Validation of a Noninvasive Device to Monitor Pulmonary Fluid Accumulation Using Changes in Bioimpedance

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Study: Pulmonary edema is a common complication of heart failure that can be severely debilitating, often necessitating hospitalization. Patients could benefit from easily usable chronic monitoring strategies to detect changes in intrapulmonary fluid levels. We developed a noninvasive device that detects pulmonary fluid accumulation (PFA) by monitoring changes in transthoracic bioimpedance.

Methods: The system consists of a circuit that measures impedance changes from attached electrodes connected to a microcontroller which outputs these changes to an LCD display. To determine viability, we tested the system in 2 acute post mortem animal models: an open-chest pig and a closed-chest sheep. Electrodes were placed longitudinally across the right lung with direct pulmonary tissue contact in the open model and were affixed to the skin in the closed model. Baseline impedance values were determined, then normal saline was incrementally (25-30 mL) added via endotracheal tube into the right lung until the calculated volume for pulmonary edema occurred (250-300 mL). Impedance was measured at 40-80 kHz in 104-Hz increments and then averaged. A network analyzer device was used as a control.

Results: Data from both models showed an inversely correlated trend between PFA and impedance changes using both devices. The prototype and control, shown in the figure as solid and dashed lines, respectively, revealed similar trends in the open-chest (r2: 0.845 vs. 0.722) and closed-chest (r2: 0.855 vs. 0.791) models. Compared to the control, the device showed a similar response with less variability. Our simple, noninvasive device was able to measure PFA in both open- and closed-chest animal models and detected relatively small changes in volume accumulation. These tests simulated the slow accumulation of fluid in the lungs during which patients are often asymptomatic. By detecting PFA, this device allows preventative action to be taken, thus decreasing patient discomfort and hospitalization.

Affordable Prosthetic Hand

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Study: Our goal is to improve the quality of life of persons who have experienced the loss of a hand by developing a reliable and clinically-viable prosthetic through biomedical research, design, and manufacturing that can be built for under $1000.

Methods: Upper limb amputees are characterized by lacking physical anatomy in one of their upper limbs. Upper limb amputation results in the loss of functionality one would normally have with a hand. Nearly 400,000 people in the US are living with upper limb loss due to amputation, with an average of 10,000 new upper limb amputations in the US each year. Most electro-mechanical prosthetic hands cost between $25,000 and $120,000. A prosthetic device in this price range is not achievable for the majority of the population and most insurance companies will not cover these costs. Because of this only 27% of upper limb amputees use a prosthetic. The project utilizes open source information from the Open Hand Project and our design will allow amputees to have autonomous control of the Open Hand. We will design the electronic controller that will execute three motion patterns for the hand through EMG signals, have instantaneous reaction to the muscle movements of the user, and immediately be put to use when attached to a patient that is used to the forearm system. The hand will run on low-power electronics to allow the battery of the forearm attachment to last for at least 12 hours and weigh less than 10 pounds.

Results: We will first test the hand in the lab setting. This will include stress testing, measuring range of motion, battery life, and failure rate. Next we will do a trial run on a group of patient to confirm the mechanical abilities of the hand. We will test performance criteria and compare results between the lab and user application. We will use patient surveys to get feedback on comfort and reliability of the hand.
Bioartificial Liver On A Chip _a Microfluidic Device For Assist Therapy

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Study: The liver is one of the most significant organs in human, when it was out of order, people would be sick and even die. The artificial liver support system may bridge patients to liver transplantation due to the system may help patients live longer for transplantation. Although artificial liver supporting systems have been improved in modern medical engineering, the assistant therapeutic effect of the artificial liver is still need to be improved. Here, we present a miniature liver on a chip for assist therapy of liver failure. The device is designed in the form of a sandwich which is composed by three polymethyl methacrylate plates that contain microchannels and two layers of chitosan macroporous membranes. The structure and function of the device mimic the liver lobule tissue after liver cells cultured in the system. In addition, the design is flexible and the device can be used in many fields such as the assist support therapy system for liver failure patients, the in vitro model for liver toxicity testing and the platform for cell co-culture. In order to prove the effectiveness of the design, several experiments were performed. The results showed that hepatocytes were cultured well in the device and the concentration of hepatoxin in medium was decreased. Therefore, the presented bio-artificial liver on a chip is a functional and versatile platform, and capable of providing support for the development of artificial liver and the therapy of liver disease.

Over-The-Wire Endovascular Device for Immediate and Complete Peripheral Artery Occlusion

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Study: This study evaluated prototypes of the Blockstent Microcatheter™ in both an acute and chronic canine artery acute occlusion model.

Methods: Metal balloons of 4 mm dia. and 9 mm length and 6 mm dia. and 10 mm length were electroformed from gold and then mounted, folded, wrapped, and compressed onto a 3.5 Fr microcatheter. Female cross-bred hounds (weight 20 - 22 kg) were sedated and heparinized (ACT > 300 sec). In an acute study of 2 dogs, a 0.018” guidewire was used to place a 0.018” guidewire into either the internal thoracic artery (ITA) or axillary artery (AA). 4 mm Blockstents were placed in the ITA (n=3) and 6 mm Blockstents were placed in the AA (n=4) through the guide sheath in an over-the-wire (OTW) fashion. Female cross-bred hounds (weight 20 - 22 kg) were sedated and heparinized (ACT > 300 sec). In an acute study of 2 dogs, a 7 Fr guide sheath was used to place a 0.018” guidewire into either the internal thoracic artery (ITA) or axillary artery (AA). 4 mm Blockstents were placed in the ITA (n=3) and 6 mm Blockstents were placed in the AA (n=4) through the guide sheath in an over-the-wire (OTW) fashion. The shape and position of the expanded devices and degree of target artery occlusion was evaluated by angiography before euthanasia and necropsy. In a chronic study of 3 dogs, bilateral AA occlusion was done by placing a 6 mm Blockstent on one side and an Amplatzer® Vascular Plug II (AVP2, 6 mm dia. and 6 mm length) on the other side. Angiography was done immediately after the procedure. Upon completion of 29-day angiography, the animals were euthanized and necropsied.

Results: The Blockstent Microcatheter provided excellent fluoroscopic visibility, good trackability, and easy placement. Devices expanded with 1–3 atm of pressure. In the acute study, immediate and complete occlusion was achieved in 7 of 7 arteries upon Blockstent expansion. In the chronic study, complete occlusion was also achieved initially with the AVP2 in 3 of 3 arteries, with occlusion occurring 7.5 - 10 min after device deployment. Complete occlusion was maintained at 29 days in 3 of 3 arteries with the Blockstent and 0 of 3 arteries with the AVP2.

The Blockstent Microcatheter is a promising new OTW device for peripheral artery occlusion, offering more rapid and durable occlusion than the AVP2 in a canine model.
Porcine Animal Model for Biocompatibility Testing of Vascular Prosthesis in Descending Thoracic Aorta  
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Study: Developing biological materials requires an in vivo preclinical assessment. The purpose of this study was to investigate whether positioning of valved conduit in porcine descending thoracic aorta could be a valid method for a preclinical study.  
Methods: A newly developed alpha-galactosidase treated valved conduit was interposed in the proximal descending aorta in seven pigs (80.5 ± 3.75 kg). The aorta was exposed through left thoracotomy via 4th intercostal space. After heparin infusion the aorta was clamped just distal to the left subclavian artery and about 10cm away from the initial clamp caudally. The aorta was transected at the mid portion of each aortic clamps and the valved conduit was interposed with 4-0 prolene continuous end-to-end anastomosis. The procedure was performed without the use of a shunt or a bypass. Intra-operative sonography was performed and the valved conduit was extracted post-operative three months.  
Results: There was no operative mortality and all pigs were alive before the sacrifice. Perioperative morbidity included paraparesis in one pig, otherwise no significant complication was observed. The mean operative time and aortic cross clamp time were 183 ± 59.7 (111–300) min and 31.4 ± 3.62 (24–36) min respectively. Intra-operative sonographic findings showed limited leaflet motion, which was open throughout the cardiac cycle in all the pigs. The leaflet was thickened and open fixed state in all the extracted conduits after three months. There was no significant narrowing in the walls of the conduits. In this porcine model, we demonstrated that, an interposing conduit in the proximal descending aorta without the use of a shunt or a bypass was a relatively safe procedure since the risk of spinal injury was not high. This model can be used to investigate vascular prosthesis in vivo assessment. Nonetheless, the descending aorta was not an adequate site for evaluating leaflet motion because it was nearly open fixed state throughout the cardiac cycle.
Control Strategy for an Implantable Rotary Blood Pump Based on Identification of Pumping States
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Study: The state of the art ventricular assist systems must ensure adequate flow under various physiologic conditions for successful treatment of the heart failure. A method for control of an implantable rotary blood pump (IRBP) is required in order to get that done. The aim of this study is to present the control strategy for an IRBP based on the following principles: adjustment of the pump flow to the required reference value, avoidance of adverse states and providing the selected treatment strategy. The last two features are achieved through the identification of pumping states: backflow of blood through the pump (BF), partial assist of the ventricle with periodically open aortic valve (PA), full assist of the ventricle (FA), and partial collapse (intermittent and continuous) of the ventricle during the cardiac cycle (PVC-I and PVC-C).

Methods: A lumped-parameter model of the cardiovascular system was used for development and testing of the proposed control strategy. A mathematical model of an IRBP takes into account the inertial and viscous properties of blood; it allows calculating the instantaneous pump flow $Q(t)$ from known values of pressure head $H(t)$, speed $\omega(t)$ and viscosity of blood $\mu$. Estimated flow is obtained by integrating $Q(t)$ in one minute. Pump speed is continuously adjusted until estimated flow will not be equal to reference flow. Pumping state is determined by analysis of the pumping state indices $PSI(t)$ derived from the pump model. New value of speed $\omega(t+1)$ is formed depending on the current pump flow, pumping state and treatment strategy. Pump speed is forcibly changed if adverse state (BF or PVC) occurs.

Results: The proposed control strategy was tested under diverse conditions (heart rate was varied from 60 to 100 bpm, left ventricular contractility ±5%, systemic and pulmonary vascular resistance ±5%). Simulation results are demonstrating the proper adjustment of the pump flow to the reference flow in all cases; identification of adverse pumping states is reasonably acceptable also.

Development of Small-caliber Decellularized Vascular Graft Modified with Bioactive Peptides for Neointima-inducing Activity
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Study: Small-caliber artificial vascular graft has been suffered from the rapid stenosis due to a thrombosis formation on the luminal surface. Therefore, autologous blood vessels are used as the bypass or vascular replacement graft. To overcome this problem, we have developed small-caliber decellularized vascular graft modified with bioactive peptides for neointima-inducing activity. The peptide contained collagen binding region and endothelial cell binding ligand. In this presentation, endothelial cell affinity of the peptide-modified decellularized tissue was evaluated in vitro. The patency of the peptide-modified graft were evaluated in rat abdominal aorta replacement model.

Methods: Decellularization was accomplished by ultra-high hydrostatic pressure technology. The decellularized vascular graft was modified with the peptide by immersing in the peptide solution. The adherent cell number was measured by fluorescence spectroscopy. The peptide-modified decellularized aorta (diameter: 1mm) was transplanted into rat abdominal aorta. Blood flow was evaluated by laser-Doppler measurements.

Results: Although the fibroblastic cells were not adhered on the modified surface, 80% of seeded endothelial cells were adhered in peptide-sequence specific manner. After one month transplantation, good patency, neointima formation, and no thrombogenic formation on the luminal surface were observed only in the case of peptide-modified graft. These results suggested that our design of the graft improved patency and neointima formation of the small-diameter grafts in vivo.
Working With FDA's Center for Devices to Advance Regulatory Science and Medical Device Innovation
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Study: The mission of FDA's Center for Devices and Radiological Health (CDRH) is to protect and promote public health by assuring that patients have continued access to medical devices that are both safe and effective. This includes an obligation to work with external stakeholders (including industry, the medical community, academia, and patient groups) to promote innovation so that improved medical devices can be utilized in patients as quickly as possible. To accomplish this goal, CDRH is actively engaged in advancing ‘regulatory science’ practices to provide scientifically-based assessment tools and approaches that can aid in the development and evaluation of new devices and technologies.

Methods: CDRH staff support regulatory science processes by 1) developing new standardized test methods and computational modeling techniques through laboratory-based device research, 2) analyzing premarket bench, animal, and clinical trial tests of new devices, 3) improving surveillance and epidemiological methods for studying currently marketed devices, 4) preparing regulatory-based information and guidance documents to assist industry, and 5) bringing together interested parties and experts to address challenges in device development and assessment.

Results: To keep pace with scientific advances and the increasing complexity of device technology, CDRH has several initiatives to collaboratively work with external stakeholders to enhance scientific research, the exchange of information, and regulatory education and interaction. Through fifteen different programs (e.g. Critical Path Initiative, Consensus Standards, Experiential Learning Program, Public Workshops, CDRH Fellowships, Guidance Documents, National Postmarket Surveillance System, Network of Experts, Medical Device Curriculum), we invite you to partner with CDRH to impact the development and evaluation of new medical devices, to facilitate patient access to these devices, and to improve public health.

Modeling a Dialysis Catheter and the Superior Vena Cava for Treatment of Infection by Heating
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Study: Bacterial biofilms cause central line infections and many complications. Treatment with antibiotics alone is ineffective; contaminated devices in most cases must be surgically removed. We have shown heating staphylococcal biofilms to 45°C increases vancomycin susceptibility 10-fold. Heating catheters may augment antibiotic treatment of central line infections. In this work we established the feasibility of catheter heating using in vitro and computational models of the superior vena cava (SVC).

Methods: A hydraulically and thermally representative model of the SVC was perfused at 2.2 L/min with 37°C. One lumen of the catheter was fitted with 3 resistance thermometers. The second lumen was perfused from a 60°C reservoir via a proportional/integral/derivative pump controller. Catheter heating performance was quantified with a coefficient of variation summed over all measured timepoints. A similar computational fluid dynamic (CFD) model was generated with Ansys/Fluent. In both the physical and computational models, we evaluated the primary efficacy and safety measures, namely the luminal and maximal plume temperatures respectively. All measurements and simulations were run in at least triplicate.

Results: The physical catheter was controlled with speed and accuracy with a summed coefficient of variation of .44. (Figure 1). CFD data showed for a range of infusion temperatures 51-71°C, the catheter’s outer surface was 37.59 +/- 0.23°C while the inner surface varied between 49.5–67.6°C. The SVC outlet temperature was 37.25 +/- .10°C. Likewise, maximum plume temperature varied between 49.6–68.1°C. (Figure 2). These data suggest that use of this system to safely augment vancomycin treatment is plausible in a clinical setting for treatment of central line infections.

Figure 1. The thermal response of the catheter to heating based on computer input. The system used 788.8 mL of water (60°C).

Figure 2. CFD results with flow velocity and temperature inputs to match the physical model.
The Effects of Left Ventricular Assist Device Implantation: Computational Comparison of the Ascending and Descending Aorta Sites
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Study: Left ventricular assist device (LVAD) has become a common approach to treat patients with heart failure, used as a bridge to transplantation, as a temporary or definitive support. Median sternotomy is the standard approach for LVAD implantation, during which the outflow graft is usually anastomosed in the ascending aorta (AA). The left thoracotomy represents a less invasive procedure, during which the anastomosis can be realized in the descending aorta (DA).

Methods: A computational study was performed in order to analyze the effects on hemodynamics of the two main sites (AA and DA). Two multi-scale models were implemented, coupling the 3D model of aorta to the lumped parameter model. Since the blood demand depends on the needs of organs and tissues, the flow rate percentage is independent from the outflow graft anastomosis location. As a consequence, the same resistance boundary condition was applied to the outlets of the two models. As an inlet boundary condition, a real flow waveform was used. Velocity pattern and wall shear stress were compared to establish the possible clinical consequences.

Results: The numerical results highlighted that recirculation flow occurred in AA, whereas a stagnation flow characterized the DA. Furthermore, the velocity in the descending aorta was orderly in AA case, while it was chaotic, swirling and with retrograde flow in DA case. Regarding the wall shear stress, high values were recorded in the areas opposite to the anastomosis. In case of AA site the emergence of epiaortic vessels is mainly subject to atherosclerotic events; in case of DA site plaque formation is favor in ascending truck. Although the DA site is adopted during a less invasive procedure, it generates a worse velocity pattern and facilitates atherosclerotic processes.

Improved PIV Method to Visualize Blood-Sided Flow Inside a Hollow-Fiber Membrane Oxygenator

Study: While Computational Fluid Dynamics (CFD) is a powerful tool to improve the overall design and development process of oxygenators, a validation is mainly done by comparing the total pressure drop of the CFD studies with the actual device. In the past, our group found that the flow visualization method Particle Image Velocimetry (PIV) can be utilized to study the blood-sided flow inside oxygenators. We recently improved this method further to study flow in the inlet, outlet, and inside the fiber bundle on a macroscopic level which allows a more detailed comparison with CFD data.

Methods: A fully transparent, scaled-up PMMA model of a wound hollow-fiber oxygenator was used for this experiment. The fibers were replaced by PMMA rods. A transparent blood mimicking fluid mixture of water, glycerol and sodium iodide was used to match the refractive index of PMMA. Fluorescent polystyrene particles were used to detect the flow, which was recorded via a Stereo-PIV setup. The experiment was based on similitude theory to ensure that PIV and CFD data are comparable. Both cameras were positioned stationary while the oxygenator model was rotated in 5° steps. This new method has two significant advantages: 1) Every image taken has the same good quality due to a consistent, reduced optical pathway between image plane and cameras 2) The duration of the experiment was shortened significantly so that particle adhesion effects, which we experienced in the past, were reduced to an acceptable level.

Results: Our improved PIV method allows a more detailed insight into the flow pattern in the fiber bundle of an oxygenator, which cannot be achieved by CFD. Macroscopic differences between PIV and CFD can be found in terms of flow tortuosity, as well as local flow acceleration and deceleration. The analysis of the data is in progress and will be presented at the ASAIO 2015. Our method not only allows a direct comparison and validation of CFD data, but will also help to improve CFD in hollow-fiber oxygenators in the future.
Acoustic Detection of Left Ventricular Assist Device Thrombosis

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Study: The use of left ventricular assist devices (LVADs) has become an increasingly common and effective treatment for advanced heart failure. Although modern continuous flow LVADs improve quality of life and survival over medical management of heart failure, device thrombosis remains a common concern. Improved non-invasive methods for assessment of LVAD function are needed for early detection of thrombosis.

Methods: An electronic stethoscope was used to record sound from the HeartMate II LVAD in vitro and in vivo, including in one patient before and after surgical exchange for device thrombosis. A HeartMate II was implanted in a viscoelastic gel whose sound transmission properties are similar to those of soft tissue and was attached to an artificial circulatory system for in vitro measurements. Data were uploaded to a computer and processed using spectral analysis.

Results: Harmonics associated with pump operation were easily visualized in a patient with stable LVAD function using a plot of amplitude versus frequency (Figure 1a). Peak harmonic frequency from in vivo samples correlated strongly with predicted values (based on pump speed) as well as with measurements taken in vitro at equivalent pump speeds (r>0.999 for all). Comparison of spectral slices for acoustic measurements taken before and after device exchange in the patient with LVAD thrombosis revealed a pattern of decreased amplitude with similar curve structure (Figure 1b). Sounds produced during LVAD operation can be reliably recorded and analyzed using an electronic stethoscope. Strong correlations between in vivo samples correlated strongly with predicted values (based on pump speed) as well as with measurements taken in vitro at equivalent pump speeds (r>0.999 for all). Comparison of spectral slices for acoustic measurements taken before and after device exchange in the patient with LVAD thrombosis indicated that sensitivity is high and that the LVAD acoustic signature is not altered during transmission through chest. Further, reduction in amplitude observed in the thrombosed LVAD may be a result of decreased flow and impaired pump function. This methodology, therefore, may represent a simple, clinically applicable, and non-invasive means for detection of LVAD thrombosis.
Heat Generation During In Vitro Operation of the HeartMate II Left Ventricular Assist Device

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Study: Heat generated during operation of left ventricular assist devices (LVADs) may be damaging to blood and surrounding tissues. Normal operation of the HeartMate II (HMII) LVAD, requires a power supply of 4–12 W. Our goal was to analyze power consumption and temperature (temp) change during in vitro operation of the HMII.

Methods: An abbreviated loop of 1.9 cm diameter vinyl tubing was connected to a HMII LVAD and filled with a solution of water and glycerin with viscosity 3.2 cP and volume 110 mL. The pump was implanted in a 1.87 kg phantom made with EcoFlex®, a viscoelastic gel with properties similar to those of soft tissue. An infrared thermometer measured temp at the surface of the pump. Temp was measured for 75 minutes at pump speeds ranging from 8,200–12,200 RPM. Pump wattage, flow, and speed were collected. Ambient air temp. was 25.4 °C.

Results: Temp increased over baseline (25.4 °C) in all trials. Higher device speeds resulted in more rapid heat generation as well as statistically significantly greater maximum temps in all cases (p<0.001). The change in temp over 65 minutes was 6.0 °C at 8200 RPM and 14.5 °C at 12,200 RPM (Figure 1). At 9,200 RPM, approximate average speed used clinically, temp increased by 6.5 °C at an average power of 6.02 ± 0.06 W. As expected, power consumption also increased with device speed; average wattage was 4.61 ± 0.23 at 8200 RPM and 14.20 ± 0.57 at 12,200 RPM, p<0.001. In our closed circulatory loop, operation of the HMII LVAD resulted in considerable increases in system temp. Increased speed resulted in greater heat generation and power consumption. Heat generation was assumed to be a result of normal electrical inefficiencies in the pump motor and friction between the rotating impeller and fixed stators. Although heat dissipation during LVAD operation in vivo will differ from the in vitro system, our laboratory system could be a promising tool for thermal analysis of long-term LVAD operation. Further studies will be needed to translate these findings into the clinical arena.
In-body Tissue Engineered Heart Valve (Bivalve) Can Be Engrafted as Vital Tissues
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Study: We are developing a novel autologous heart valve with a special method named in-body tissue engineering, which is simple, safe and economical. In this study, we investigated how the implanted biovalves have been engrafted in the native tissue in a goat model.

Methods: Biovalve Stents were prepared by 2-month embedding of the molds, assembled using plastic rods and a metallic stent for catheter implantation, in the subcutaneous spaces of goats. After extracting the molds and removing the plastic rods only, Biovalve Stents with tri-leaflet valves similar to those of the native aortic valves were constituted from completely autologous connective tissues. Sixteen out of 23 Biovalve Stents were implanted in the aorta in situ and other 7 Biovalve Stents were implanted in the pulmonary artery (PA) in situ with transcatheter technique.

Results: In both aortic and PA cases, the Biovalve Stents were successfully implanted. Angiography showed smooth movement of the leaflets with a little regurgitation under the systemic and pulmonary circulation. The Biovalve Stents were extracted 1, 2 or 5 months after implantation. The leaflets of the Biovalve kept their shape and elasticity even after 5 months and neither calcification nor thrombi were observed. Histological examination showed the cell populations inside the valves and endothelial cells covering the laminar surface of the valve leaflets. In conclusion, the Biovalve satisfied the higher requirements of systemic and pulmonary circulation in goats for 6 months. It can survive as an autologous tissue in the native body.

PFOB Emulsion Stability Study Under Different Preparation Processes
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Study: Perfluorooctyl bromide (PFOB) emulsions used as intravascular oxygen carriers have been widely studied and characterized. Our previous in vitro studies showed emulsion instability after being stored for short periods (<40 days), generating a strong acidification and an increase in droplet size. In vivo results showed allergic reactions due to the vegetal origin of surfactant used in the formulation. Acidification and increase in pH could be associated with unfavorable sterile conditions that promote microorganisms’ presence and/or product transformation processes indicators. Likewise, changes in droplet size indicate system equilibrium destabilization.

Methods: In this paper results after changing preparation process conditions to improve in vitro stability and avoid in vivo allergic reactions are presented. To achieve this goal, the following procedures were carried out: (1) steam sterilization, (2) increase in α-tocopherol concentration used as antioxidant, (3) Nitrogen bubbling before glass sealing, (4) changes in pressure and cycles during microfluidization process, and (5) sodium oleate addition used as cosurfactant to strength lecithin surfactant. For all above cases, soy lecithin was changed by egg yolk lecithin to minimize allergic reactions.

Results: Results showed that steam sterilization and microfluidization conditions affect positively and significantly emulsions stability. Stable emulsions were obtained throughout 84 days of characterization, and further studies for longer periods are required.
The Influence of Non-Newtonian Effects on Inferior Vena Cava Hemodynamics

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Study: Blood is a non-Newtonian shear-thinning fluid with a viscosity that depends non-linearly on shear rate. In most computational studies of blood flow, shear rates are assumed to be sufficiently high (i.e., greater than approximately 100 s⁻¹) to justify the approximation of blood as a Newtonian fluid. However, shear rates lower than 100 s⁻¹ occur in some regions of the circulation. In this study, non-Newtonian effects on blood flow were investigated to determine the appropriateness of the Newtonian approximation in the human inferior vena cava (IVC), where the lowest shear rates in the human circulation occur.

Methods: Newtonian and non-Newtonian blood flow was investigated in three IVC geometries: a straight-tube IVC, a patient-averaged IVC, and a patient-specific, left-sided IVC anomaly. Newtonian computational fluid dynamics (CFD) simulations were performed using two viscosities: 1) a high shear rate asymptotic viscosity, and 2) a characteristic viscosity based on a volumetric average of internal shear rate. Non-Newtonian simulations were performed using the Carreau model. Partial occlusion of the IVC by an IVC filter and a thrombus was also considered using a finite-element based virtual-placement procedure developed previously. The error resulting from the Newtonian approximation was then quantified for flow parameters including shear rate, velocity, and wall shear stress.

Results: More than 87% of the IVC volume was found to contain flow in the nonlinear region of the shear rate - viscosity curve for blood in all cases. Newtonian simulations performed using the asymptotic viscosity for blood over-estimated the Reynolds numbers by more than a factor of two and under-predicted mean wall shear stress fields by 15% to 55%. Use of a characteristic Newtonian viscosity resulted in better agreement with the non-Newtonian simulations, though mean wall shear stresses were still over-predicted by 7% to 19%. In future studies, non-Newtonian simulations are recommended for modelling flow in the human IVC.

Hydraulic Development of Miniature Axial Flow Blood Pump

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Study: Use of left ventricular assist devices (LVADs) as a treatment for end-stage heart failure has become common practice as a bridge-to-transplant or as destination therapy. More recently, there has been interest in less invasive partial assist bridge-to-recovery devices. Developing miniaturized pumps for less invasive use has many unique engineering challenges regarding implantation and removal, anchoring and minimizing the risk of hemolysis and thrombosis. Our group has begun development of a miniaturized LVAD to provide partial ventricular unloading.

Methods: The development approach applied to this new miniature pump focuses first on identifying optimal pump geometries (impeller/inlet straightener/outlet diffuser) which create the most physiologically compatible pressure/flow curves. Multiple pump geometries are prototyped on a 3D printer and tested in an automated flow loop consisting of a variable speed motor to drive the impeller, a pneumatic pinch valve to vary resistance, an electropneumatic regulator to adjust the pinch valve, a flow meter, and pressure transducers on the inlet and outlet of the pump. Computational fluid dynamics will be performed to evaluate micro-flow features and provide pump optimization characterization.

Results: Proof-of-concept testing shows that a pump geometry that fits within a 10 mm diameter and 15 mm length housing can achieve a pump flow of 3 LPM with a differential pressure of 100 mmHg. Our aim is to optimize hydraulic performance including pump efficiency and pressure/flow capacity while decreasing the pump geometry to fit in a smaller housing.
**On Replacement of Sickle Hemoglobin (HbS) in RBCs of SCD Patients with Healthy Donor Hb**

L. A. Ziegler, S. E. Olia, J. H. Waters, M. V. Kameneva. 

**Study:** Sickle-cell disease (SCD) causes abnormal shape and rigidity of red blood cells (RBCs) due to a pathological hemoglobin (HbS) which, when sickled, results in vaso-occlusion, tissue hypoxia and many other severe and painful events. Current long-term treatments for SCD are limited and cause serious complications. Pharmacotherapy with hydroxyurea leads to both leukopenia and thrombocytopenia while repeated blood transfusions result in alloimmunization in over 50% of patients. In this work, we propose to replace HbS with healthy donor Hb, and subsequently return these modified RBCs to the patient. Once fully developed, it is hoped that this therapy will minimize or eliminate vaso-occlusion and alloimmunization.

**Methods:** Currently, proof-of-concept experiments are being performed using healthy donor RBCs. Removal of endogenous Hb is carried out by lysing the RBCs with a low-osmolarity solution. Encapsulation of exogenous donor Hb into the lysed RBCs is accomplished through a multi-step process, designed to capture normal hemoglobin and then to reseal the RBCs. Hb encapsulation is evaluated by total hemoglobin concentration in the modified RBCs (OSM3 Hemoximeter) and is compared to a control group encapsulated with PBS.

**Results:** Encapsulation of exogenous donor Hb into RBCs has been performed, achieving complete equilibrium of Hb concentration between the membrane interior and the external Hb solution. The figure below demonstrates an example of pellets of experimental RBCs containing 5.5 g/dl total intracellular Hb which compares to the 1.75 g/dl original intracellular Hb leftover present in the control RBCs (cells are washed at the end of experiment and re-suspended in PBS following centrifugation). Based on these reproducible results, encapsulation of much higher concentrations of Hb is assumed and currently under examination in on-going studies. In addition, rheological and morphological properties of these modified RBCs are being tested using Linkam Shearing device.
Suction Recognition for the Cleveland Clinic Continuous-Flow Total Artificial Heart

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Study: The Cleveland Clinic Continuous-Flow Total Artificial Heart (CFTAH), like all other implantable circulatory assist devices, must avoid suction at its inlets to prevent clinically significant reductions in flow. We have developed three algorithms that enable the CFTAH controller to detect bellwether conditions in real time and automatically reduce speed to prevent suction. We have tested each of these during in vivo experiments in calves.

Methods: Under normal operating conditions the motor current waveform is the same shape as the programmed speed waveform. In algorithm 1, the normalized current (current/speed) is fit to the speed waveform. As suction approaches, the current wave changes, increasing the standard error of the fit. Imminent suction is recognized when the error passes a preset trigger value. The second algorithm employs the hysteresis loop of normalized power (power/speed^2) vs. speed to sense the differential pressure between the atria in pre-suction conditions. The controller calculates this area, normalizes it by speed range, and compares the resulting integrated suction parameter to a set target value. The third algorithm uses the axial position of the free-floating rotating assembly to sense the differential pressure between the atria in pre-suction conditions. Sensors were installed to monitor the axial position of the rotating assembly and provide a relative axial position signal. The normalized relative position was then integrated with respect to speed and divided by the speed range resulting in another integrated suction parameter which is compared to a set trigger value.

Results: All three methods were able to detect conditions that would lead to suction in time for the controller to temporarily decrement mean speed thereby avoiding clinically relevant suction events. The methods can be combined to make a more robust system. While the third algorithm is slightly more difficult to implement, it provides advantages over the other two.

Roller Pump Circulation System For Preventing Filter Clogging During Cell-free and Concentrated Ascites Reinfusion Therapy (CART)


Study: Cell-free and concentrated ascites reinfusion therapy (CART) involves filtration, concentration, and reinfusion of drained ascites. The clogging of the filtration filter makes the reuse of a reasonable quantity of ascites difficult, and produces toxic substances such as inflammatory cytokines. In order to prevent filtration filter clogging, we developed a roller pump circulation system that causes the ascites to circulate through the filter and the circulation circuit. However, physical stimulation by the roller pump and the filter membrane in this system may increase the levels of cytokines of the filtrated ascites. Therefore, we evaluated safety of roller pump circulation system by measuring the changes of ascites cytokine levels using in vitro models.

Methods: Three experimental groups were set up: roller pump group (n=6), roller pump/filter group (n=6), and control group (n=6). Ascites extracted from patients with carcinomatous peritonitis or liver cirrhosis was placed in a reservoir bag and circulated using the roller pump at a flow rate of 50 mL/min in the roller pump and roller pump/filter groups. In the roller pump/filter group, an ascites filtration filter was placed in the circulation circuit. Each group was studied at room temperature or 37 °C. The levels of cytokines (IL-2, IL-4, IL-6, IL-8, IL-10, GM-CSF, IFN-γ, and TNF-α) in ascites in the reservoir bag were measured at 0, 10, 30, 60, and 120 min after the start of ascites circulation.

Results: No significant changes were observed in the levels of cytokines under physical stimulation by roller pump and filter membrane in any of the experimental groups. Furthermore, the cytokine levels were unaffected by temperature. These results indicate that the roller pump circulation system can maintain the circulation flow for preventing filter clogging safely without increase ascites cytokine levels during CART.
Control System for Diagnostic and Failure Treatment Applied to a Ventricular Assist Device
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StudY: Many obstacles can be found on the control of Ventricular Assist Devices (VAD). But a big challenge is a safety control of VAD. Then is necessary a high safety levels control because in case of fault, the consequences are severe.

Methods: The present work proposes applying mechatronic concepts to the development of control systems for VADs, considering the nature of the fault indicating signals, as well as the Discrete Event Systems (DES) theory and through the application of tools for risk analysis, and fault diagnostic and treatment techniques aiming the development of control models based on modular and distributed architectures. This control architecture features the diagnostic and treatment of faults, where methods for faults classification where developed, and according to the severity each fault is proposed a control system that performs the regeneration or degeneration of the VAD to a secure state and is according to medical standards and safety techniques. This systematic is based on HAZOP (Hazard and Operability Studies).

Results: From the knowledge acquired about the system behavior during critical conditions, formal models are developed employing Bayesian Networks and Petri Nets for the diagnostic and treatment of faults. The proposed procedure was applied on the VAD development, which was performed by a team of researchers from the Escola Politecnica da USP and from the Instituto Dante Pazzanese de Cardiologia. Thus, is possible to achieve an autonomous and safe control system that complies with the applicable technical standards, as well as the strict project requirements for this class of system.
Endothelialization of Sintered Inflow Cannulas of LVAD With Allogeneic Mhc-silenced Endothelial Cells
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Study: Advances in regenerative medicine, show that endothelial cell (EC) seeding optimize hemocompatibility of artificial organs, but it is limited by insufficient autologous EC harvest. To improve hemocompatibility of LVAD, sintered inflow cannulas (SIC) were endothelialised using allogeneic EC. To prevent EC rejection due to Major Histocompatibility Complex (MHC) incompatibility, EC MHC expression was stably silenced. EC functionality and immunogenicity were analyzed.

Methods: A lentiviral vector was used to deliver β2-microglobulin (shβ2m)-specific shRNAs. Non-specific shRNA (shNS) sequence was used as control. MHC-expressing or silenced ECs were seeded on SIC. EC growth/seeding efficiency and thrombocyte adhesion were assessed by microscopy. Efficiency of MHC-silencing/EC phenotype were analyzed by qRT-PCR and flow cytometry. Cytokine secretion profiles were evaluated by Luminex technology. EC specific activation and thrombogenic state markers (ESATS) were quantified by real-time RT-PCR. Biologic reactivity was tested in IFNγ-/TNFα-stimulation assays. Allogeneic T-cell responses were analyzed by flow cytometry.

Results: EC transduction efficiencies of 96% were achieved. Delivery of shβ2m induced reduction of 92% of β2m mRNA levels, causing knockdown of MHC surface expression of 93%. No significant differences between shβ2m-EC and shNS-EC were observed regarding EC growth/endothelialisation of SIC resulting in improved hemocompatibility. EC phenotype, cytokine profile and ESATS remained unaffected by MHC-silencing, or by cell-to-SIC contact, but their expression could be upregulated by TNFα-stimulation. Upon IFN-γ stimulation, non-transduced ECs showed a 3-fold upregulation of MHC expression, but shβ2m could block it. MHC-silenced EC abrogated T-cell responses and escaped antibody-mediated complement-dependent cytotoxicity. These results may bring LVAD biologisation for better hemocompatibility closer the reality.

Table 1. SA distributions of the microfluidic unit and the HMII.

<table>
<thead>
<tr>
<th></th>
<th>10th percentile [Pa s]</th>
<th>50th percentile [Pa s]</th>
<th>90th percentile [Pa s]</th>
</tr>
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<tbody>
<tr>
<td>HMII VAD</td>
<td>0.3</td>
<td>0.8</td>
<td>2.9</td>
</tr>
<tr>
<td>HMII microfluidic</td>
<td>0.3</td>
<td>0.9</td>
<td>2.8</td>
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Preparation and Characterization of Small Intestine Submucosa-Chitosan Sponges for Use in Deep Wound Repair
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Study: Deep wound management remains a medical challenge because of the separation that occurs in the different layers of soft tissue, making a bandage insufficient in promoting the regeneration of tissue. Among alternative wound dressings, there have been advancements in some natural materials such as small intestine submucosa (SIS), which can generate an environment that promotes tissue regeneration, and chitosan (Ch), a natural polymer used in many biomedical applications, which has also been used as a scaffold for wound repair. We aim to develop a sponge made of SIS and chitosan and compare its properties with sponges made of pure SIS.

Methods: As an initial step, this study developed a methodology that integrates chitosan and the crosslinking agent, glutaraldehyde (GA), with SIS. Four types of sponges were studied: Two containing SIS-Ch and two with only SIS, the difference between the same mixtures was the percentage of GA used to crosslink the components. The sponges were characterized by measuring water uptake, mass loss, microstructure, porosity, mechanical strength and a chemical analysis of the components that were integrated.

Results: There was no statistical difference in the water uptake, porosity or mechanical compressive strength across all groups; the different compositions also showed a similar microstructure. FTIR was then used to validate the components of the scaffold, with the characteristic bands for SIS and Ch found in the mixed structures. On the other hand, a lower mass loss was obtained with the SIS-Ch sponges, indicating that the Ch improves the mass loss behavior. We suggest further studies of the material using cell cultures and higher concentrations of chitosan to determine the biocompatibility and regenerative capacity.

Concept of the Table Estimation Method of Blood Viscosity Adjusted Pressure and Pump Flow
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Study: Sensor less estimation of pressure and pump flow has been an important subject for artificial hearts. However, the estimated values are sometimes incorrect influenced by the change in blood viscosity. In this study, we propose the novel method to realize blood viscosity adjusted estimation.

Methods: When we adopt a pulsatile mode using continuous flow pumps, pump parameters can be obtained in systolic and diastolic phases. Within a short period of one pulse, changes in blood viscosity and peripheral resistance are thought to be neglected. In this condition, blood viscosity is thought to be estimated from the two motor information of systolic and diastolic phases. Thus, if we have viscosity based reference tables in relation to motor information and peripheral resistance, we can estimate blood viscosity, and thus, blood viscosity adjusted pressure and pump flow. To investigate the proposed method, the helical flow pump was connected to the mock circulation and data were gathered to construct viscosity based reference tables.

Results: When using two conditions of continuous flow data that were regarded to systolic and diastolic phases, the more different two conditions were, the more accurately viscosity was estimated. Accuracy of estimated pressure and pump flow depended on the accuracy of estimated viscosity. When using data of pulsatile flow, almost the same results were obtained by adding some correction. Possibility of the proposed estimation method was demonstrated.
Low Cost Control System for Reproducing In Vivo Pressure and Flowrate at the Benchtop

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Study: Blood and other fluids in vivo are pulsatile and oscillatory. Medical devices for implantation in the vasculature must be rigorously tested for hemolysis and thrombus formation at the benchtop prior to implant. Accurate in vitro testing requires flow systems that recapitulate in vivo fluid dynamics. We engineered a low cost fluidic control system to mimic in vivo pulsatile flow and pressure.

Methods: Hardware for the fluidic control system included a microcontroller, pressure regulator, pressure transducer, and peristaltic pump. Hardware was controlled via a custom program developed using National Instruments Lab View allowing independent input of time dependent flow and pressure conditions. The pressure regulator was controlled by closed loop feedback from the pressure transducer. Dampering of the feedback enabled the system to maintain an average pressure despite pulsatile perturbations from a pump. In vivo and bench top flowrates were measured with Doppler ultrasound (SonoHeart Plus, SonoSite). A phantom device with flow conduit was designed to record flowrates using the same ultrasound that was used in vivo.

Results: Comparing ultrasound images from a canine, we were able to choose pressure and flow parameters approximating in vivo flow at the benchtop. The pressure feedback loop parameters were adjusted to maintain a mean pressure of 100 mmHg (matching the mean arterial pressure of a canine) despite perturbations from the pump. Figure 1A shows flowrate vs. time in a canine model measured by Doppler ultrasound. Figure 1B illustrates our ability to mimic in vivo pulsatile flow using the same ultrasound device. Parts, excluding the pump, totaled $560. We were able to engineer a low cost system to adjust flowrate and pressure simultaneously to accurately model in vivo flow and pressure at the benchtop.

A Low-Cost Digital Particle Image Velocimetry (DPIV) System

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Study: Digital Particle Image Velocimetry (DPIV) allows for detailed analysis of fluid dynamics for different applications, including cardiovascular flow modeling. Commercially available systems may cost $100,000 or more while seeding particles may cost $100 or more per gram. Although this costly purpose-built equipment provides an abundance of information about fluid dynamics in a flow system, the complexity and abundance of features is not necessary for all applications. In response to a need for basic DPIV, low-cost systems have been constructed using alternative laser sources, imaging hardware, and analysis software. Recognizing that new-generation smartphones offer impressive high-speed/slow motion digital imaging, we produced a basic DPIV system using the camera on the iPhone 5s and inexpensive readily-available hardware.

Methods: Hardware for the fluidic control system included a microcontroller, pressure regulator, pressure transducer, and peristaltic pump. Hardware was controlled via a custom program developed using National Instruments Lab View allowing independent input of time dependent flow and pressure conditions. The pressure regulator was controlled by closed loop feedback from the pressure transducer. Dampering of the feedback enabled the system to maintain an average pressure despite pulsatile perturbations from a pump. In vivo and bench top flowrates were measured with Doppler ultrasound (SonoHeart Plus, SonoSite). A phantom device with flow conduit was designed to record flowrates using the same ultrasound that was used in vivo.

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Design and Preclinical Evaluation of a Hemostatic Collagen Plug for Percutaneous Biopsy: 72% Less Bleeding and 100% Cessation

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Study: Percutaneous liver and renal biopsy can lead to dangerous hemorrhages, especially in patients with coagulopathies. Current option with transjugular biopsy is associated with increased costs, and complications and poor quality of samples. Our purpose was to design and evaluate a hemostatic collagen plug to halt bleeding after percutaneous biopsies.

Methods: We designed a 1 mm OD, 25 cm long collagen plug to be inserted through a Tru-cut needle sheath. Safety and biocompatibility were evaluated in an animal model (Yorkshire swine, 20 ± 2kg, n=14) and assessed after 30 days by histopathology (H&E). Efficacy was evaluated in a transplant-discarded human livers model (n=14), by performing two biopsies followed by implantation of the plug and two no-plug control biopsies. The order, segment of the liver and use of the plug were randomized. Bleeding from the biopsies was collected in gauze for 3 minutes. The clotting ability of the plug (n=7) was assessed by measuring change in diameter after in-vitro exposure with human blood without anticoagulant.

Results: We found a minimal inflammatory reaction restricted to the plug material in the animal model, with no inflammatory cell migration to the parenchyma. Bleeding in human biopsies was reduced by the plug by 72% and stopped within 3 minutes after the biopsy in 100% of the cases, whereas controls only ceased to bleed in 7% of the cases. In vitro clotting ability showed an increase of the diameter of 22.6%. Our study provides data demonstrating that the collagen hemostatic plug is histologically safe, and effectively reduces and stops bleeding after percutaneous biopsies. Clinical trials are forthcoming.

Analyzing Interactions of Ventricular Assist Devices and Thromboemboli - An In Vitro Model

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Study: Ventricular Assist Devices (VADs) are commonly used as a bridge-to-transplant therapy for heart failure patients. However, thrombus formation and embolization associated with mechanical failure remain pertinent issues. A “power spike” seen clinically on the VAD controller has been associated with a thrombus passing through the device, and sometimes results in an exchange surgery. To learn more about the interaction of VADs and thromboemboli, we have developed an in vitro model to characterize the response of VADs to synthetic clots.

Methods: Clots were fabricated by adding CaCl₂ to citrated donor equine blood. Clots were introduced into a glycerin/water filled-flow loop that contained a peristaltic pump in parallel with a mock centrifugal flow VAD. The pressure and flow rate were continuously monitored as the clot interacted with the VAD. The system ran for approximately 30 seconds and resulting deposits were collected for histology.

Results: The flow meter (located ~65 cm distal to the VAD) detected irregular flow rates approximately 6 seconds after the clot was introduced to the VAD (Fig 1). Pieces of the clot were visible distal to the VAD, indicating that the impeller (1900 RPM) broke up the clot. Histology of the control clot (that is, not subjected to the VAD) showed uniformity across the section (Fig 2A), while the clot subjected to the VAD showed laminations similar to those seen in clinical VADs (Fig 2B). This model can be used to evaluate centrifugal, uniaxial, and pulsatile flow VADs. By changing the parameters within the system (flow rates, temperatures, pressures, etc.), this model can simulate conditions experienced by heart failure patients and better characterize how the VAD will respond to thromboemboli. Findings resemble features seen clinically and may provide context for in vivo VAD controller phenomena.
Real-time Analysis of Flow-induced Thrombus Formation Within a Defined Crevice

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Study: Although the majority of ventricular assist device (VAD) manufacturers attempt to make the blood contacting surfaces of their devices as smooth as possible, all VADs are composed of combined components that inevitably generate crevices and steps along the flow path. These regions are often the nidus of thrombus formation, however few studies have examined real time platelet deposition within these features. Using hemoglobin depleted red blood cells (RBC ghosts), long working optics, and a custom designed parallel plate chamber, we sought to perform this analysis.

Methods: A whole blood analog composed of RBC ghosts and fluorescently labeled platelet rich plasma (PRP) was perfused through a polydimethylsiloxane (PDMS) parallel plate flow chamber containing a crevice of defined dimensions (54 ± 4 x 122 ± 1 µm², 95 ± 3 x 122 ± 1 µm², 136 ± 4 x 122 ± 1µm²) across a titanium alloy (Ti6Al4V) for 10 min at a wall shear rate of 1000 s⁻¹. Ti6Al4V was chosen to emulate the blood-wetted surfaces of VADS. Platelet deposition was visualized with an inverted epifluorescent microscope and a 40x long working distance objective.

Results: Probability maps were generated from acquired fluorescent images of platelet deposition utilizing a custom designed Matlab program. Sample images were taken at 2.5, 5, 7.5 and 10 min of perfusion (Figure 1). For both the 54 ± 4 x 122 ± 1 µm² (N=8) and 95 ± 3 x 122 ± 1 µm² (N=5) crevice, the greatest deposition occurred at the bottom, front corner, with the probability of thrombus formation being > 80% at this location after 10 min of perfusion. In the 136 ± 4 x 122 ± 1µm² crevice platelets adhered mainly along the bottom wall. However deposition was less likely to occur in the largest crevice size with a maximum probability of platelet adhesion < 50% after 10 min of perfusion. The results indicate that this is a viable method for evaluating the effect of common geometric irregularities found in cardiovascular devices on platelet deposition.
Development of a Novel Centrifugal Pump for Compact Heart-Lung Equipment

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Study: Heart-lung equipments are useful to save life of acute heart failure and respiratory distress patients. However, these equipments are usually big in size. To realize a compact heart-lung equipment, the pump that generates high pressure with low flow and has suitable port design for connecting it to the artificial lung is necessary. To meet the purpose, we have been developing a novel centrifugal pump named sequential flow pump (SFP).

Methods: In the SFP, centrifugal force is given sequentially two times to the fluid with a single impeller. To realize smooth connection to the artificial lung, inlet and outlet ports are open at axial and radial sides, respectively, which is reverse order of common centrifugal pumps. The SFP was designed to have 60 mm in impeller diameter, hydrodynamic bearing and magnet coupling method to drive the impeller. Pump performances were analyzed with computer fluid dynamics (CFD) analysis and an actual model.

Results: In CFD analysis, with conditions of 3000 rpm of rotational speed and 5 l/min of flow rate, 343 mmHg and 271 mmHg of outflow pressures could be obtained in the SFP and in the normal centrifugal pump having the same impeller, respectively. In actual model, 5 l/min of flow rate against 350 mmHg of pressure head was obtained with 3150 rpm of rotational speed. The results showed that the SFP had a potential to be a suitable built-in blood pump for a compact heart-lung equipment.
**Visualization of Thrombus Growth in a Hollow Fiber Membrane Oxygenator Using µCT**

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**Study:** Over the last decades the development of new materials and the optimization of the flow distribution has brought many breakthroughs in the field of membrane oxygenators. However, the long term application of fiber membrane oxygenators remains limited by its hemocompatibility. Especially, thrombus formation represents fatal risks for patients since embolic events and mechanical failure of the device might occur.

**Methods:** This study aims for a time-resolved visualization of thrombus formation in order to detect hotspots that are prone to thrombus formation. For this purpose an oxygenator and test circuit was developed that satisfies the requirements of accessibility using a µCT. An anticoagulation strategy was established in pre tests to ensure thrombus formation within 2 to 6 hours. Contrast agent was added to the blood flow with an increasing concentration. Flow and pressure are recorded, ACT was measured in intervals of 1 hour and hemograms were performed every 20 minutes.

**Results:** Thrombus formation was found in the fiber bundle near the oxygenator outlet in all pre tests and occasionally at the inlet. A correlation between increase of pressure and thrombus growth was observed. The tests in the µCT showed an initial thrombus at the outlet after 30 minutes. Further growth of this thrombus was detected with a growth rate of 0.182 mm³/min. At 90 minutes the thrombus was washed out. In summary, a reproducible and comparable anticoagulation strategy was found to evaluate the thrombogenic potential of an oxygenator within an appropriate time for testing in vitro. Further results will be used for modelling the flow induced thrombus growth in computational fluid dynamics (CFD) in order to benefit from the less cost and time consuming character of simulation aided development of oxygenators.

**Visualization of Flow Measurements in an Oxygenator Model with Particle Tracking**


**Study:** Experimental investigations of flow fields in oxygenators is important but still remains difficult. Recent work has shown, that particle image velocimetry (PIV) flow measurements could be successfully carried out in an upscaled model of an oxygenator. However, there are still limitations concerning image quality and particle density in the fluid, mainly due to the enormous amount of Plexiglas fibers in the flow field, which are the dummies for the original oxygenator fibers. Besides this, the PIV algorithm is only able to resolve in squares with a minimum size of 16x16Px, which is interfering with the fiber geometry. In this work we applied particle tracking algorithms to PIV images to investigate their ability to improve the outcome of flow measurements in oxygenators.

**Methods:** Flow data originally recorded for PIV purposes has been analyzed. The data was collected in a transparent upscaled model of a membrane oxygenator. All model parameters were adjusted to mimic physiological blood flow through the original oxygenator. The fluid was enriched with fluorescent micro particles. A laser illuminated the particle seeded flow, a camera captured the particle movements. The resolution of the images was ~20µm/Pixel. A set of 100 images, recorded with a frequency of 10Hz was analyzed with commercial particle tracking algorithms (Dantec Dynamics). The resulting particle tracks have been post-processed and visualized with Matlab and Tecplot.

**Results:** A comparison of PIV and particle tracking is shown in figure 1. It is clearly shown, that the fibers are mapped better with particle tracking and that the resulting flow distribution is finer than with PIV, whereby measurement errors are reduced. The applied methods will further improve experimental flow investigation in oxygenators and other membrane devices with a high contact surface (especially fibers). This opens up new possibilities of insights to flow patterns in those devices.
Importance of a Hybrid Cardiovascular Simulator during the development of an Automatic Rotational Speed Control of an Implantable Centrifugal Blood Pump

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Study: This work shows the usage of a Hybrid Cardiovascular Simulator (HCS) as tool for the development of a control system that adjusts automatically the rotational speed of an Implantable Centrifugal Blood Pump (ICBP) to avoid backflow, ventricle suction and aortic valve collapse. In order to evaluate the ICBP controller (e.g. control strategies), a HCS was used. The HCS is a closed hybrid system composed by a numerical section, modeling right ventricle and pulmonary circulation, and a physical section, figure, composed by an electromechanical pump, mimicking the left ventricle, a compliance chamber and resistance module, modeling the systemic arteries. Baroreflex control is addressed using mean arterial pressure measurement.

Methods: ICBP was connected to HCS physical section, simulating implantation from left ventricle to aorta. According to clinical cases from literature, HCS was set to reproduce heart disease conditions. Pressure and flow data were acquired and recorded.

Results: HCS allowed us to observe hemodynamic changes at left ventricle, aortic valve behavior and at right ventricle. Also, ICBP speed control strategy showed improvement in cardiac output with higher mean aortic pressure, lower heart rate and keeping the aortic valve opening, comparing to fixed ICBP rotational speed. Conclusion: From test results, we observed that the usage of HCS was important to demonstrate that an accurate rotational speed control for ICBP avoids blood backflow, ventricle suction and aortic valve collapse. In addition, HCS was able to simulate clinical cases, allowing to observe cardiovascular circulation improvement when a ICBP is operating.

In Vitro Benchmarking Study of VADs in Current Clinical Use

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Study: The MiniVAD™ is a new VAD that utilises a novel layout to potentially improve implantability, manufacturability and haemocompatibility. The hope is that this will lead to reduced device cost and complication rates, improving the overall health-economic proposition. To understand how the haemocompatibility of the MiniVAD compares to current market leading devices, an in vitro benchmarking study was carried out.

Methods: The MiniVAD™ was compared to the HeartWare HVAD, the Thoratec CentriMag (CMAG) and the Thoratec HeartMate 2 (HM2) and a static control in a standard 500 ml mock circulatory loop using bovine blood. Samples were withdrawn at regular intervals and complete blood counts were analysed by automated haematology; haemolysis by the Harboe assay; leukocyte microparticles and platelet activation by flow cytometry and von Willebrand factor by immunoblotting. Limitations of the study include HVADs and HM2s being explanted pumps where pre-use could impact pump performance. To mitigate this bias, pumps were carefully cleaned and inspected, and several pump versions from different sources were tested multiple times.

Results: This study is ongoing to increase the sample size with a targeted completion date in April 2015. Results to date: NIH (g/100L): CMAG = 0.0011, MiniVAD = 0.0012, HVAD = 0.0061, HM2 = 0.025. Leukocyte microparticles: fold change increase at 360 min compared to static control at 5 min: CMAG: 5.3, MiniVAD: 13.7, HM2: 24.5. These preliminary results indicate that it is possible to observe clear differences in haemocompatibility between different pump designs during in vitro testing. Future work will attempt to assess how these differences may translate into clinical performance.
Exogenous Nitric Oxide Supplementation to Enhance The Outcome of Fluid Resuscitation From Hemorrhagic Shock
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Study: Nitric oxide (NO) production is impaired in hemorrhagic shock (HS) by: reduction on endothelial shear stress; free radicals that uncouple endothelial NO synthase; and hypoxia. We propose to supplement NO during resuscitation, using nanoparticles (NO-np). This study investigated the systemic and microcirculation changes and 8-day survival outcome of NO-np infusion (10, 15 and 20 mg/kg).

Methods: Syrian hamsters with dorsal window chamber were used. Resuscitation with NO-np solution was performed after HS. Vessel diameter, red blood cell velocity, and functional capillary density were evaluated. Blood gases, MAP, HR, Nitrite, nitrate and S-nitrosothiol were monitored. Measurements were performed at baseline, after shock, and after treatment.

Results: MAP and HR were affected by NO-np, indicating vasodilatation and chronotropic effect of NO. With NO, pH improved to baseline levels, BE was positive and higher, indicating the acid-base restoration. Venular blood and diameter were also improved. FCD improved by 1.7 times. These effects show the microvasodilatation, shunt prevention and improved perfusion effect of NO-np. Systemic pO2 levels were higher in NO groups. Nitrite concentration was 1.7 times higher, S-nitrosothiol levels were 2.5 times higher and 8-day survival was dramatically improved, showing NO homeostasis in the circulatory compartment benefiting HS outcome. NO alters organ function by regulating regional blood flow and organ perfusion. NO prevented cardiovascular collapse, allowing animals to maintain superior systemic and microvascular hemodynamic conditions and increasing survival. Our previous experience has proven that tissue and organ survival requires maintenance of FCD and that perfusion is not always related to systemic pressure values.

Development of an Extracorporeal Neutrophil Reprogramming Device for the Treatment of Acute Inflammatory Disorders
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Study: As one of the first responders to sites of inflammation, neutrophils play a critical role in the progression of acute inflammatory conditions such as sepsis. High quantities of neutrophils migrating to remote organs such as the lungs has been associated with increased morbidity and mortality by initiating multiple organ dysfunction or immune paralysis in septic patients. The migration and activation of neutrophils is regulated by CXCR-1 and CXCR-2, g-protein coupled receptors that bind to interleukin-8 (CXCL-8). In this study a prototype neutrophil reprogramming device was constructed to attenuate neutrophil response to chemotactic signaling by exposing neutrophils to immobilized CXCL-8 within an artificial microcirculation. Additionally the prototype device efficacy was evaluated by examining CXCR-1/2 surface receptor expression of neutrophils after whole blood recirculation.

Methods: First oxygen-gas plasma surface treatment was employed to deposit amine groups on the outer surface of polymethylpentene oxygenator fibers. Next, CXCL-8 was covalently immobilized on the outer surface of the amine functionalized fibers using glutaraldehyde coupling. Modified fibers were then potted into a polycarbonate housing. Whole blood was recirculated through the device for 60 minutes with blood samples taken at fixed intervals for analysis. Neutrophil surface expression of CXCR-1/2 was evaluated using flow cytometry.

Results: In scaled devices neutrophil surface receptor expression of CXCR-1 and CXCR-2 decreased by 28% and 36% respectively when compared to baseline plain blood. This indicates reduced migration towards CXCL-8 stimulation. Further testing is being conducted to evaluate the functional response of reprogrammed neutrophils to a chemotactic gradient. A similar device platform may be applied to alternative disease states which are regulated by cell-cell interactions.
Development of Rotational Automatic Control Method to an Implantable Centrifugal Blood Pump

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Study: This paper shows the development of an Automatic Control System (ACS) capable to adjust the rotational speed of an Implantable Centrifugal Blood Pump (ICBP) in order to provide an adequate assistance to the left ventricle in different patient conditions. The usage of continuous flow blood pumps as Left Ventricle Assist Device (LVAD) introduces main questions: How strong ventricle assistance is necessary to keep organs perfusion at an adequate level without introduce a ventricle and/or valves hazard? If we are considering LVAD as a bridge to heart recovery, how LVAD must be controlled to progressively reduce LVAD assistance?

Methods: A new rotational speed control system is proposed in two layers: LVAD Blood Flow Control (FwC) through flow and pressure estimator, and a Fuzzy Control (FcC), generating a blood flow reference. Fuzzy input variables are: estimated blood flow; estimated aortic pressure, patient’s activity, functional class (e.g. NYHA). The control strategy has been studied in a Hybrid Cardiovascular Simulator (HCS) as a tool that allows the physical connection of ICBP under evaluation. In addition, HCS allows changes of some cardiovascular parameters in order to simulate specific heart disease: Ejection Fraction (10 - 25%) and heart rate (50 - 110 bpm).

Results: FwC was able to adjust the blood flow error less than 2%. FcC was able to provide appropriate flow with 95% of accuracy when compared to a recommended flow from a specialist physician, even under typical heart failure conditions. Conclusion: Results demonstrated that ACS increases rotational speed to avoid backflow during heart diastolic phase while decreases rotational speed to avoid aortic valve dysfunction during heart systolic phase.

Shear-induced Platelet Dysfunction by Non-physiological High Shear Stress With Short Exposure Time: Activation and Receptor Shedding

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Study: Platelet receptors play the vital role in physiological hemostasis and pathophysiological thrombosis. The aim of this study was to investigate shear-induced platelet activation and platelet receptor shedding by non-physiological high shear stress with short exposure time.

Methods: A blood shearing system was constructed for generating non-physiological shearing conditions. Healthy human donor blood was subjected to two levels of shear stresses (25Pa and 125Pa) with short exposure time of 0.5s. The shear-induced platelet activation indicated by surface P-selectin expression, glycoprotein IIb/IIIa (GPIIb/IIIa) activation and generation of platelet-derived microparticles (PMPs), and the shear-induced shedding of platelet functional receptors (GPIbα, GPVI and GPIIb/IIIa) were quantified with flow cytometry.

Results: The results showed that the number of activated platelets, as indicated by surface P-selectin expression and GPIIb/IIIa activation and generation of PMPs increased significantly when exposed to the non-physiological high shear stress with short exposure time. It was observed that the same level non-physiological shear stress caused the reduction of receptors (GPIbα, GPVI and GPIIb/IIIa) in platelet surface. The loss of these receptors may impair the normal hemostatic function of platelets. The non-physiological high shear stress could not only activate the platelets increasing the risk of thrombosis, but also cause the shedding of platelet functional receptors increasing the propensity of bleeding.
Disc and Disc Holders of Polish Mechanical Heart Valve Modifications Supported by Numerical Methods

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Study: A new construction of MOLL tilting heart valve for pulsatile heart assist pumps Religa Heart PED and Religa Heart EKT has been developed. The new valve is based on its prototypes: first, constructed by prof. J. MOLL patented in 1987 [Moll J.J. patent USA 4.661.106, 1987; Moll J.J. patent USA 4.725.275, 1987] and second, constructed by Lodz University of Technology. Aim of study was valve construction optimization in numerical simulations. Modifications were focused on reduction of wall shear stress and streamline profile improvement. Additionally, new shape of disc holders were constructed in order to reduce the deformation of this elements during valve assembling.

Methods: Construction modifications of disc thickness and valve ring disc holders shape utilizing CAD 3D parametric modeling were introduced. Valve model was examined in numerical flow simulations. Based on numerical results model parameters were being modified until desirable results were obtained. New disc holders were examined using digital microscopy after valve assembling - results were compared with previous construction.

Results: Modifications reduced valve resistance by 40 percent: from 2,5 mmHg to 1,5 mmHg (for 10 L/min flow) and decreased shear stress in area of disc holders. New design of disc holders has provided its smaller surface deformation after valve assembling. The research was financially supported by The National Centre of Research and Development (PBS1/A7/1/2012).

Blood Damage Assessment: Erythrocyte Microparticle Formation During Sub-hemolytic Mechanical Trauma Using Flow Cytometry

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Study: The improvement of ventricular assist device (VAD) and artificial heart design relies on the advancement of blood trauma analysis.

Methods: Freshly collected human blood was washed and then red blood cells (RBCs) were isolated and resuspended in Ringer’s/albumin solution. Fluorescent markers CD235A-FITC for RBC identification and Annexin V-Alexa Fluor 647 for apoptotic activity measurement were used to identify RBC-derived microparticle formation as shear stress levels were increased from 100 to 1300 dyn/cm^2. Cells were exposed to shear stress for 2 minutes in a couette viscometer that ensures uniformly sheared samples.

Results: Control (non-sheared RBCs) samples contained 1.7 ± 0.28 RBC microparticles/µL, while 100, 500, 900, and 1300 dyn/cm^2 shear environments significantly increased RBC microparticle generation to 2.7 ± 0.40, 3.5 ± 0.27, 5.1 ± 0.95, and 8.6 ± 0.03 microparticles/µL (p<0.05 via ANOVA). Increased RBC microparticle formation correlated with increased hemolysis which may suggest that hemoglobin release occurs as microvesicles separate from the lipid bilayer. Elevated fluorescence intensity of microparticles compared to apoptotic RBCs (143,012 ± 10,298 FL-Units versus 15,510 ± 2,020 FL-Units for the control sample) indicated a higher concentration of phosphatidylserine found on microparticle membranes.

Conclusions: RBC microparticle concentrations significantly increased following exposure to increased shear stress magnitude. Quantification of RBC microparticles may provide a more subtle measure of blood trauma than overt hemolysis. The microparticles express high levels of negatively charge phospholipids are supportive of coagulation cascade reactions, offering a potential link between RBC trauma and thrombosis. Measurement of shear-induced RBC microparticle generation and apoptosis may offer more sensitive measures of blood trauma to evaluate VAD design and performance.
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**Albumin Retention by an Implanted Silicon Nanopore Hemofilter**

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**Study:** We are currently developing an implantable hemofiltration device using high efficiency silicon nanopore membranes (SNMs). The goal of this study was to evaluate the albumin retention characteristics of the SNMs during short term implantation in a canine model.

**Methods:** SNMs were fabricated using previously established silicon nanofabrication techniques. SNMs were coated with polyethylene glycol to prevent biofouling. Membrane pore size and selectivity were evaluated prior to implantation by measuring hydraulic permeability and Ficoll sieving coefficient. SNMs (n=4) were housed in a custom made flow device and anastomosed to the abdominal vasculature in a canine. Systemic blood pressure provided the primary drive for filtration through the SNMs for a period of 3–4 days. Filtrate was collected from each SNM and albumin concentration was measured with an ACE Alera Chemistry System, Alfa Wassermann. Albumin sieving coefficient was taken as the ratio of filtrate albumin concentration to blood albumin concentration.

**Results:** Pre-implant hydraulic permeability of the membranes showed an average critical pore size of 5.9 ± 0.6 nm; slightly smaller than the hydrodynamic diameter of albumin (7.0 nm). All four filtrate collection bags had clear effluent and showed average albumin sieving of 0.26 ± 0.03. The average albumin sieving closely matched the Ficoll sieving, 0.27 ± 0.06, at hydrodynamic diameter 4.0 nm. Though 4.0 nm Ficoll is smaller than the hydrodynamic diameter albumin (7.0 nm), it is similar to the small dimension of the ellipsoidal albumin protein (4.0 nm). These experiments demonstrate the ability for silicon nanopore membranes to retain albumin in vivo during short term implantation in a canine model. Refinement of the pore size will allow tuning of albumin retention for further testing in the in vivo model.

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**Direct Measurement of LV-Aortic Differential Pressure Using the TORVAD Ventricular Assist Device**

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**Study:** The two-piston, positive displacement pumping mechanism used in the TORVAD™ ventricular assist device is electromechanically-actuated, providing a means to infer pressure between the left ventricle (LV) and the aorta. This capability is integrated within the pump controller, providing additional insight into the state of the cardiovascular system without additional sensors. The method has been tested both in vitro and in vivo.

**Methods:** The design of the TORVAD™ relies on two pistons individually actuated and moving within a toroidal pumping chamber. One piston is temporarily held stationary to prevent flow between the inlet and outlet ports while the other is driven to eject fluid via the outlet cannula to the aorta. A static sensing mode holds both pistons momentarily thereby using the sensed motor currents to infer differential pressure across each piston. In addition to being used to estimate mean aortic and diastolic pressure, this information can also be used to aid clinicians in optimizing TORVAD™ operation. Along with other data and a computational cardiovascular system model, the differential pressure can be used to estimate important patient parameters such as systemic vascular resistance, cardiac output, and ventricular contractility.

**Results:** During acute experiments with a bovine model (n=4), testing was completed to evaluate synchronous TORVAD™ pumping. In this mode, pumping is timed based on sensed ECG signals, allowing pump ejection at different times within the cardiac cycle. During these tests, the differential pressure sensing function was used to monitor the pressure between the aorta and left ventricle. A comparison with pressure values measured using catheters (Mikro-Tip, Millar, Houston, TX) placed in the left ventricle and aorta is shown below.
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In Vitro Pulsatile Performance Evaluation of the HeartMate Percutaneous Heart Pump (PHP)

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Study: The HeartMate PHP is a catheter pump inserted through a 13 F sheath and expands to 24F to provide minimally invasive acute hemodynamic stabilization and left ventricular unloading in both prophylactic and emergent clinical settings. This study evaluates the performance and ventricular unloading characteristics of Heartmate PHP through in vitro pulsatile bench testing.

Methods: A custom-built pulsatile heart simulator was tuned to generate physiological flow pressure waveforms while mimicking the preload responsiveness of the native heart. An expanded PHP was mounted across the aortic valve similar to in-vivo device placement. The systemic vascular impedance of the heart simulator was adjusted to simulate typical pre-op hemodynamics of cardiogenic shock. Total and native cardiac output (CO) were measured with ultrasonic flow sensors. Ventricular unloading characteristics were assessed by analyzing pressure-volume (PV) loops, end-diastolic volume (EDV), and stroke work (area under PV loop) at 16k, 18k and 20k RPM pump speeds.

Results: Physiological aortic flow and pressure waveforms representative of a cardiogenic shock state were generated. Upon activation, PHP (at 20k RPM set speed) increased mean arterial and diastolic pressure from 70 and 45 mm Hg to 95 and 80 mm Hg respectively. PV loops shifted leftwards as EDV reduced from 165 to 140 mL depending on the pump speed. Total CO increased from 3.0 to 4.5 ± 0.5 LPM while a substantial reduction (40–80%) in native CO and stroke work (-35%) was achieved as a result of ventricular unloading. These preliminary results demonstrate the performance of the HeartMate PHP under pulsatile loading conditions and demonstrate its effective ventricular unloading capability. Additional testing is in progress to fully characterize PHP performance in a variety of simulated physiologic conditions. "Device in development. Not available for commercial use".

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A Biomimetic Antibacterial Coating for an Artificial Cornea Device

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Study: Artificial corneal devices are the last option for restoring sight when corneal transplants are unavailable or contraindicated. Biofilm-induced infection of corneal devices can require systemic antibiotic treatment and even explantation. To combat biofilm formation, much emphasis has been placed on anti-adhesion and antibiotic chemical coatings, but these strategies are not long lasting. Antibacterial surfaces have been found in nature (insect wings, shark skin) and fabricated (roughened surfaces, multi-scale wrinkles), but none are scalable or easily fabricated on FDA-approved polymers.

Methods: We employed nanoimprint lithography to generate biomimetic antibacterial nanostructures on the surfaces of poly(methylmethacrylate) (PMMA). We replicated the nanofeatures of a cicada wing on PMMA thin films. We also used commercially available molds to imprint biomimetic nanopillars on thin PMMA films over square centimeter areas.

Results: Compared to flat films, biomimetic nanopillars 1) reduced surface adhesion of live E. coli determined by a standard fluorescence based viability assay, and 2) killed these bacteria, evidenced by a decrease in colony forming units in suspension over time (up to 24 hours). SEM and AFM imaging of fixed bacterial cells (Figure 1) indicate a mechanical cell-wall breaching mechanism that is unlikely to develop resistance. Decreased pillar size improves bactericidal efficiency on PMMA surfaces. Such surfaces could be used for a wide variety of environmental and medical applications.

Figure 1: Pulsatile heart simulator: (a) aortic chamber, (b) aortic valve, (c) HeartMate PHP, (d) ventricle chamber, (e) aortic flow sensor, (f) flow pressure waveforms, (g) PHP at the aortic position, (h) PV Loops
Improving Biocompatibility of Centrifugal Pump with MHD Bearings
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Study: DuraHeart II (DHII) is a small (30 cc, 120G) centrifugal pump delivering up to 10LPM flow against 80mmHg pressure. The pump uses hybrid magnetic and hydrodynamic (MHD) bearings for impeller levitation inside the blood chamber. Previously conducted in vivo studies indicated vulnerability of small hydrodynamic bearing gaps to thrombus formation. The new motor control method allowing for the impeller position modulation (IPM) was developed to actively change hydrodynamic bearing gaps with the intent to increase bearing washout.
Methods: To evaluate the effect of changing bearing gaps on hemolysis In vitro test with bovine blood was conducted using 3 DHII pumps with IPM, 2 w/o IPM and BPX80 as a control. The initial pump thrombogenicity assessment was done in vitro using 6 mock circulation loops filled with heparinized (3unit/ml) bovine blood. The pumps operated with actively changing impeller-chamber gaps were compared to those that used the conventional control method. For in vivo study four Holstein calves (98-119kg) were implanted with DHII pumps through the left thoracotomy using off pump procedure. The pumps operated in speeds between 2200 and 2600RPM delivering flows between 2.0 and 6.5LPM. Anticoagulation regimen included in op heparin for ACT>500 sec and post op Coumadin to maintain INR 1.5–2.5.
Results: Normalized index of hemolysis in all DHII pumps was 40% below than that of BPX80. In vitro thrombogenicity test results while favored pumps with IPM were inconclusive due to the loop thrombosis. During in vivo test postoperative complications included one animal bleeding and one animal infection. Within 7 days after surgery in all animals PFH levels were less than 10mg/dl and LDH returned to the pre-op level indicating no hemolysis problem created by the pump. All animals were electively sacrificed on POD 28. Explanted pump were free of thrombi.
Conclusion: The novel pump control method improved the pump capability to resist hydrodynamic bearing thrombosis while remaining gentle to blood cells.

Test Method to Quantify the VWF Compatibility of Rotary Blood Pumps
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Study: Gastrointestinal bleeding occurs in 20–30% of patients per year receiving rotary blood pumps (RBP) due, in part, to the loss of high molecular weight von Willebrand Factor (hVWF) multimers. Changes in hVWF multimers and function potentially offer a new, more sensitive biomarker to evaluate hemocompatibility, yet there is no standard test to measure VWF compatibility. In this study, we developed a benchtop method to quantitatively compare the changes in hVWF multimers and function in RBPs.
Methods: Human plasma was circulated through flow loops with the Thoratec HeartMate II (HMII) and CentriMag (CM - the current gold standard for hemocompatibility) and HeartWare HVAD and Levacor RBPs. A loop without a pump served as a control. Pumps generated flow rates of 4L/min against an afterload of 75mmHg. Samples were collected prior to operation, and then hourly for 6 hrs of RBP operation and analyzed for VWF function. VWF collagen binding activity (VWF:CB) and VWF antigen level (VWF:Ag) were measured with ELISAs. VWF multimer profiles were assessed using gel electrophoresis and near-infrared in-gel visualization and quantified using densitometric analysis.
Results: VWF collagen binding efficiency (VWF:CB/VWF:Ag) in the HMII, CentriMag and HVAD significantly decreased by an average (N=5) of 46%, 44%, and 36% from baseline after 6 hours of operation. Multimer profiles showed significant losses of hVWF for these pumps in the first 30 minutes of operation. VWF:CB/VWF:Ag was unchanged and hVWF multimers were preserved in the Levacor and control loops. We developed a repeatable benchtop method to quantitatively compare the changes in hVWF multimers and function in RBPs. The data indicate three RBPs, including axial and centrifugal designs, and varied bearing approaches, all deplete hVWF, while the mag-lev Levacor pump did not. This test differentiated the hemocompatibility performance of the CM and Levacor, even both have extremely low hemolysis (NIH < 0.002 g/100L). This approach could be employed to evaluate new RBPs designed for improved hemocompatibility.
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Aggregation and Breakup Model for Platelets in CFD
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Study: The thrombogenic characteristics of blood-contacting devices are difficult to be predicted because of complex dynamics involving platelets, flow and surface. Platelet aggregation can only occur when activated platelets physically contact each other. In the flowing blood, these collisions are a consequence of local velocity gradients. Coincidentally, velocity gradients are also directly related to shear stresses which prevent platelet aggregation by breaking platelet-to-platelet bonds before they are stable. We apply kinetic theory in conjunction with computation fluid dynamics (CFD) to improve the predictability of thrombus initiation in medical devices. Other authors have used empirical models that have to be calibrated for specific flow fields. Our objective is to develop a more general model to be valid for any flow condition.

Methods: We created a kinetic model to predict the population distribution of platelets in aggregates of different sizes. Competition between aggregation and breakup rates determines the profile of this distribution according to the flow condition. The aggregation rates are predicted by the Smoluchowski aggregation model (1916), and the breakup rates are calculated by the breakup model of Pandya and Spielman (1982). The parameters used in the model were obtained by correlating experiments of Xia and Frojmovic (1994) to the aggregation-breakup model. This kinetic model yields a set of ordinary differential equations which is solved numerically for each cell of a CFD simulation.

Results: Predictions of fraction of aggregated platelets quantitatively agree with the experiments of Xia and Frojmovic in simple shear flow. Moreover, simulations were conducted of flow and aggregation in the microchannels investigated by Nesbitt et al. (2009), and the results qualitatively reproduced the experimental results. In general flow fields aggregation occurs more prominently in low shear rate regions just downstream of high shear rate regions.

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Improved Canine Surgical Model for an Implantable Hemofilter
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Study: Patients with end-stage renal disease have high mortality and morbidity rates on dialysis. Transplantation offers the best treatment option; however, donor kidneys are in short supply. An artificial kidney using silicon nanoporous membranes is in development to address this problem. The objective of these experiments was to determine a reproducible surgical model to continue preclinical evaluations.

Methods: Our Institutional Animal Care and Use Committee approved the operative protocol for hemofilter placement in Class A canines. A laparotomy incision is made to enter the peritoneal cavity. Intravenous heparin is administered to achieve adequate levels of anticoagulation during the operation. The abdominal viscera is medially rotated to expose the left retroperitoneum. The aorta and inferior vena cava (IVC) are dissected free of tissue. Seven millimeter, ringed, Polytetrafluoroethylene (PTFE) grafts are used to create the venous and arterial anastomosis to the IVC and aorta, respectively (graft length 2.5–3.0 centimeters). The arterial inflow and venous outflow PTFE grafts are connected to the hemofilter. Blood flow is established through the hemofilter. The hemofilter is secured to the psoas muscle adjacent to the inferior pole of the left kidney. Effluent reservoir bags that collect filtered fluid from across each membrane are placed in the abdomen. The midline incision is re-approximated. The canine receives 3 mg/kg of acetylsalicylic acid per day post-operatively.

Results: The surgical approach and post-operative anti-platelet therapy described above has been implemented successfully in five experiments. There has been no complications or thrombosis formation. The experiments have averaged 9 days. These experiments highlight a successful and reproducible surgical model, as well as the efficacy and safety of post-operative anti-platelet therapy strengthening the foundation for further preclinical experiments aimed towards the future realization of an implantable artificial kidney.
Applicability of Reynolds, Total, Viscous and Wall Shear Stresses in Different Power Law Models
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Study: The blood trauma power law model, a function of exposure time and shear stress, has been commonly employed to analyze medical device design. These models were derived from viscometer experiments using laminar flow, although turbulence frequently occurs in blood-contacting devices. Shear stress in the viscometers is calculated from torque, dimensions and operational speed, yet a single number cannot represent a complex flow field. In this study, we investigate the benefits of employing area averaged Reynolds, total, viscous, and wall shear stresses in different power law models.

Methods: ANSYS FLUENT was used to predict the detailed structure of turbulence utilizing k-ε and k-ω SST models and four power law models to investigate area averaged, time averaged Reynolds, total, viscous, and wall shear stresses in improving hemolysis predictions for experimental conditions in a capillary tube. Standard errors between experimental hemolysis data and theoretical calculation were calculated.

Results: Simulations showed that the Zhang power law model gives the lowest error, while Giersiepen’s model yields the highest. When results were compared examining different stresses (e.g. viscous vs. total stresses), both the best and the worst agreement between experimental data and a power law models were obtained using wall shear stress. When the k-ε and k-ω SST models were compared, the k-ω SST model, in which total stress is calculated from viscous stress, provided better agreement overall with the experimental data. Turbulence models combined with different shear stress parameters and refined power law models improved simulation accuracy and could be applied to improve analysis of blood-contacting medical device designs.

Development of a Computational Model for Predictions of Thrombosis in Regions of Flow Separation
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Study: Thrombosis remains an obstacle in current blood-contacting devices, primarily due to regions of disturbed flow. Specifically, regions of high shear stress activate platelets, and regions of low wall shear rate (WSR) allow for platelet adhesion and thrombus growth. Both of these phenomena occur in regions of flow separation. A computational model capable of predicting device-induced thrombosis on a macroscopic scale and relatively quickly, compared to existing models, would be useful in the device development process.

Methods: A single-scale thrombosis model was taken from literature and modified to predict device-induced thrombosis. Bulk concentrations of platelets (non-activated and activated), a chemical activator, and platelet-platelet links are considered. A power law model is used to predict platelet activation based on the local shear stress, and a non-linear weighting function is used to quantify thrombus deposition based on the local WSR. Finally, a modified Brinkman term is added to the Navier-Stokes equations to account for a growing thrombus by modeling it as a porous material. The model was tested under laminar conditions in a 2D asymmetric sudden expansion, which produces flow separation.

Results: The model correctly predicted thrombus growth in the low WSR region caused by the flow separation. Flow through the thrombus was greatly reduced compared to the free stream velocity, although not zero. The simulated thrombus was thickest near the expansion and decreased in cross-sectional area in the downstream direction. This matched the findings of a published in vitro thrombosis study in a similar geometry [1].

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Assessment of Outlet Flow From the HeartMate II Continuous Flow Ventricular Assist Device Under Physiological Pulsatile Conditions Using Laser Doppler Velocimetry

Study: Left ventricular assist devices (LVADs) are used in patients with a diseased ventricle as a bridge to transplant. Patients with an implanted LVAD, such as the HeartMate II (HMII), have experienced bleeding in the abdomen region due to the possible cleaving or proteolytic breakdown of the von Willebrand Factor, an integral protein in the clotting cascade. Therefore, an in vitro study is used to characterize flow conditions near the outlet of the HMII under physiological conditions.

Methods: Laser Doppler velocimetry (LDV) was used to measure velocities, turbulence intensities, and stresses in an acrylic model of the outlet cannula for the HMII at the same cross sections as a previous study under steady flow conditions in three regions downstream of the flow. The in vitro study combined the HMII LVAD, a pulsatile pump, and compliance chamber in series to mimic a standard patient with the implanted device. The pulsatile pump was operated under pathophysiologic conditions at a rate of 95 beats per minute with a stroke volume of approximately 50 mL.

Results: This two component velocity data was compared throughout the cardiac cycle to the previous study, and the velocity during systole in the center of the pulsatile flow was observed to be nearly double the velocity observed in the previous steady flow data. The velocity components during diastole were observed to be approximately the same magnitude as the velocities in the steady flow. Turbulence intensities and shear stresses were also observed to be higher under pulsatile conditions in comparison to the steady experiment.

Figure 1.

A) The 500 mL intraventricular blood pump reservoir assembly and B) the velocity pathlines at a flow rate of 3 L/min.

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CFD Optimized Reservoir for In-Vitro Testing of Intraventricular Rotary Blood Pumps
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Study: Benchtop evaluation of intraventricular rotary blood pumps (RBPs) is a unique challenge owing to features on the pump surfaces which impacts hemocompatibility, but are covered or obstructed by attachment to tubing, compliant blood bags, or clinical hard-shell reservoirs. Maintaining inlet clearance and adequate mixing is crucial at lower flows associated with pediatric and partial support ventricular assist devices (VADs). A new blood reservoir was developed, addressing the growing pool of transmyocardial-type VADs, to enable improved in-vitro hemolysis assessment.

Methods: A two-piece, bottom-mount, cylindrical reservoir was designed in SolidWorks® for SLA-printing using an optically clear, ABS-like, biocompatible resin. The assembly consists of a lug-type lid which mates flush with the inner lumen of the reservoir base with radial seal outside of the chamber. The reservoir inlet barb, tangent to the reservoir base, accepts 3/8” ID tubing while the pump insertion site consists of a 1.0 cm long interference fit. CFD was performed to determine optimal reservoir entrance inlet angle and floor slope.

Results: The tapered interference fit successfully secured and sealed around the transmyocardial portion of a RBP prototype. The three luer fittings (Figure 1A) enable fluid sampling, temperature measurement, and venting of the reservoir. A total capacity of 300 or 500 mL is achieved through interchangeable lids with varied heights. A 30° upward inlet angle and 10° slope through CFD analysis (Figure 1B) provided complete mixing within the reservoir while allowing for air emboli to be collected at a vent port in a domed section of the lid. This reservoir has been successfully fabricated and hemolysis experiments for intraventricular RBPs are ongoing.
Hemodynamics Associated with a Pediatric Ventricular Assist Device Using a Viscoelastic Blood Model

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Study: Congenital heart disease is the leading cause of infant death in the United States with over 36,000 newborns affected each year. Despite this growing problem there are few cardiovascular devices designed specifically for pediatric and neonate patients. Previous computational fluid dynamics (CFD) research has been done investigating blood flow in the aorta in both healthy and diseased patients under different levels of cardiac support from a pediatric assist device (PVAD). This work, however, assumed blood to be a Newtonian fluid, ignoring its viscoelastic and shear-thinning properties. Due to the altered flow patterns in the aorta caused by the PVAD outlet cannula, a more accurate blood model should be used to predict hemodynamics and regions of graft failure.

Methods: A new CFD solver that incorporates a modified Oldroyd-B viscoelastic model designed specifically for pediatric blood is used to investigate important hemodynamic parameters in a pediatric aortic geometry under pulsatile flow conditions. The model is compared to Newtonian blood simulations to determine the viscoelastic effect on the hemodynamics throughout the cardiac cycle. Additionally, the viscoelastic model is fit to three sets of pediatric blood viscosity data (20, 40 and 60% hematocrit) representing the broad range of physiological pediatric hematocrits.

Results: Significant differences are seen in the development of flow in the ascending aorta and in the jet leaving the PVAD outlet cannula. Additionally, shear stress, which plays a key role in platelet activation and deposition, hemolysis, and graft failure varies significantly between the models and hematocrits throughout the entire cardiac cycle.

Effects of Fluid Shear Stress on the Functional Radius of VWF-Coated Beads in an Optical Trap

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Study: Many patients worldwide suffer from Acquired von Willebrand Syndrome, a condition that arises when the von Willebrand Factor does not function properly and spontaneous bleeding events occur. The leading cause is thought to be the elevated shear stress levels that often occur after the implantation of a left ventricular assist device (LVAD). Determining the threshold shear stress necessary for a conformation change of von Willebrand Factor would allow the makers of cardiac assist devices to avoid creating certain flow patterns with their devices, and thus, reducing the incidence of Acquired von Willebrand Syndrome. An experimental setup, which can test and quantify these thresholds for shear stress would thus be invaluable to future medical device research and development.

Methods: VWF is extracted from human plasma, purified through column chromatography, identified using a Western Blot and imaging, and finally attached to polystyrene beads. The polystyrene beads are then fixed in place by the use of an optical trap. The stiffness of the trap is calculated then software is used to track the motion of a bead within a flow chamber of DPBS solution by movement of a piezoelectric stage. Phase shift between fluid velocity and bead motion and the produced amplitude are measured for the following bead groups: non-vWF coated beads, vWF coated beads with no shear, vWF coated beads with 3 cycles of a 157 s⁻¹ shear rate, and vWF coated beads with 5 cycles of a 157 s⁻¹ shear rate.

Results: Preliminary results show no difference in phase shift between the four groups, but a difference in amplitude of motion is observed. This is presumably caused by an increase in the functional radius of the bead due to the characteristic unraveling of the vWF protein under significant amounts of shear stress.
Computational Analysis of the 12cc Penn State Pediatric Ventricular Assist Device

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Study: There are limited options of pediatric patients awaiting a heart transplant. As part of Penn State’s ongoing effort to provide an alternative, we are performing a numerical analysis in order to characterize the 12cc pneumatic pediatric ventricular assist device (VAD) fluid mechanics.

Methods: A computational fluid dynamic (CFD) simulation was performed focusing on the fluid dynamics, while a fluid structure interaction (FSI) study that couples the blood and air inside the VAD was also performed. For the CFD simulation, a moving boundary was adopted to characterize and describe the fluid dynamics inside the device. In order to do this, a finite element simulation was conducted using ABAQUS 6.10 (SIMULIA©) to quantitatively assess membrane deformation and extract its kinematics. The time-dependent nodal displacements of the diaphragm were used as boundary conditions in the subsequent CFD analysis, simulated with FLUENT v13.0 (ANSYS©), implementing a user-defined function to update the mesh within each time step. FSI was used to simulate the dynamic interaction of air, blood, and the thin membrane separating the two fluids. The computational challenges addressed include a realistic and quantitative description of the buckling motion kinematics of the membrane. These were performed with the explicit solver LS-DYNA R6 (LSTC©). The blood and air reservoirs were characterized with pressure waveforms extracted from experiments, obtaining comparable working conditions between the computational model and the mock circulatory loop.

Results: Computational velocities were comparable with the experimental ones, acquired by means of particle image velocimetry. Both the numerical inlet and outlet velocities were within the experimental range, with a maximum velocity between 0.5 and 0.7 m/sec. The kinematic parameters, velocities, and displacements obtained from the FSI model compared well with the ones extracted from high-speed video.

Assessment of Potential Hemolysis and Platelet Activation in the Hinge Region of a Bileaflet Mechanical Heart Valve Using Laser Doppler Velocimetry

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Study: While many patients needing a replacement heart valve receive a homo- or xeno-graft tissue valve, mechanical heart valves (MHVs) are still routinely used in pulsatile ventricular assist devices and total artificial hearts. One of the most common MHVs is a bileaflet valve, which has been shown to cause hemolysis and platelet activation due to regurgitant jets in the hinge regions. To help improve computational models of the hemodynamics of MHVs, an in vitro study is used to characterize the flow field in the hinge region during valve closure.

Methods: Laser Doppler velocimetry is used to collect 2D velocity data over short time windows (near valve closure) in the hinge region of a mitral bileaflet MHV. The valve was mounted in a test chamber that allowed for continuous opening and closing of the valve, and a non-Newtonian blood analog was used as the fluid. The opening/closing of the valve was dictated by applying physiologically relevant pressures to the ventricular chamber, which produced a dP/dt of approximately 1650 mmHg/s during valve closure.

Results: The results showed the highest regurgitant jet velocities and Reynolds stresses in the 2–3 ms around closure. Mean velocities near 1 m/s, with peak velocities reaching nearly 2.5 m/s, were found near the leaflet edge. Principal Reynolds shear stresses up to 3000 dyn/cm² were calculated, which exceed established thresholds necessary to cause hemolysis and platelet activation.

Effect of Reynolds Stresses on Hemolysis

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Study: Prosthetic heart devices expose blood to non-physiological conditions, such as turbulent blood flow, causing locally high shear stresses in blood and medical complications like hemolysis. It is commonly accepted that turbulence affects red blood cell damage. While an increase in hemolysis is observed when cells are exposed to turbulent stresses, the structure of turbulence in proximity to the blood cells and the mechanism by which cells are injured remains unclear. Therefore, understanding and predicting the effect of turbulent stresses on erythrocytes is a major concern when designing prosthetic heart devices. In this study we explore the effect of Reynolds stresses (RS) on hemolysis using computations.

Methods: A finite volume method (FLUENT) has been used to study the effect of RS on hemolysis. The relation between the hemolysis seen experimentally to the RS in the flow was investigated by using Reynolds-Averaged Navier-Stokes models of turbulence (k-ε turbulence model) to simulate different experimental conditions in a capillary tube and 7 experimental conditions in a Couette viscometer.

Results: Simulations for both capillary tube and Couette viscometer were completed by assuming our system is well mixed and cells spent the same amount of time in any location inside the flow field. Results showed, for both capillary flow and flow in a Couette viscometer, that there was no evidence of a threshold for hemolysis in terms of RS. Therefore, RS is not a good predictor of hemolysis.
CFD-Based Design of Pump Integrated Gas Exchanger
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Study: We are developing a compact one piece pump integrated gas exchanger device (PIGED) for an ambulatory paracorporeal artificial lung. In artificial lung design, an even blood flow pattern is essential for least thrombogenesis and best gas exchange performance. Computational fluid dynamics (CFD) was used for PIGED design to achieve even blood flow pattern.

Methods: The PIGED is a diaphragm displacement cylinder pump embedded inside a gas exchanger (Fig. 1A). A membrane fiber bundle is positioned around the cylinder pump. A cone is used to redirect blood flow to evenly perfuse PIGED inlet fiber bundle. An outlet flow baffle is used to regulate blood flow evenly through PIGED outlet end fiber bundle. The 3D computational domain involved the inlet channel, the outlet blood flow collector, and the hollow fiber membrane. CFD was performed at 2–4 l/min constant flow rates, using the laminar flow model. The fiber bundle was treated as a porous medium, and the blood flow behavior through the fibers was approximated by the Ergun equation. Blood was assumed to be a Newtonian fluid. The finite volume method was used for governing equations discretization.

Results: This CFD study predicted the optimized gas exchanger design at 2–4 l/min flow rates. The blood flow rediector cone allowed even flow distribution. At the lowest flow rate (2 l/min), the minimal velocity was above 2 mm/s within the PIGED inlet fiber bundle and above 1.9 mm/s in the outlet end fiber bundle (Fig. 1B). At the highest flow rate (4 l/min), the shear stress was 168 Pa. The PIGED resistance was 14 and 28 WU at 2 and 4 l/min blood flows, respectively. 

Conclusion: The CFD-based PIGED design achieved an even blood flow distribution through the hollow fiber bundle with minimal velocity above 1.9 mm/s at 2 l/min blood flow. The shear stress at 4 l/min flow rate was slightly larger than the minimum threshold for blood damage (150 Pa) which may cause blood hemolysis.

An Experimental and Computational Study of the Inferior Vena Cava Hemodynamics during Respiration
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Study: Inferior vena cava (IVC) filters have been used for over five decades as an alternative to anticoagulation therapy in the treatment of venous thromboembolic disease. However, complications associated with IVC filters, including failure in embolus capture, wall perforation, filter tilt, filter migration, and filter fracture remain common. Though many studies have investigated blood flow in the IVC, the effects of respiration-induced IVC compression have not been evaluated and may have an influence on IVC filter performance. Therefore, hemodynamics in uncompressed and compressed IVC configurations was investigated using in vitro flow experiments and computational simulations.

Methods: Particle image velocimetry was used to measure the hemodynamics in a compliant model of the human IVC. Flow was studied under uncompressed and compressed configurations, with the minor diameter of the IVC reduced by 30% in the compressed state. Rest and exercise flow conditions were investigated, corresponding to suprarenal flow rates of 2 lpm and 5.5 lpm, respectively. Computational simulations were performed using a geometry derived from a computed tomography scan of the compliant IVC model in the uncompressed configuration. The finite element analysis (FEA) program ABAQUS was then used to reproduce the compressed configuration of the IVC. Computational fluid dynamics (CFD) simulations were performed in FLUENT using the uncompressed and compressed geometries, and the CFD results were compared to the experimental data.

Results: Velocity results in the uncompressed and compressed IVCs were similar, with flow from the left and right iliac veins merging to form a central jet in the infrarenal IVC. Compression of the minor axis of the IVC by 30% resulted in an increase in the major axis of the IVC by 23%, thus reducing the wall velocity gradients on average. However, three-dimensional changes in the flow following IVC compression caused an increase in wall velocity gradients in some regions.
Effects of Hemodynamic Factors on Hemolysis in Shear Flows
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Study: Rotary ventricular assist devices (VADs) usually contain portions where Taylor-Couette flow occurs. Simulation of this type of flow have been performed to predict hemolysis based on flow parameters such as extensional stress, viscous shear stress and exposure time. In this study, Direct Numerical Simulation (DNS) was employed to determine instantaneous flow field parameters and then apply blood damage algorithms to predict hemolysis.

Methods: A plane Couette flow with a moving top wall and a stationary bottom wall was simulated to calculate flow characteristics, using DNS. DNS is a computational method to solve the Navier-Stokes equations directly, with high accuracy and without modeling small scale turbulence. Our method was based on a pseudo-spectral numerical technique that has been validated experimentally [1]. A complete velocity field was obtained and parameters of interest then determined, at several Reynolds numbers. Then simulations using Lagrangian Particle Tracking (LPT) were performed to track individual cells in the flow field. Hemolysis was calculated for each particle trajectory, based on previously published power-law based hemolysis prediction models, using 34,200 particles introduced into the flow field.

Results: We used this method to predict hemolysis in an experiment in our lab. The experiment was performed at laminar regime in a Taylor-Couette viscometer, at shear stress of 10, 50 and 90 Pa. Good agreement was found. By using the DNS/LPT method and hemolysis prediction models, hemolysis was calculated for each particle, based on instantaneous hemodynamic values. DNS/LPT has proved to be more accurate than other fluid dynamics models, especially in turbulent regimes, and has yielded some agreement with experimental data in predicting hemolysis. This method could offer better prediction of hemolysis at different designs and working conditions, which is crucial in optimizing VADs.

CFD Analysis of a Paired Membrane Umbrella Double Lumen Cannula for Failing Fontan Support
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Study: We are developing a new paired membrane umbrella double lumen cannula (DLC) to support failing Fontan patients. The objectives of this computational fluid dynamics (CFD) study were to evaluate the performance/flow pattern and the potential for blood thrombosis of the paired umbrella DLC.

Methods: The paired umbrella DLC is inserted from the right jugular vein and superior vena cava (SVC) into the total cavopulmonary connection (TCPC). Blood is withdrawn from the SVC and the inferior vena cava (IVC) through the drainage lumen and reinfused into the pulmonary artery (PA) via the infusion lumen. A realistic 3D geometry of the paired umbrella DLC and an idealized 3D geometry of the TCPC were constructed. The two paired membrane umbrellas were positioned at a distance of 8 cm from each other, and the infusion outlet was designed 4 cm above the PA anastomosis (Fig). CFD was performed at 2–5 l/min flow rates. The laminar flow model was used for Reynolds number (Re) less than 4000. The shear-stress transport (SST) k-ω turbulent model was implemented for Re greater than 4000. Blood was assumed to be a Newtonian fluid. The finite volume method was used for governing equations discretization.

Results: This CFD study predicted that our paired membrane umbrella DLC can perfuse both the right and left PA, eliminating the strict alignment requirement and guaranteeing adequate performance. However, blood stagnancy, which may increase thrombosis risk, was found close to the two paired membrane umbrellas for all flow rates (2–5 l/min). The stagnant blood flow volume (for a velocity <1 mm/s) decreased from 1.48 mm³ at 2 l/min to 0.04 mm³ at 5 l/min.

Conclusion: The paired membrane umbrella DLC perfused both the right and left PA, ensuring adequate performance. Although blood stagnancy was found, the volume was very small (<1 mm³). Long-term studies will be necessary to determine thrombosis risk.
Development of a Low-Cost Audiogram and Proof of Concept for an Affordable Integrated Audiogram and Hearing Aid
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Study: 360 million people have mild to severe sensorineural hearing loss (SHL) worldwide, most in developing countries and cannot afford a hearing test or hearing aid. Since hearing tests are conducted separately from the fitting of a hearing aid, a doctor or audiologist is required to program the hearing aid, limiting access. As a result, SHL often goes undiagnosed and untreated.

Methods: A low-cost, automated audiogram solution was created on a Raspberry Pi ($45) and Auvio Pearl earbuds ($10) as a high school sophomore design project. An algorithm was created to play clinical audiogram files and record user input through external buttons. A clinical test (n=12 patients) was conducted to compare the results of the RPi audiogram to the clinical audiogram at standard audiogram test frequencies of 125 Hz, 250 Hz, 500 Hz, 1 kHz, 2 kHz, 4 kHz, and 8 kHz.

Results: The RPi audiogram matched the corresponding results of a standard audiogram within 10 dB with a 96% accuracy in a controlled environment (ambient noise < 50 dB). These results demonstrate that the RPi audiogram may be an affordable solution (< $60) to diagnose SHL in developing countries. A low-cost hearing aid is currently being developed in conjunction with the low-cost audiogram with the hearing aid autonomously self programming based on the results of the audiogram.

Total Artificial Heart and Mock Circulation System: A Simulation Tool for Comparative Analysis of Mechanical Circulatory Support Devices
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Study: Mock circulatory systems have been used extensively to evaluate in vitro hemodynamic and hydrodynamic performance of mechanical circulatory support (MCS) devices. However, the ability to easily compare MCS devices and perform relevant clinical scenarios remains extremely limited. In our lab, we have physiologically characterized a mock circulation system, comprised of a SynCardia Total Artificial Heart (TAH-t) and Donovan Mock Circulatory System (DMCS), to mimic clinical heart failure scenarios by operating the TAH-t in a reduced cardiac output mode.

Methods: Herein, we compared 3 different continuous flow ventricular assist device (cfVAD) at a wide range of clinical pump speed: HeartWare (2400-2800RPM), HeartMateII (9000-1100RPM), and HeartAssist5 (7500–12000 RPM). These cfVADs were attached using two T-junctions, separated by a one-way bi-leaflet open pivot artificial heart valve, between the LV outflow and the inflow to the aortic pressure (AoP) chamber of the DMCS (Fig. 1A-B). Pressures and flows at the aorta, left atrium, and left ventricle were measured using the Millar systems and Transonic flow meters.

Results: Under the left ventricle heart failure (LV-HF) condition, the TAH had increased sensitivity to variations in afterload and had reduced Frank-Starling like mechanisms. Before the addition of the cfVAD, left atrial pressure increased by 48% (p<0.01), and cardiac output decreased by 11% (p=0.06) compared to normal operating conditions. When a cfVAD was incorporated into the system, LV-HF was resolved; augmenting the low cardiac output (Fig. 1C) and unloading of left atrial pressure (Fig. 1D). This left ventricular heart failure model allows comparison of the hemodynamic augmentation provided by differing cfVADs, defining inter-VAD differences in performance under identical test conditions. This system can successfully be used to compare MCS devices and be used as a training module for patients and clinicians.
A Method to Increase Radiopacity of PLA Backbone Scaffolds for Preclinical Micro-CT Imaging

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Study: Stent implantation is a popular and effective treatment for narrowed arterial lumens. Metallic stents have been FDA-approved since the 1990s but in recent years, considerable research has been directed towards the development of biodegradable scaffolds. As part of the preclinical study protocol for stents and biodegradable scaffolds, the effect of the implanted device on surrounding tissue is evaluated through histology. Integration of histology and micro-computed tomography (micro-CT) allows for precision-guided histologic sections of stents. Imaging of implanted stents by micro-CT can generate high-resolution images that help identify sites of interest within the tissue-stent context. Newer polymer-backbone biodegradable scaffolds are challenging to visualize en bloc with micro-CT, due to the radiolucency of these materials and the similar radiopacity of the scaffold to surrounding soft tissue. The difficulty of visualizing these polymer-based stents has motivated the development of a technique to increase stent radiopacity post-explant for micro-CT.

Methods: We evaluated common imaging contrast agents for their capacity to increase PLA scaffold radiopacity. A plastic tube filled with water was used to simulate coronary artery soft tissue attenuation. Using 3D printed mockups of a generic PLA backbone stents, a circulatory loop system was used to simulate perfusion of stented coronary arteries. Various micro-CT contrast agents were introduced into the loop for times ranging from 30 minutes to 2 hours allowing the agent to passively permeate the stent prior to imaging.

Results: Preliminary results indicate an increase in visualization of polymer stent features with contrast enhanced perfusion for micro-CT in the pulsatile loop system. Additional contrast media and variations on the perfusion protocol are being evaluated to identify optimal contrast agent and perfusion strategy for in situ micro-CT of implanted polymer based stents.

Frequency Spectrum Analysis of Rotary Blood Pump Vibration

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Study: Analysis of vibration is common with industrial applications of pumps, but has not been studied with significance in the area of rotary blood pumps (RBPs). In particular, the frequency spectrum of pump vibration has been characterized to define mechanical and hydraulic issues such as whip and whirl, imbalance, bearing instability or defects, contact, etc. All such mechanisms could lead to decreased hemocompatibility or durability of RBPs.

Methods: Six RBPs were examined for frequency spectrum of pump vibration (HeartMate II, CentriMag, HVAD, VentrAssist, Levacor, and Jarvik 2000) using an accelerometer and spectrum analyzer with a 2.5 cP glycerin-water working fluid. The acoustic spectrum was quantified in g-force units as a function of impeller speed.

Results: The six RBPs exhibited sub-synchronous and super-synchronous acoustic vibration patterns related to bearing type, stability, or pump construction. The CentriMag showed the highest vibration peaks, primarily due to the mechanical system setup of the polymeric flow path set within the motor driver. Vibration peaks of 1–2 g’s were measured on the VentrAssist, with the remaining four devices below a maximum of 1 g. The Levacor displayed the lowest vibration peaks <.25 g. The frequency spectrum of mechanical and hydraulic vibration varies due to the pump design and construction. Vibration detection can be used to quantify impeller stability and hemodynamic performance. The long-term viability of pump hemocompatibility is likely impacted by its acoustic waveform signature.
Prophylactic Intra-Aortic Balloon Pumping Support before Ventricular Assist Device Implantation Improves Post-operative Clinical Course in Patients with INTERMACS Profile 2
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Study: Intra-aortic balloon pumping (IABP) is sometimes used before the cardiac surgery such as coronary artery bypass grafting targeting better postoperative clinical courses in high-risk patients, clinical impact of prophylactic IABP support before left ventricular assist device (LVAD) implantation in patients with worsening hemodynamics due to advanced heart failure (HF) has remained unknown.

Methods: We experienced 22 patients with worsening hemodynamics who had received IABP before LVAD implantation (IABP group). We also enrolled 22 patients receiving neither IABP nor extracorporeal membrane oxygenation before LVAD implantation, who were selected by the propensity score matching analyses (Non-IABP group).

Results: Although both groups had comparable preoperative background, the IABP group had shorter postoperative intensive care unit (ICU) stay, and more improved hemodynamics (p<0.05 for all). Serum levels of total bilirubin and creatinine decreased significantly in the IABP group over the non-IABP group during post-LVAD 1 month (p<0.05 for both). Medical expenses during perioperative ICU stay was significantly lower in the IABP group over those without IABP, even considering the cost of prophylactic IABP support (p<0.05). In conclusion, prophylactic IABP support in HF patients with worsening hemodynamics improves post-LVAD clinical outcomes and medical expenses.

Can Cardiac Resynchronization Therapy be a Rescue Therapy for Inotrope-Dependent Patients with Advanced Heart Failure or not?
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Study: Although the "off-label usage" of cardiac resynchronization therapy with defibrillator (CRT-D) has spread recently in advanced heart failure (HF) patients in the real-world practice, its clinical effect remained uncertain.

Methods: A total of 84 in-hospital <65-year old patients with advanced HF undergoing CRT-D were enrolled. Seventeen patients (20%) had been dependent on inotropes at the time of CRT-D implantation, and 17 suffered cardiac death within a year. We investigated predictors of such early cardiac death among baseline variables.

Results: Both inotrope dependence and elevated plasma levels of B-type natriuretic peptide (BNP) (>690 pg/mL) at the time of CRT-D implantation were independent predictors of cardiac death within a year by Cox regression analyses (p<0.05 for both). These 2 parameters could significantly stratify 1-year ventricular assist device (VAD)-free survival: inotrope-free low (1) or high BNP (2), or inotrope-dependent low (3) or high BNP groups (4) (98, 77, 57, and 17%, respectively, p<0.001, Fig A). In contrast, there were no significant differences in actual 1-year survival among the four groups (Fig B). Logistic regression analyses demonstrated that baseline left bundle branch block and left atrial diameter 10% during six months (p<0.05 for both). In conclusion, CRT-D may not rescue inotrope-dependent patients with advanced HF. LVAD treatment should be considered instead of CRT-D in such too sick patients.
Perioperative Bronchoscopic Visualization of Left Ventricular Assist Device Thrombus
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Study: Left ventricular assist device (LVAD) malfunction related to formation of intra-pump thrombus can result in hemolysis and can necessitate surgical exchange for a new device. Often the precise etiology of the hemolytic episode is unclear and post-explantation pump analysis by the manufacturer can take weeks. We describe a method for direct visualization of intra-pump thrombus immediately upon explantation.

Methods: Following surgical removal of 4 HeartMate II LVADs, the devices were irrigated with saline solution to remove any remaining blood. An Olympus Evis Exera II Bronchovideoscope was used to visualize the interior of the inflow tract, device housing, and outflow tract. The articulating video probe permits navigation through the 90 degree inflow and outflow elbows as well as the flexible Dacron outflow graft. Digital images were used to record location and architecture of any thrombus.

Results: All patients undergoing exchange presented with clinical indication of hemolysis including lactate dehydrogenase levels at least twice baseline, spikes in pump power, and hemoglobinuria. Following device explantation, thrombus material was visualized using the described bronchoscopic method in each patient. Primary thrombus formation occurred at the bearing surface between the inflow stator and the impeller in all cases. This method allowed for visual assessment of thrombus material—each appeared as organized, white clot located proximal to the device impeller (Figure 1). We report a novel method for visualization of thrombus within explanted LVADs using a bronchovideoscope, a tool readily available in most ORs. The method was successful in locating thrombus in all 4 patients undergoing device exchange for hemolysis and allowed surgical staff to easily and accurately describe the nature and position of the clot. It should be noted that this method is unable to detect the presence of thrombus located in the HeartMate II device housing between the inflow and outflow stator bearings.
Pre-Operative Serum Sodium and Atrial Fibrillation Predict Improvement in Cognitive Function Following Left Ventricular Assist Device Implantation

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Study: Cognitive impairment is common in heart failure patients and can negatively impact quality of life, functional capacity, and survival. Though the effects of hemodynamic support on cognitive function (CF) remain poorly investigated, a recent study indicated substantial improvement following left ventricular assist device (LVAD) implantation. We investigated pre-operative predictors of improvement in CF following LVAD.

Methods: The Montreal Cognitive Assessment (MoCA) was used to evaluate CF in 56 patients prior to and 8 months after LVAD implantation. Demographic, hemodynamic, echocardiographic, and laboratory data were collected concurrently with MoCA testing. Patients were divided into two groups- those with improved and non-improved MoCA scores. Time dependent change in variables was assessed using paired t-tests, and a multivariate logistic model was used to evaluate predictors of improvement in MoCA score.

Results: When the cohort was subdivided based on change in MoCA score, 20 (35.7%) patients did not improve at follow up while and 36 (64.3%) improved. Within these groups, those who improved had significantly lower pre-implant MoCA than those who did not improve (22.8 ± 3.7 vs 25.0 ± 2.7, p=0.049). Mean pulmonary artery pressure, serum sodium, albumin, B-type natriuretic peptide (BNP), and incidence of atrial fibrillation indicated a trend towards a more advanced disease state in the group whose MoCA scores improved compared to those whose scores did not improve or remained the same (Table 1). Noting these worsened clinical indicators in the group with improved MoCA, a multivariate binary logistic model was tested using these variables. Pre-operative serum sodium levels and history of atrial fibrillation were found to be independent predictors for improvement in MoCA score after LVAD implantation (OR: 0.84 CI:0.71–0.99 p=0.02, OR:0.28 CI:0.08–1.02 p=0.05, respectively).

Comparison Between Improved and Non-Improved Groups

<table>
<thead>
<tr>
<th></th>
<th>Non-Improved MoCA (n=20)</th>
<th>Improved MoCA (n=36)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Implant MoCA</td>
<td>25.00 ± 2.70</td>
<td>22.83 ± 3.78</td>
<td>0.049</td>
</tr>
<tr>
<td>Post-Implant MoCA</td>
<td>23.50 ± 3.50</td>
<td>25.06 ± 3.03</td>
<td>0.008</td>
</tr>
<tr>
<td>Age (years)</td>
<td>56.05 ± 12.03</td>
<td>56.76 ± 14.05</td>
<td>0.850</td>
</tr>
<tr>
<td>Mean Pulm. Artery Pressure (mmHg)</td>
<td>29.90 ± 10.44</td>
<td>37.95 ± 10.74</td>
<td>0.039</td>
</tr>
<tr>
<td>Pulmonary Artery Saturation (%)</td>
<td>57.75 ± 7.03</td>
<td>49.68 ± 11.49</td>
<td>0.086</td>
</tr>
<tr>
<td>Sodium (mg/dL)</td>
<td>135.73 ± 2.52</td>
<td>133.21 ± 4.57</td>
<td>0.011</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.26 ± 0.50</td>
<td>2.93 ± 0.47</td>
<td>0.040</td>
</tr>
<tr>
<td>BNP (pg/dL)</td>
<td>350.55 ± 215.32</td>
<td>854.74 ± 880.23</td>
<td>0.020</td>
</tr>
<tr>
<td>A. Fibrillation (count %)</td>
<td>4 (20%)</td>
<td>16 (47.1%)</td>
<td>0.047</td>
</tr>
</tbody>
</table>
First Successful Salvage Impella Support in Failing Fontan Patients - A Novel Approach

J. W. Smith,1 B. H. Morray,2 S. J. Patel,3 C. W. Don,3 K. K. Stout,2 E. V. Krieges,1 C. Masri,1 J. A. Beckman,1 A. C. Stempien-Otero,1 J. D. Pal,1 T. F. Dardas,1 R. K. Cheng,1 T. K. Jones,2 A. E. Rubio,2 E. D. Verrier,3 N. A. Mokadam,1 C. Mahr,1 1Cardiac Surgery, University of Washington, Seattle, WA;2Cardiology, Seattle Children’s Hospital, Seattle, WA;3Cardiology, University of Washington, Seattle, WA.

Study: Experience with MCS in single ventricle (SV) anatomy is limited.

Methods: We report the first successful use of an Impella device in two SV patients with Fontan circulation in cardiogenic shock.

Results: Case 1: 19 YO M male with hypoplastic left heart syndrome S/P Fontan. He presented with altered mental status, low cardiac output and renal failure. There was severe SV dysfunction, cardiac index of 1.6 L/min/m², elevated Fontan pressures of 23 mmHg and PAWP of 19 mmHg. Despite inotropic support he developed worsening end-organ function, INTERMACS Profile 1. An Impella CP was placed via R axillary artery cutdown through a 6 mm Dacron graft and into the RV with immediate hemodynamic improvement. CO and end-organ function improved and the Impella was removed after 13 days. Case 2: 31 YO M with double inlet LV, S/P Fontan and DSK procedures, pacemaker for complete heart block. He presented following PEA arrest with severe LV dysfunction, low CO, elevated Fontan pressures of 20 mmHg and LVEDP of 10 mmHg. Despite inotropic support he developed worsening end-organ function, INTERMACS Profile 1. An Impella 5.0 was placed via right axillary artery cutdown through a 10 mm Dacron graft. Initial device position across the native pulmonary valve was poorly tolerated with acute hypotension secondary to catheter related regurgitation. Re-positioning the Impella across the native AV resulted in prompt hemodynamic improvement. He was transitioned to a HeartWare HVAD after 10 days.

Conclusions: We report the first use of Impella support of failing SV in Fontan patients. There were immediate improvements in filling pressures, CO and ventricular function. No significant hemolysis or device complications occurred. Impella is a viable option in centers with advanced heart failure, MCS and CHD expertise for emergent support of failing SV physiology, either as a bridge to durable advanced therapy or to recovery.

Inotrope Therapy Prior to Left Ventricular Assist Device Implantation: Analysis of Indications and Impact on Outcomes

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Study: Inotropic medications are utilized prior to left ventricular assist device (LVAD) implantation for a variety of indications. Since no study has specifically examined the indications for inotropic therapy pre-implant and whether there is differing impact on outcomes based on these, we review our experience.

Methods: Between March 2009 and August 2014, 251 patients (205 male) underwent primary LVAD implantation at our Clinic. Median age at implant was 62 years (range, 19–82). Etiology of heart failure was ischemic in 117 patients (47%) and indication for LVAD therapy was destination therapy in 157 (63%). Pre-implant inotropes were utilized in 163 patients (65%) for a median of 5 days (range, 1–875 days), 1 agent was used in 129 patients (79%), 2 agents in 29 (18%) and 3 agents in 5 (3%). Indications for inotropes were hemodynamic rescue (Group 1) in 34 (21%), planned optimization (Group 2) in 114 (70%) and as part of prior bridge to transplant strategy (Group 3) in 15 (9%). Group 0 included all patients in whom pre-implant inotropes were not utilized.

Results: Follow-up was available in all patients for a median of 1.1 years (max. 7 years) and for a total of 400.1 patient-years of support. Early outcomes are presented in Figure 1; Group 1 had significantly more respiratory failure compared to the other groups (p=0.04) and there was a trend toward more RV dysfunction in Group 1 (p=0.07). Kaplan-Meier survival curve demonstrates no significant difference in late survival according to indication for pre-implant inotropes (Figure 1).
Costs and Outcomes in the Care of Bi-ventricular Support as a Bridge to Cardiac Transplant


Study: Bi-ventricular mechanical circulatory support is commonly used as a bridge to cardiac transplant. However, the optimal strategy resulting in good clinical outcomes while remaining cost effective is unknown. We examined the outcomes, as well as the costs in the use of bi-ventricular support as a bridge to cardiac transplant.

Methods: From 2001–2014, three different bi-ventricular (Bi-V) support strategies were utilized: 1) Para-corporeal ventricular assist device (PVAD-2001–2006), 2) Heartmate II left ventricular assist device in conjunction with a Centrimag right ventricular assist device (HMII+CMAG-2006–2012), and the total artificial heart (TAH-2012–2014). Total costs were derived from the hospitalization at implant and post-implant costs defined as equipment and re-hospitalizations prior to transplantation.

Results: Sixty-two (31 PVAD’s, 20 HMII+CMAG, and 11 TAH’s) devices were used as a bridge for transplant. There were no differences in implant variables including age, renal/liver function, INTERMACS score, or implant length of stay. While the wait list mortality was not different between groups (PVAD-32%, HMII+CMAG-45%, TAH-54%; p=0.3), the percentage of patients transplanted was highest in the PVAD group (PVAD-61%, HMII+CMAG-30%, TAH-18%; p=0.01). The duration of Bi-V support was greatest within the HMII+CMAG group (PVAD-0.3 ± 0.5, HMII+CMAG-2.8 ± 1.9, TAH-0.4 ± 0.4 years; p=0.01). Total costs were not significantly different between groups (PVAD-$9,264 ± 21381, HMII+CMAG-$278,958 ± 135,324, TAH-$321,387 ± 212477; p=0.5) (Figure 1). Breakdown of costs demonstrated significantly higher post-implant costs within the HMII+CMAG group (PVAD-$306,166 ± 247,839, HMII+CMAG-$278,958 ± 135,324, TAH-$321,387 ± 212477; p=0.01).

Conclusion: Despite variations in therapy, outcomes and total costs for patients requiring Bi-V support as a bridge to cardiac transplant have remained constant over the past decade.

Figure 1.

<table>
<thead>
<tr>
<th>Total Costs (Dollars)</th>
<th>PVAD</th>
<th>HMII+CMAG</th>
<th>TAH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implant</td>
<td>20000</td>
<td>60000</td>
<td>0</td>
</tr>
<tr>
<td>Post-Implant</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Abbreviations: PVAD-Para-corporeal Ventricular Assist Device, HMII+CMAG-Heartmate II Left Ventricular Assist Device + Centrimag Right Ventricular Assist Device, TAH-Total Artificial Heart

Accuracy of Detecting the Presence of Left Ventricular Thrombus With Pre- and Intraoperative Echocardiogram in Patients Undergoing Left Ventricular Assist Device Implantation

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Study: A persistent left ventricular thrombus (LVT) poses risks of pump thrombosis and stroke in left ventricular assist device (LVAD) recipients. Transthoracic (TTE) and transesophageal echocardiograms (TEE) are commonly used to detect the presence of LVT. However, the relationship between preoperative echocardiography and findings at LVAD implantation has not previously been studied.

Methods: A retrospective review examined all patients undergoing continuous-flow LVAD placement or exchange from October 2011 to March 2014 at a single institution. Preoperative TTE and TEE data were compared with the presence of LVT during direct inspection at LVAD placement. The findings were analyzed quantitatively and the discriminative powers of these modalities were analyzed.

Results: Between October 2011 and March 2014, 99 patients underwent 107 LVAD implants or exchanges. The median age was 61 (IQR 51–66) with 19 (19.2%) female patients. TTE was available in 94 (87.9%) cases, while preoperative TEE was available in 37 cases (34.6%) and intraoperative TEE in 99 cases (92.5%). Intraoperative inspection revealed LVT in 14 cases. On preoperative TEE, LVT was correctly identified in only two cases. Conversely, preoperative TEE did not identify any of the LVT and there were two false positive reports. Intraoperative TEE also failed to identify thrombi and there was one false positive report. Receiver operating characteristics analysis yielded unsatisfactory areas under the curve for all three modalities (<60%).

Conclusion: Preoperative echocardiogram offers low accuracy for presence of LVT. Overall, the sensitivity is too low to reliably exclude thrombus. This could have significant implications in planning off-pump LVAD exchange as thrombus could be missed. More data are necessary to determine whether this could have significant effects on thromboembolic complications and survival.

Comparison of Preoperative TTE, TEE and Intraoperative TEE Detection of LVT

<table>
<thead>
<tr>
<th></th>
<th>Median Days Prior to Surgery</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Accuracy</th>
<th>Area Under the Curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>TTE</td>
<td>22.5</td>
<td>16.7</td>
<td>100</td>
<td>100</td>
<td>89.1</td>
<td>89.2</td>
<td>0.58</td>
</tr>
<tr>
<td>TEE</td>
<td>4</td>
<td>93.8</td>
<td>0</td>
<td>81.1</td>
<td>75.7</td>
<td>0.47</td>
<td></td>
</tr>
<tr>
<td>Intra-Operative TEE</td>
<td>0</td>
<td>98.9</td>
<td>0</td>
<td>87.8</td>
<td>86.7</td>
<td>0.49</td>
<td></td>
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</tbody>
</table>

Abbreviations: PVAD-Para-corporeal Ventricular Assist Device, HMII+CMAG-Heartmate II Left Ventricular Assist Device + Centrimag Right Ventricular Assist Device, TAH-Total Artificial Heart
The Role of Acid Suppression Therapy to Reduce GI Bleeding Events in LVAD Patients

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Study: Gastrointestinal bleeding (GIB) is a common complication of LVAD therapy occurring in 18 to 40% of patients. As approximately 50% of these bleeds originate in the upper GI tract, we sought to assess the effect of acid suppression therapy (AST) on GIB incidence in LVAD patients.

Methods: Using our institutional registry, we identified 100 patients who were discharged after continuous flow LVAD placement between 1/1/2011 and 8/31/2014. We analyzed the primary outcome of GIB based on the outpatient prescription of AST (H2-blocker or proton pump inhibitor). Patients were excluded for GIB immediately after LVAD implantation (n=5) or death within 30-days of device implant (n=2).

Results: Of the included patients, 75% (n=70) received AST and 25% (n=23) did not. Baseline characteristics such as age, device indication, INTERMACS Profile, history of GIB, did not differ between the two groups (data not presented). The median time to GIB was 92 days [48–141] in the no AST group and 186 days [95–328] in the AST group (p=0.5). Survival free of GIB was not affected by AST (p=0.85, Figure 1). Further, no effect was found of AST when patients were analyzed by upper v. lower GIB (p=0.87 v. 0.69), and AST had no effect on re-bleeding rates (11%, p=0.43). Arterio-venous malformations were the most common cause of GIB (Table 1). Overall, the AST group experienced 0.32 GIBs per patient-year v. 0.3 GIBs per patient-year in the no AST group. There was no difference in long-term survival between those who experienced GIB and those who did not (p=0.85). These results seem to indicate that prescription of AST as an outpatient is not effective in reducing GIB events in LVAD recipients. This is important as AST has its own side effects.

### Table 1 - Bleeding Locations by Category

<table>
<thead>
<tr>
<th>Bleeding Location</th>
<th>AST</th>
<th>No AST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper GI AVM</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Esophagitis</td>
<td>1</td>
<td>***</td>
</tr>
<tr>
<td>Gastritis</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Peptic Ulcer</td>
<td>1</td>
<td>***</td>
</tr>
<tr>
<td>Lower GI AVM</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Hemorrhoids</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Diverticulosis</td>
<td>***</td>
<td>1</td>
</tr>
<tr>
<td>Unidentified</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>
The Effect Of Blood Contact Surface Area Reduction During Extracorporeal Circulation In A Rat Cardiopulmonary Bypass Model
Y. Fujii,1 M. Shirai,1 Y. Takewa,1 E. Tatsumi.1 1Department of Artificial Organs, National Cerebral and Cardiovascular Center Research Institute, Suita, JAPAN.

Study: Systemic inflammatory responses in patients receiving cardiac surgery supported by extracorporeal circulation (ECC) significantly contribute to ECC associated morbidity and mortality. Previous studies have suggested that the interaction of blood and large artificial surface contributes to inflammatory response during ECC. As a result of a series of chain reactions, the numerous powerful inflammatory mediators are formed and released. We hypothesized that small ECC circuit which reduces priming volume and blood contact surface area attenuates the systemic inflammatory response with a reduction of cytokine levels during ECC.

Methods: Rats were divided into the large surface area ECC (priming volume: 15 ml, surface area: 0.044 m2) group and the small surface area ECC (priming volume: 7 ml, surface area: 0.036 m2) group. ECC pump flow was maintained at 80 ml/kg/min. Blood samples were collected pre, 60 min and 120 min after initiation of ECC. We measured the serum cytokine levels (TNF-α, IL-6, IL-10), biochemical markers (LDH, AST, ALT) and wet-to-dry (W/D) weight ratio of the left lung tissues postmortem after 120 min ECC.

Results: Pro-inflammatory markers (TNF-α, IL-6) and biochemical markers were significantly elevated in the large surface area ECC group compared with the small surface area ECC group at 60 min (TNF-α: large vs small: 856 ± 65 vs. 444 ± 34 pg/ml, IL-6: large vs small: 695 ± 62 vs: 292 ± 85 pg/ml). At 120 min, however, none of the markers was statistically different between the 2 groups (TNF-α: large vs small:1237 ± 61 vs. 1129 ± 137 pg/ml, IL-6: large vs small: 1226 ± 132 vs. 1158 ± 150 pg/ml). The W/D ratio increased significantly more in the large surface area (high priming volume) ECC group than in the small surface area (low priming volume) group (6.01 ± 0.11 vs 5.46 ± 0.09). These data suggested that in addition to the blood contact surface area factor, the ECC exposure duration is also an important factor for causing the systemic inflammatory response.

Assessment of Preload-Recruitable Stroke Work During Biventricular Ex Vivo Heart Perfusion: A Novel Approach Eliminating The Pressure-Volume Loop Catheter
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Study: Ex vivo heart perfusion may facilitate resuscitation of non-utilized donor hearts. A reliable means of demonstrating organ viability prior to transplantation is required. Preload recruitable stroke work (PRSW) is a load independent metric of myocardial function obtained using a pressure-volume loop catheter; however, the expensive, cumbersome, and invasive nature of the equipment limits clinical translation. Therefore, we sought to develop a non-invasive method of measuring PRSW in an ex vivo, bi-ventricular, working heart device.

Methods: A bi-ventricular working heart device was developed (Figure 1), and a computer program was written for control and integration of pressure (left atrial, right atrial, aortic, and pulmonary arterial) and flow (left atrial, and right atrial) data. The hearts of 40 kg pigs were procured, perfused with a blood-STEEN solution, and transitioned into a working mode by increasing the revolutions per minute on the preload pump. The partial occlusion clamp was adjusted to ensure right atrial flow did not exceed left atrial flow (Figure 1). Stroke volume was calculated as follows: stroke volume (mL/beat) = atrial flow (mL/min) / heart rate (beats/min). Stroke work was calculated as follows: stroke work (mmHg*mL) = [mean arterial pressure - atrial pressure] x stroke volume (mL).

Results: Stroke work was measured during a computer-controlled reduction in revolutions per minute on the preload centrifugal pump, producing a linear reduction in atrial pressure. PRSW was determined by calculating the linear regression of stroke work and atrial pressure (Figure 2). PRSW can be measured in a non-invasive fashion during ex vivo heart perfusion in a biventricular-working mode, without the need for pressure-volume loop catheters. This method of myocardial functional assessment may aid in selecting viable donor hearts for transplantation in the future.
Impact of an Outpatient Anticoagulation Protocol on Thrombotic and Bleeding Complications of LVAD Therapy
K. M. Poppiti, M. Bradbury, D. B. Goffman, R. Connelly, S. S. Desai, N. A. Burton, P. Shah. Inova Fairfax Hospital, Falls Church, VA.

Study: Patients with left ventricular assist devices (LVADs) are predisposed to thrombotic and bleeding complications. The optimal anticoagulation regimen in this population is unknown. In October 2012, we implemented a standardized outpatient anticoagulation protocol. The purpose of this study was to determine the protocol's efficacy in preventing LVAD complications.

Methods: Using our institutional registry, we investigated outcomes in 100 outpatients implanted with a continuous-flow LVAD between 1/1/2011 and 8/31/2014. Three patients were excluded for lack of INR follow-up. Protocol efficacy was analyzed by comparing the incidence of hemolysis, stroke or major bleeding before and after protocol use. Percent time in therapeutic range (%TTR) with warfarin was calculated.

Results: Baseline demographics were similar between groups. We analyzed 3,572 INR values. There was a significant difference in %TTR between the pre-protocol and post-protocol cohorts (49.6 ± 22.3 v. 58.0 ± 17.0, p=0.04). Pre-protocol, the rates of hemolysis and stroke were 0.26 events per patient-year (EPPY) and 0.20 EPPY, respectively. Event rates were similar after protocol initiation (0.20 EPPY and 0.24 EPPY, p=0.77 and p=0.19, respectively). The post-protocol group had a higher incidence of major bleeding versus the pre-protocol group (0.51 EPPY v. 0.24 EPPY, respectively, p < 0.01) and an increased relative risk of major bleeding (3.3, 95% CI 1.7 to 6.5, p < 0.01). At time of bleeding, the median INR was 2.4 (IQR 1.9–3.2) in the pre-protocol group and 2.7 (IQR 1.6–2.5) in the post-protocol group. Figure 1 depicts survival free from bleeding, hemolysis or stroke stratified by protocol and percent-time in therapeutic range.

A standardized outpatient anticoagulation protocol was associated with increased %TTR without impact on rates of hemolysis or stroke. However, there was an increase in major bleeding events, cautioning aggressive anticoagulation protocols.

In Vitro Evaluation of a Minimally Invasive Mechanical Circulatory Support Device for Assisting Renal Blood Circulation
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Study: In previous study, we have proposed the new technique for assisting renal blood circulation selectively using an extracorporeal circulation circuit in acute cardiorenal syndrome (ACRS) and have shown its effectiveness in a goat model. The purpose of this study is to develop a minimally invasive mechanical circulatory support (MCS) device which can perform renal selective blood perfusion (RSP) on renal ischemic dysfunction in ACRS. This time, we developed a catheter-based miniature intravascular blood pump for the minimally invasive MCS device and evaluated its hydrodynamic performances in in vitro test.

Methods: The minimally invasive MCS device consisted of the miniature blood pump, a catheter and an external drive unit. The miniature blood pump which was set on the catheter tip was composed of an impeller, a brushless DC motor, a motor housing and a pump casing and ejects the blood by rotating the impeller which was installed inside the pump casing by the brushless DC motor. The miniature blood pump has two outlet ports against one inlet port in order to be put in the abdominal aorta near the renal artery and to assist simultaneously to both renal arteries. The diameter and total length of a prototype blood pump was 9 mm and 37 mm, respectively. The hydraulic performance of the prototype blood pump was evaluated using a mock circulation circuit which included renal arterial branch under pulsatile systemic hemodynamic condition.

Results: Upon simulation of ACRS condition by decreasing cardiac output, renal arterial flow (RAF) and renal arterial pressure (RAP) of both renal arteries decreased to 71 and 60% of the respective baseline values of normal heart condition. Then, RSP by prototype blood pump increased RAF and RAP of both renal arteries up to 95 and 92% of baseline values, respectively. The prototype blood pump displayed sufficient performance for RSP and its MCS device may offer a new treatment strategy for patients with ACRS.
Precision Sensorless Flow Rate Estimation with On-line Viscosity Compensation in a Magnetically Levitated Centrifugal Blood Pump

W. Hijikata, Y. Suzumori, J. Rao, S. Takatani, T. Shinshi

Precision and Intelligence Laboratory, Tokyo Institute of Technology, Yokohama, JAPAN; Interdisciplinary Graduate School of Science and Engineering, Tokyo Institute of Technology, Yokohama, JAPAN; MedTech Heart Inc., Tokyo, JAPAN.

Study: A sensorless technology for estimating the flow rate in a rotary blood pump without using a flow meter is crucial in order to realize a compact and reliable ventricular assist system. Even though various methods to estimate the flow rate have been proposed, a method for estimating the flow rate with on-line viscosity compensation has yet been realized. In this study, we have developed a sensorless method for measuring viscosity in a magnetically-levitated centrifugal blood pump, an impeller of which was supported by a magnetic bearing.

Methods: By applying lateral vibrational excitation to the impeller using the magnetic bearing and measuring a phase difference between the current in the magnetic bearing and the displacement of the impeller as shown in the figure, we measured viscosity of working fluid. For evaluating the accuracy of the sensorless viscosity measurement, we used several glycerol water mixtures as blood analog fluids with viscosities ranging from 1.18 to 5.12 mPa∙s. By using the torque and rotational speed of a motor, estimation of the flow rate compensated by the measured viscosity was also carried out.

Results: The mean absolute deviation between the measured viscosity and reference viscosity, which was measured by a vibrational viscometer, was 0.12 mPa∙s in the range from 1.18 to 5.12 mPa∙s. The mean absolute deviations between estimated flow rate and reference flow rate were 1.83 L/min without viscosity compensation and 0.36 L/min with viscosity compensation in the range from 1 to 5 L/min. The results showed the proposed method for measuring the viscosity was sufficiently accurate to be used for the flow rate estimation.
Mechanistic Insight of Platelet Apoptosis Leading to Non-Surgical Bleeding Among Heart Failure Patients Supported by Continuous-Flow Left Ventricular Assist Devices

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Study: Non-surgical bleeding (NSB) is the most common clinical complication among heart failure (HF) patients supported by continuous-flow left ventricular assist devices (CF-LVADs). The incidence of platelet apoptosis in mediating bleeding was reported in our previous study. But the exact molecular mechanism of platelet apoptosis in bleeding CF-LVAD patients remains unknown. The goal of this study was to identify the molecular mechanism of platelet apoptosis and associated signalling pathway on the incidence of bleeding after CF-LVAD implantation.

Methods: We recruited 25 HF patients implanted with CF-LVADs. Eight patients developed NSB (bleeder group) within 1 month after CF-LVAD implantation while the others were considered non-bleeder group (n = 17). Generation of reactive oxygen species (ROS) from platelets, change in platelet mitochondrial membrane potential (Δψm), expression of pro-survival (Bcl-2, Bcl-xL) and pro-apoptotic (BAX) proteins, release of cytochrome C, activation of caspases, gelsolin cleavage and platelet apoptosis were studied.

Results: Intraplatelet ROS generation was found to be significantly elevated in the bleeder group in comparison to the non-bleeder group. Pro-survival proteins in the bleeder group significantly decreased compared to the non-bleeder group. Translocation of Bax into platelet mitochondria membrane and subsequent release of cytochrome c were clearly evident in the bleeder group. Progressive rise in % positive depolarized platelets, activation of caspases, gelsolin cleavage and platelet apoptosis were studied.

Results: Intraplatelet ROS generation was found to be significantly elevated in the bleeder group in comparison to the non-bleeder group. Pro-survival proteins in the bleeder group significantly decreased compared to the non-bleeder group. Translocation of Bax into platelet mitochondria membrane and subsequent release of cytochrome c were clearly evident in the bleeder group. Progressive rise in % positive depolarized platelets, activation of caspases, gelsolin cleavage and phosphatidylserine (PS) exposure in the bleeder group were observed. These multiple indicators of platelet apoptosis suggest the platelet damage played an important role in bleeding incidence. In conclusion, our results may offer mechanistic insights into the bleeding complication in patients with CF-LVAD support (Fig. 1).

E-health Based Management of Patients With Left Ventricular Assist Device in Their Home Environment


Study: Leftventricular assist device (LVAD) implantation are increasing in prevalence to treat end stage heart failure. Post-implantation follow-up is important for monitoring device function and patient condition to avoid anticoagulation related life-threatening side effects or VAD malfunction. However, practise is inconsistent, and according to physician preference. Thus, in this study we evaluated and described an intelligent e-health platform for wireless remote monitoring of cardiac performance and anti-coagulation status in VAD patients to identify salient problems rapidly.

Methods: We designed and established a project pathway to conceptualise the deployment of this e-health service innovation. Using insights of technical and conceptual needs (status-quo process) and a patient survey (capture of willingness to apply modern information technology and demands related to e-health) were combined to develop step by step a full scope-telemonitoring platform in VAD population.

Results: Cardiac implantable electronic devices (ICD) and anticoagulation management (CoaguCheck®) are identified as potential enabler for health care process optimization and data flow. Using our e-health platform all data coming from the ICD or CoaguCheck® are recorded, evaluated and stored in a electronic health record and periodically analyzed for 50 consecutive patients. For data transmission no additional action is required. Potentially impaired health status, arrhythmias, disturbances or differences to define ranges of INR levels are highlighted automatically as alerts. Consequently, both the patient and the stakeholders are informed for further action. Most of the patients are appreciate e-health technology, but they have concerns about the security of data transmission and data confidentiality.
Factors Influencing Simulation Results and Hemolysis Estimates for the FDA CPI CFD/Blood Damage Project

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Study: In an effort to standardize the use of computational fluid dynamics (CFD) analysis for preclinical assessment of medical devices, the Food and Drug Administration (FDA) released a simplified centrifugal blood pump model as part of the Critical Path Initiative (CPI) program. The results of this numerical study will be compared with experimental results obtained by the FDA to establish the accuracy of numerical approaches and blood damage prediction for the design and optimization of medical devices.

Methods: The computational domain of the model pump was generated using ANSYS ICEM CFD 14. All meshes were unstructured and optimized based on mesh orthogonal quality and grid independence. Solutions were obtained using ANSYS FLUENT using 2nd order upwind spatial and temporal discretization.

Results: The maximum scalar shear stresses varied by >50% between laminar and turbulent flow models, while average residence times and particle distributions were found to vary substantially. The frame of reference used to estimate hemolysis may result in damage indices that differ by as much as 90% for identical flow conditions. The inclusion of models for shear-thinning viscosity of blood results in a 15% increase in peak scalar shear stresses. The quantitative differences between the viscous and rheological models were illustrated using CFD visualization techniques, such as the scalar shear stress contours shown in Figure 1, which provide useful and experimentally unattainable insight into the physics of fluid flow through blood pumps. The results of the CFD analysis of the FDA CPI model pump indicated a strong dependence on the selection of input model assumptions such as laminar vs. turbulent flow and viscosity models. These selections, in turn, impact the predicted hydraulic and blood damage performance of the blood pump. Upon release of the experimental findings by the FDA, the impact of these selections can be determined and the CFD model refined to improve prediction accuracy.

Contours of Scalar Shear Stress [s] Pa

Laminar (Newtonian) Laminar (non-Newtonian) Turbulent (Newtonian)

Development and Chronic in vivo Testing of a Fully Implantable Extraventricular Counterpulsation Device

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Study: The C-Pulse® extra-aortic counterpulsation system has shown preliminary indications of safety and improvement in functional status and QoL in a feasibility study (n=20) and is currently in a US IDE study (Counter HF) and a European post market study (Options HF). One limitation of all current MCS systems is the requirement for a percutaneous driveline and the associated risk of infections. To eliminate the driveline a second generation C-Pulse system is being developed that consists of a fully implantable electrohydraulic pump and extra-aortic cuff, that will be powered via a TET system intended for chronic cardiac support.

Methods: Testing of the implantable pump and extra-aortic cuff included; in vitro performance evaluation on a mock loop conducted with the current C-Pulse system as control; anatomic fit and implantation assessment in cadavers (n=3); an acute bovine model (n=2) investigation of short term performance; and chronic in vivo performance evaluation in calves (n=2) up to 90 days to investigate device-tissue interactions.

Results: In vitro testing demonstrated reductions of aortic end-diastolic pressures greater than 10mmHg, a similar afterload reduction as seen with the first generation C-Pulse system. Implantation of the system was achieved in cadavers via both a right anterior thoracotomy and a hemi-sternotomy surgical approach. In animals, counterpulsation with significant diastolic aortic pressure augmentation (20mmHg) was achieved both acutely and following 90 days implantation. Necropsy revealed no restrictive fibrous capsule around the device. Histopathology confirmed the intimal surface and the endothelium of the aorta at the cuff was intact and normal. There was no evidence of any end-organ pathology.

Conclusion: Preliminary studies demonstrate feasibility of a fully implantable counterpulsation pump and extra-aortic cuff. Further testing with the TET powered system is currently being planned prior to first clinical use of the system.
Antibody Production is Not Increased in Total Artificial Heart Patients Despite Multiple Blood Transfusions

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Study: Detection of circulating antibodies after placement of a mechanical circulatory assist device (MCSD) is well reported. Continuous flow MCSD may have less development of circulating antibodies due to fewer blood transfusions and to more benign contact blood surfaces within the device. It is known that packed red blood cell transfusions can lead to the development of circulating antibodies. It is not clear whether specific devices have different incidence of development of circulating antibodies.

Methods: We assessed 53 MCSD patients awaiting heart transplant who had no circulating antibodies prior to device insertion. Patients were divided based on the type of implanted device: HeartMate II (HMI), HeartWare (HW) and Total Artificial Heart (TAH). We assessed the incidence of de novo antibody development for each device used.

Results: Patients who received a TAH had the lowest incidence of de novo antibody development post-implant despite receiving the highest amount of blood transfusions. Patients who received a HW device had the highest incidence of de novo antibody production despite receiving the least amount of blood products while on the device. (See table)

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>HeartMate II (n=23)</th>
<th>Heartware (n=14)</th>
<th>Total Artificial Heart (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 month Actuarial Freedom from de novo antibody development</td>
<td>81.5%</td>
<td>69.2%</td>
<td>100%*</td>
</tr>
<tr>
<td>Average Units of Total Blood Products while on MCS</td>
<td>43.4 ± 25.2</td>
<td>18.4 ± 13.4**</td>
<td>44.7 ± 55.8</td>
</tr>
<tr>
<td>Average Units of Packed RBCs while on MCS</td>
<td>20.0 ± 18.5</td>
<td>8.6 ± 8.8**</td>
<td>20.3 ± 28.0</td>
</tr>
<tr>
<td>Average Units of Platelets while on MCS</td>
<td>4 ± 2.6</td>
<td>2.3 ± 2.9</td>
<td>3.9 ± 5.2</td>
</tr>
<tr>
<td>Average Units of Pooled Cryo while on MCS</td>
<td>2.8 ± 2.1</td>
<td>1.1 ± 1.4**</td>
<td>1.4 ± 2.1**</td>
</tr>
<tr>
<td>Average Units of Thawed Plasma while on MCS</td>
<td>16.6 ± 9.7</td>
<td>6.4 ± 6.3**</td>
<td>19.1 ± 23.2</td>
</tr>
</tbody>
</table>

*P<0.05 compared to HeartWare group.
**P<0.05 compared to Heartmate II group.

Conclusion: Despite the need for multiple blood transfusions in TAH patients, antibody production is low. A larger number of patients is needed to confirm these findings.

Mechanical Behavior of Porcine Aortic Valve Leaflet under Cantilever Bending Fatigue Test

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Study: Aortic valve failure involves high rates of mortality and some current designs of prosthetic valves have shown lack of long term reliability. Fatigue bending stress is reported as the main cause of prosthetic valve failure. Designing a new valve prosthesis requires an understanding of the leaflets mechanical properties under quasi-static (QS) and dynamic conditions. Biomechanical characterization of the leaflets has been mainly done under QS conditions due to the complexity of dynamic studies. This project aims to study the fatigue of aortic valve leaflets by proposing a mathematical model based on a middle term experiment. An experimental setup is implemented to measure bending stresses under cycling loads. Then the mathematical model is proposed to predict the design stress of an aortic leaflet as a function of its displacement and the number of load cycles.

Methods: Porcine aortic leaflets were sectioned and stored. An experimental setup was built to test aortic leaflets under cantilever bending at aqueous condition. Two experiments were conducted: a bending cantilever test at QS conditions and a fatigue test at 2.5x10^5 cycles at 0.1 Hz. The mathematical model is proposed based on Continuum Damage Mechanics. The model consists of two parts: the first one based on the QS experiment, relates displacement with maximum bending stress; the second part describes the reduction of the mechanical response due to fatigue. The damage behavior was based on the dynamic experimental data.

Results: The experimental setup allowed to measure the leaflet loads at cantilever arrangement. The aqueous condition permitted to maintain leaflet consistency during the dynamic experiment. The mathematical model was able to describe experimental response of the leaflet at both experiments. A function to describe the damage of the leaflet due to the number of load cycles is proposed. The mathematical model would help to design new bioprosthetic aortic valve based on long term mechanical behavior.

Efficacy of Oral Antimicrobial Management of LVAD Driveline Infections


Study: Driveline infections (DLIs) remain one of the most common complications in continuous-flow left ventricular assist device (CF-LVAD) populations. Limited data exists, however, to guide treatment for affected patients, resulting in well-documented practice variability. We sought to characterize the current management of DLIs, with a focus on patients who could be successfully treated with oral antibiotics alone.

Methods: All durable CF-LVAD implants from Aug 2007-Aug 2014 at our institution were retrospectively analyzed. Collected data included patient demographics, comorbidities, treatment strategy, microbiology, and outcome. Patients had been initially stratified by infection stage to either oral antibiotics (minor or superficial) or IV antibiotics/debridement (deep). For those treated with oral therapy, success was defined as documented clinical resolution in the absence of re-hospitalization, subsequent use of parenteral antibiotics, or operative intervention for at least 3 months.

Results: A total of 159 adult patients were implanted with a CF-LVAD during the study period. 42 (26%) of these patients developed a DLI (median time to first infection = 282 days). Among those with a DLI, 27 (64%) were treated solely with oral antibiotics - success was achieved in 17 (63%), while 10 (37%) required escalation in care. From 2009–2014, oral antibiotic success improved to 73%. Escalation in management was most often associated with MRSA infection. Commonly used empiric therapies included ciprofloxacin (100% success rate from 2009–2014), doxycycline (100%), trimethoprim-sulfa (80%), and levofloxacin (43%). This preliminary data demonstrates that oral antibiotics may be used successfully to eradicate minor DLIs, while deep and/or MRSA DLIs are likely best managed with a more aggressive strategy. This should facilitate the development and subsequent validation of an empiric treatment protocol that may reduce the need for hospitalization, IV antibiotics, or debridement in select patients.
Aortic Valve Regurgitation and Outflow Graft Anastomosis Site Design After Left Ventricular Assist Device Implantation
K. Iizuka, T. Nishinaka, T. Katsube, K. Yamazaki. Cardiovascular Surgery, Tokyo Women’s Medical University, Tokyo, JAPAN.

Study: Aortic valve regurgitation (AR) is a serious complication under left ventricular assist device (LVAD) support. We investigated time-course changes of AR and related factors.

Methods: 21 patients, who had continuous-flow LVAD (EVAHEART®, SunMedical Technology Research Co., Japan) implant supported for more than 3 months, were investigated. AR score (none=0, trivial=0.5, mild=1, mild-moderate=1.5, moderate=2, moderate-severe=2.5, severe=3), LV diastolic and systolic diameter (LVDd and Ds), fractional shortening (FS), and aortic annulus dimension were evaluated with echocardiography. Computed tomography scan was performed in 20 patients postoperatively. The angle of outflow graft to the aorta (O-A angle) was evaluated.

Results: The age of patients was 39 ± 11. Average support duration was 686 ± 354 days. AR score (0.4 ± 0.3, 0.5 ± 0.4, 0.7 ± 0.3, 0.8 ± 0.3, 0.9 ± 0.4, 0.9 ± 0.5, 0.8 ± 0.5; preoperatively, at 1, 3, 6, 12, 18, and 24 months of LVAD support, respectively) tended to increase, being maintained around mild. No patient needed any intervention to aortic valve. The aortic valves of 81.0% of patients were closed continuously. LVDd (69 ± 10, 56 ± 10, 58 ± 10, 60 ± 8, 65 ± 8, 66 ± 6, and 64 ± 9mm) and LVDs (68 ± 8, 51 ± 11, 54 ± 7, 52 ± 10, 58 ± 10, 59 ± 7, and 56 ± 10mm) tended to decrease by LVAD implant. FS (0.09 ± 0.04, 0.09 ± 0.06, 0.09 ± 0.04, 0.10 ± 0.05, 0.12 ± 0.07, 0.11 ± 0.05, and 0.11 ± 0.05) and aortic annulus dimension (20 ± 2, 21 ± 2, 21 ± 2, 21 ± 3, 23 ± 1, 22 ± 3, and 20.1 ± 2mm) had no correlation to AR score. The O-A angle, which is speculated to have some impact on blood flow pattern around aortic valve was correlated with AR level.
Impact of Left Ventricular Assist Device Support on Regional Cerebral Oxygen Saturation

J. Huang, J. Trivedi, A. Cheng, M. Slaughter. Cardiovascular & Thoracic Surgery, Jewish Hospital & University of Louisville, Louisville, KY.

Study: Left ventricular assist device (LVAD) placement has become the mainstay for treatment of end-stage heart failure. Currently, there is no reliable, real time parameter to assess LVAD function and patient outcome. We hypothesize LVAD support improves regional cerebral oxygen saturation (rSO2) after implantation and that baseline rSO2 might be a predictor of postoperative clinical outcomes.

Methods: 218 consecutive patients had a continuous flow LVAD implanted between 2008 and 2014. rSO2 at baseline and skin closure were measured and recorded in medical records. Clinical outcomes were further analyzed between baseline rSO2 less than 40 group and equal or above 40 group for possible association. Student t test was used to compare the mean and standard deviation of various outcomes.

Results: Thirty-eight (18%) patients presented to the operating room with baseline rSO2 below 40 and one hundred and seventy (82%) were equal or above 40. Average baseline rSO2 was 50.8±12.6 and was improved to 61.4±10.2 at skin closure after initiating LVAD support. However, there was no statistically difference between rSO2 less than 40 group and rSO2 equal or above 40 group for in hospital mortality, Intensive Care Unit time, length of stay, stroke, renal failure and 1 year mortality. In conclusion, LVAD initiation improved rSO2 by 21% and rSO2 might serve as a real time measurement of LVAD function. However, baseline rSO2 alone does not predict early postoperative clinical outcomes in LVAD surgery.

rSO2 and LVAD Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Baseline rSO2 &lt; 40 (n=38)</th>
<th>Baseline rSO2 ≥=40 (n=170)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>53.2±13.4</td>
<td>55.5±13.5</td>
<td>0.3</td>
</tr>
<tr>
<td>Gender-Male</td>
<td>68.4%</td>
<td>81.4%</td>
<td>0.07</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>7.9%</td>
<td>4.6%</td>
<td>0.4</td>
</tr>
<tr>
<td>Intensive Care Unit time</td>
<td>235.5±368.9</td>
<td>194.3±239</td>
<td>0.4</td>
</tr>
<tr>
<td>(hours)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of Stay</td>
<td>23.8±17.7</td>
<td>21.2±15.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.6%</td>
<td>2.9%</td>
<td>0.9</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>2.6%</td>
<td>6.4%</td>
<td>0.3</td>
</tr>
<tr>
<td>1 year mortality</td>
<td>15.6%</td>
<td>17.9%</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Cellular Microparticles as Predictive Markers for Thrombosis and Other Clinical Events in Patients with Implanted LVADs

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Study: Current methods that identify left ventricular assist device (LVAD)-associated adverse events have low sensitivity hindering early prediction and timely clinical intervention. Microparticles (MP), formed upon cellular activation or exposure to altered shear stress, may mediate hemostatic or inflammatory alterations. The aim of this study is to determine whether changes in blood MP levels are observed prior to the occurrence of adverse events in LVAD patients.

Methods: Blood samples collected from patients implanted with a HeartMate II LVAD (Thoratec) were centrifuged to platelet poor plasma, ultracentrifuged to pellet the MP, stained with a membrane dye and either CD41 (platelets), CD45 (WBC), CD146 (endothelium) or CD235 (RBC), then analyzed by flow cytometry. Six healthy individuals served to establish normal levels.

Results: From 21 patients studied, confirmed thrombosis or elevated LDH occurred 9 times in 7 patients (mean 155 ± 111 days post-implant; range 34–350 days). Months prior to thrombosis, elevated CD41+ (2–6 SD above normal), CD45+ (3–5 SD) and CD146+ (5–8 SD) MP were observed. CD41+ (3–6 SD), CD45+ (2–5 SD), CD146+ (1–8 SD) and CD235+ (2–5 SD) MP were increased 2 months prior to LDH elevation. Elevations >6 SD above normal in all MP were noted in one patient 3 days prior to hemolysis, but were not observed in a separate patient’s sample collected 43 days prior to hemolysis. All patients had MP within 1 SD of normal for the first 2 months following implant; patients without events remained within or near normal range. Quantitation of MP may be useful to identify thrombosis in patients with implanted LVADs in a timely manner allowing for early intervention and correction. Further evaluation of MP in a larger population is warranted.
Body Mass Index Does Not Affect Survival and Is a Reliable Independent Risk Factor of Ventricular Assist Device (VAD) Thrombosis

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Study: Obesity is a known cardiovascular risk factor. However, the literature provides conflicting data when correlating BMI to survival benefit in patients who received a VAD (Ventricular Assist Device). In this study, we sought to compare our institutional survival data with BMI and develop a risk score to predict adverse outcomes after VAD implantation.

Methods: We performed a retrospective analysis of 252 patients implanted with VADs from August 2008 to May 2014. Patients were divided in 4 BMI (kg/m²) groups: normal weight (18 - 24.9), overweight (25 - 29.9), obese (30 - 34.9) and morbidly obese (≥ 35). The primary endpoint was survival at 30 days and 1 year after VAD implant. Secondary endpoints were post-operative complications, including VAD thrombosis. We also performed a multivariable single entry logistic regression to identify whether BMI is an independent risk factor for VAD thrombosis.

Results: Pre-operative demographics and comorbidities were similar in all groups. The morbidly obese group was the youngest (53 yrs, p = 0.002) and had a higher incidence of type 2 diabetes (58%, p = 0.018). There were no statistical differences in post-operative outcomes, including drive line infection rates (p = 0.784) among all groups, except for a higher rate of VAD thrombosis in the morbidly obese group (26%, p = 0.007) (Table 1). Multivariable analysis showed that BMI and COPD were independent risk predictors of VAD thrombosis with an odds ratio of 1.109 (p = 0.001) and 3.42 (p = 0.011) respectively. Kaplan-Meier survival estimates at 30 day (p = 0.857) and 1 year (p = 0.164) after VAD implantation were similar among all groups (Fig 1). We concluded that BMI does not affect short and mid-term survival in patients implanted with a VAD. BMI does have an association with VAD thrombosis and initial multivariable analysis identifies it as an independent risk factor.

Table 1: Demographics and Outcomes. (IQR): Interquartile Range.

<table>
<thead>
<tr>
<th>Demographics &amp; Outcomes</th>
<th>Normal Weight (n=77)</th>
<th>Overweight (n=83)</th>
<th>Obese (n=55)</th>
<th>Morbidly Obese (n=38)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age, years (IQR)</td>
<td>62 (16)</td>
<td>58 (17)</td>
<td>57 (16)</td>
<td>53 (26)</td>
<td>0.0020</td>
</tr>
<tr>
<td>Ischemic Cardiomyopathy, (n%)</td>
<td>43 (57)</td>
<td>38 (48)</td>
<td>28 (55)</td>
<td>13 (34)</td>
<td>0.3030</td>
</tr>
<tr>
<td>Type 2 Diabetes, (n%)</td>
<td>25 (33)</td>
<td>31 (37)</td>
<td>29 (53)</td>
<td>22 (58)</td>
<td>0.0180</td>
</tr>
<tr>
<td>Chronic Lung Disease, (n%)</td>
<td>13 (17)</td>
<td>11 (13)</td>
<td>12 (22)</td>
<td>3 (8)</td>
<td>0.2900</td>
</tr>
<tr>
<td>Red Blood Cell Transfusion, units (IQR)</td>
<td>4 (10)</td>
<td>4 (11)</td>
<td>7 (15)</td>
<td>2 (13)</td>
<td>0.1170</td>
</tr>
<tr>
<td>Stroke, (n%)</td>
<td>8 (10)</td>
<td>9 (11)</td>
<td>7 (13)</td>
<td>5 (13)</td>
<td>0.9470</td>
</tr>
<tr>
<td>VAD Thrombosis, (n%)</td>
<td>6 (8)</td>
<td>5 (6)</td>
<td>7 (13)</td>
<td>10 (26)</td>
<td>0.0070</td>
</tr>
<tr>
<td>Surgical Exploration for Bleeding, (n%)</td>
<td>20 (26)</td>
<td>20 (24)</td>
<td>12 (23)</td>
<td>8 (21)</td>
<td>0.9270</td>
</tr>
<tr>
<td>Total Hospital Length of Stay, days (IQR)</td>
<td>24 (23)</td>
<td>20 (20)</td>
<td>23 (24)</td>
<td>19 (24)</td>
<td>0.3440</td>
</tr>
</tbody>
</table>
Psychosocial Evaluation in Patients Undergoing Left Ventricular Assist Device Implantation Using the Transplant Evaluation Risk Scale
G. Yost, K. Ibrahim, A. Karountzos, E. Mahoney, G. Bhat. Center for Heart Transplant and Assist Devices, Advocate Christ Medical Center, Oak Lawn, IL.

Study: It has been recommended that all candidates for left ventricular assist device (LVAD) implantation undergo preoperative psychological evaluation for risk assessment. The transplant evaluation rating scale (TERS) has not been investigated as an assessment for patients undergoing LVAD implantation.

Methods: This study retrospectively analyzed data of 125 advanced heart failure patients who were evaluated by the TERS before continuous-flow LVAD implantation. Postoperative follow-up included postoperative length of stay, number of out-of-hospital days, and adverse events. The cohort was stratified according to the TERS scores into low, moderate, and high risk groups. The outcomes were analyzed to evaluate whether the TERS score was associated with post LVAD adverse events.

Results: The TERS stratified the patients into 3 risk groups showing significant difference in all of the psychosocial domains, indicating the internal validity of this test (Total TERS Score: Low Risk: 27.9 ± 1.1, Moderate Risk: 33.0 ± 2.4, High Risk 42.5 ± 3.9, p<0.001). Low risk patients spent significantly more time out of the hospital after LVAD implantation than did moderate and high risk patients (p<0.001) (Table 1). This study indicates that the TERS was successful in stratifying the LVAD patients into 3 risk groups, with all psychological domains contributing consistently to the TERS risk groups. The TERS score is associated with time spent out of the hospital, an important component of postoperative quality of life.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Low Risk</th>
<th>Moderate Risk</th>
<th>High Risk</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-Op Length of Stay (days)</td>
<td>25.8 ± 18.61</td>
<td>32.52 ± 28.86</td>
<td>24.93 ± 12.54</td>
<td>0.484</td>
</tr>
<tr>
<td>Days out of Hospital</td>
<td>557.83 ± 275.77</td>
<td>129.18 ± 82.31</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>LVAD Exchange</td>
<td>2 ± 4.9%</td>
<td>2 ± 3.6%</td>
<td>3 ± 1.1%</td>
<td>0.394</td>
</tr>
<tr>
<td>Adverse Events per Patient</td>
<td>0.25 ± 0.72</td>
<td>0.16 ± 0.50</td>
<td>0.29 ± 0.76</td>
<td>0.908</td>
</tr>
<tr>
<td>VAD-Infection</td>
<td>0.32 ± 0.65</td>
<td>0.46 ± 1.08</td>
<td>0.29 ± 0.71</td>
<td>0.763</td>
</tr>
<tr>
<td>Gastrointestinal Bleed</td>
<td>0.05 ± 0.31</td>
<td>0.13 ± 0.60</td>
<td>0.14 ± 0.59</td>
<td>0.65</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>0.17 ± 0.54</td>
<td>0.36 ± 0.70</td>
<td>0.32 ± 0.72</td>
<td>0.281</td>
</tr>
</tbody>
</table>

Sodium Paradox: Serum Sodium as a Predictor of Survival in Patients with Mechanical Circulatory Support
G. Yost, B. Mohamedali, A. Tatooles, G. Bhat. Center for Heart Transplant and Assist Devices, Advocate Christ Medical Center, Oak Lawn, IL.

Study: Hyponatremia is a known marker for fluid status and cardiac dysfunction in patients with heart failure. Low sodium levels are associated with volume overload and are considered an indicator of poor prognosis. We investigated serum sodium levels in patients who received temporary mechanical circulatory support (MCS) with CentriMag.

Methods: This retrospective study enrolled 97 patients implanted with MCS between February 2006 -13. Admission sodium levels, relevant laboratory data, hemodynamics, type of MCS, and outcomes were collected. Patients were divided into Group A (Na+<135) and Group B (Na+≥135). Data were analyzed using non-parametric Mann-Whitney, Chi-square, and Kaplan-Meier survival analyses.

Results: Group A (n=32) had mean age 54.4 ± 15.7 years with mean admission sodium of 130.9 ± 3.2 mmol/l. Group B (n=65) had mean age 57.1 ± 15.8 years with mean admission sodium of 141.4 ± 5.9 mmol/l. Patients in group A with lower sodium survived significantly longer following surgical placement of the CentriMag system than those with higher sodium levels in group B (124.9 days (IQR=172.8) vs. 25.5 days (IQR=30), p=0.04) (Figure 1). The reduced survival in group B following intervention with temporary CentriMag support appears paradoxical. It has been demonstrated that, in a critical care setting, high sodium levels correlate with adverse outcomes. A similar association is possible in critically ill CentriMag patients and may be a result of impaired thirst mechanisms or lack of aggressive replacement of free water deficit.
Ventilation Time Predicts Length of Stay after Surgical Implantation of Left Ventricular Assist Device

G. Yost, B. Mohamedali, A. Tatooles, G. Bhat. Center for Heart Transplant and Assist Devices, Advocate Christ Medical Center, Oak Lawn, IL.

Study: Ventilation status is associated with adverse health outcomes and decreased probability of survival in hospitalized patients. Surgical implantation of left ventricular assist devices (LVADs) requires full sternotomy or left thoracotomy, cardiopulmonary bypass, and intraoperative sedation. Patients are transitioned to mechanical ventilation following surgery. We investigated the relationship between immediate post-operative ventilator support and clinical outcomes.

Methods: This retrospective study enrolled 103 patients who underwent LVAD implantation at our center between 2006–13. Patients were divided into two groups: those who were weaned from ventilator in fewer than 24 hours (group A), and those who remained on ventilator for greater than 24 hours post-operatively (group B). Risk factors, demographics, and clinical outcomes (survival and length of stay (LOS), were compared between the groups using chi-square, Mann-Whitney U, and Kaplan-Meier analyses.

Results: Within our cohort, 25 patients, with mean age 64.7 ± 10.3 years, were implanted with HW while 52 patients, with mean age 59.8 ± 13 years, were implanted with HMII. Comparisons of the two groups revealed significant differences in height and body surface area (BSA) at admission, and AST, ALT, and lactate dehydrogenase (LDH) at discharge. Differences in AST, ALT, and LDH were not significant at the time of admission or implantation (Table 1). The significantly lower averages for height and BSA at admission is an expected result and is likely driven by selection of smaller patients for implantation with HW. Significantly higher discharge AST, ALT, and LDH levels were noted in the HMII group compared to the HW group. Given similar baseline laboratory values at implantation, differences at discharge are assumed to accrue in the post-implant period. Since LDH is being used as a diagnostic marker for hemolysis suggesting thrombus, these baseline differences need to be accounted for in clinical management of axial and centrifugal LVADs.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>HVAD (n=25)</th>
<th>HeartMate II (n=52)</th>
<th>p-value</th>
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<tr>
<td>Height (cm)</td>
<td>170.8 ± 9.26</td>
<td>176.8 ± 10.37</td>
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<tr>
<td>BSA (m2)</td>
<td>1.95 ± 0.29</td>
<td>2.07 ± 0.29</td>
<td>0.042</td>
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<tr>
<td>Right Heart Failure</td>
<td>9 (36%)</td>
<td>25 (48%)</td>
<td>0.321</td>
</tr>
<tr>
<td>Implant AST (IU/L)</td>
<td>31.68 ± 17.18</td>
<td>36.06 ± 20.42</td>
<td>0.333</td>
</tr>
<tr>
<td>Discharge AST (IU/L)</td>
<td>26.72 ± 7.61</td>
<td>45.06 ± 33.26</td>
<td>0.001</td>
</tr>
<tr>
<td>Implant ALT (IU/L)</td>
<td>46.2 ± 36.35</td>
<td>51.29 ± 34.46</td>
<td>0.140</td>
</tr>
<tr>
<td>Discharge ALT (IU/L)</td>
<td>38.59 ± 13.76</td>
<td>56.09 ± 37.25</td>
<td>0.017</td>
</tr>
<tr>
<td>Implant LDH (IU/L)</td>
<td>285.8 ± 84.74</td>
<td>310.00 ± 94.95</td>
<td>0.249</td>
</tr>
<tr>
<td>Discharge LDH (IU/L)</td>
<td>285.27 ± 52.07</td>
<td>455.58 ± 272.07</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Differential Lactate Dehydrogenase Levels in HeartMate II and HeartWare Left Ventricular Assist Devices

G. Yost, B. Mohamedali, A. Tatooles, G. Bhat. Center for Heart Transplant and Assist Devices, Advocate Christ Medical Center, Oak Lawn, IL.

Study: As the treatment of advanced heart failure with left ventricular assist devices (LVADs) becomes more popular, differences in operation, physiological effects, and clinical outcomes resulting from pump design are continuing to be explored. Increasingly these differences are used to inform patient selection and post-operative care. We investigated demographic and laboratory values in groups of patients implanted with HeartMate II (HMII) and HeartWare HVAD (HW) LVADs.

Methods: This retrospective study enrolled 77 patients implanted with LVADs between 2010 and 2012. Patients were divided into HMII and HW groups. Demographic and laboratory data were collected for all patients at admission, day of implantation, and discharge. Student’s t and Mann-Whitney U tests were used to compare means between the HMII and HW groups.

Results: Within our cohort, 25 patients, with mean age 64.7 ± 10.3 years, were implanted with HW while 52 patients, with mean age 59.8 ± 13 years, were implanted with HMII. Comparisons of the two groups revealed significant differences in height and body surface area (BSA) at admission, and AST, ALT, and lactate dehydrogenase (LDH) at discharge. Differences in AST, ALT, and LDH were not significant at the time of admission or implantation (Table 1). The significantly lower averages for height and BSA at admission is an expected result and is likely driven by selection of smaller patients for implantation with HW. Significantly higher discharge AST, ALT, and LDH levels were noted in the HMII group compared to the HW group. Given similar baseline laboratory values at implantation, differences at discharge are assumed to accrue in the post-implant period. Since LDH is being used as a diagnostic marker for hemolysis suggesting thrombus, these baseline differences need to be accounted for in clinical management of axial and centrifugal LVADs.
Integration of Electronic Controllers into a Miniaturized Centrifugal Blood Pump with Total Magnetic Suspension

K. Chen, C. Chen, F. Lin, X. Ma, C. Yin, D. Liu, X. Tan, Y. Ma, P. Yang. CH Biomedical (USA) Inc, Torrance, CA; CH Biomedical Inc, Suzhou Industrial Park, CHINA; *Cardiac surgery, The fourth military medical university, Xi’an, CHINA; 4Soochow University, Suzhou, CHINA.

Study: Electronic controllers for driving and controlling electric motor and/or active magnetic bearings in a blood pump are conventionally placed in an extracorporeal control unit. CH Biomedical Inc accomplished a design that packs such electronics inside the pump body. This reduced the number of wires in the percutaneous cable into merely two pairs—one for delivery of electric power and the other for non-real-time communication with the extracorporeal unit. This study addressed feasibility of the design, especially concern of heat removal from the pump.

Methods: Design optimization resulted in a pump envelope of 2 inch in diameter and 1 inch in thickness. The percutaneous cable is 3.5 mm in diameter and very flexible without need of electric shielding. One animal experiment on sheep was conducted and terminated on the 54th day postoperatively due to break down of a wire junction at the feedthrough, which was corrected afterwards. The highest temperature from 7 sensors placed near the presumably hot spot inside the pump has less than 4°C rise over the body temperature during the experiment period. Necropsy revealed no evidence of thromboembolism in the major organs, and blood contact surfaces in the pump were found extremely clean. More bench tests and animal studies are slated.

Results: This preliminary study has demonstrated feasibility of our pump design, which is believed to be smaller and has fewer wires in percutaneous cable than the state of art fully magnetically suspended device in clinical trial. Significant reduction of the wires in the percutaneous cable will improve system reliability, infection prevention, and electromagnetic compatibility.

Preoperative Intravascular Volume Is a Predictive Factor for Early Mortality After Extracorporeal Pulsatile Ventricular Assist Device Implantation

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Study: In Japan, not a little patients still receive emergent pulsatile extra-corporeal left ventricular assist device (Nipro-VAD®) because implantable LVADs are available only for patients with stable hemodynamics targeting heart transplantation. To predict early mortality after VAD implantation is difficult because multiple factors are related in early term. The aim of this study is to investigate predictive factors for early mortality (within 90 days) after Nipro-VAD implantation.

Methods: We included patients who received Nipro-VAD implantation at the University of Tokyo Hospital between 2006–2014 performing hemodynamic study preoperatively, and excluded patients with biventricular mechanical support and children. Finally 43 patients are enrolled for the analysis. We included operation time, intraoperative bleeding and blood transfusion volume as perioperative factors in addition to various preoperative factors.

Results: Five patients died within 90 days after Nipro-VAD implantation. Among the deceased, 2 patients developed intestinal edema and one of them died sepsis from ischemic colitis. From a univariate analysis, the non-survivor group presented significantly higher preoperative mean right atrial pressure (mRAP), higher rate of continuous hemodiafiltration support, longer operation time, and more intraoperative bleeding and blood transfusion volume. There was no significant difference about right ventricular stroke work index. From a multivariate logistic analysis, both mRAP and operation time were revealed to be independent predictors (p<0.05, respectively). Mean RAP is also a significant factor about early mortality after Nipro-VAD implantation in addition to operation time.

To control preoperative intravascular volume strictly may be effective to prevent organ edema including intestine and early mortality after VAD implantation.
Mimicking Native Flow During Heart Surgery: A Novel Cannula Design

T. A. S. Kaufmann,1 R. Borchardt,2 P. Schlanstein,1 U. Steinseifer,1 S. Sonntag.1 1RWTH Aachen University, Aachen, GERMANY; 2enmodes GmbH, Aachen, GERMANY.

Study: Stroke remains a major complication with prevalence of 1–3% during cardiopulmonary bypass. This is further increased in patients with specific risk factors such as the elderly or patients suffering from atherosclerosis, diabetes, high blood pressure or impaired autoregulation. The current lifetime costs for stroke are estimated at 140,000 USD per patient. Furthermore, the number of stroke patients is expected to rise by 129% until 2030. Stroke is therefore a major burden to the society. In this study, we present a new arterial outflow cannula which was designed to mimic native flow and thereby decrease the risk for stroke in high risk patients.

Methods: The initial design was developed using validated computational fluid dynamics and initial blood testing. It was iteratively improved to optimize hemodynamics and hemocompatibility, and cardiac surgeons were consulted to assure easy handling. The final design features an inner wall to induce helical flow, which is transported to the aortic arch via a novel tip design. Thereby, cerebral perfusion is kept at native levels during surgery, jet velocity is decreased and forces acting on potentially sclerotic aortic walls are reduced. The tip design minimizes the incision site while granting washout of the proximal aortic root during surgery. The final design was tested in-silico and in-vitro.

Results: The cannula was manufactured using a standard body and two additional injection molded parts. At 5l/min bypass flow, it provides cerebral blood flow of approx. 715ml/min and jet velocities below 1.5m/s. The pressure drop over the cannula body is 10% lower compared to a standard elbow cannula. Qualitative ink testing also revealed increased jet widening of the novel design. The initial results prove the feasibility of the novel cannula design. This is currently investigated in ongoing blood and animal trials. The certification process will be launched in late 2015.

First Report of 90-Day Chronic In Vivo Support with Single-Piece Continuous-Flow Total Artificial Heart in Calves

J. H. Karimov, N. Moazami, M. Kobayashi, S. Sale, K. Such, N. Byram, G. Sunagawa, D. Horvath, S. Gao, B. Kuban, L. Golding, K. Fukamachi. The Cleveland Clinic, Cleveland, OH.

Study: The Cleveland Clinic continuous-flow total artificial heart (CFTAH) is a single-piece, valveless, pulsatile pump that provides self-regulated hemodynamic output to the left and right circulation. The study purpose was to evaluate chronic in vivo pump performance, pump-related physiologic and hemodynamic parameters, and biocompatibility of CFTAH.

Methods: The CFTAH was implanted in seventeen animals (Jersey calves, weight range 77.0 – 93.9 kg) through a median sternotomy (n=9) or a right thoracotomy (n=8). The native ventricles were removed, and the pump was connected through right and left inflow cuffs and outflow grafts. The pulmonary and systemic pump performance parameters were recorded.

Results: In vivo experiments demonstrated excellent hemodynamic performance (pump flow of 7.3 ± 0.7 l/min; left atrial pressure (LAP) of 16 ± 3 mm Hg; right atrial pressure (RAP) of 17 ± 3 mm Hg; RAP-LAP difference of 1 ± 2 mm Hg; mean arterial pressure of 103 ± 7 mm Hg; arterial pulse pressure of 30 ± 11 mm Hg; pulmonary arterial pressure of 34 ± 5 mm Hg). The CFTAH operated within design specifications and with no failure. The last 6 implants with improved pump design after implementing geometry change in the journal bearing showed no chronic hemolysis. The most recent three animals (C15, C16, C17) showed longest planned in vivo duration of 30, 90 and 90 days respectively. None of these cases used anticoagulation. Terminations in the earlier experiment series were caused by respiratory (n=1), bowel dysfunction (n=2), bleeding (n=2), other issues caused by intraoperative complications (n=3), hemolysis (n=2), and controller-related issue (n=1). All longest survival cases showed excellent biocompatibility with no organ thromboembolism.

Conclusion: The single-piece CFTAH pump has demonstrated biocompatibility without anticoagulation, and the self-regulation of hemodynamic output throughout 90 day chronic implantation in calves.
Hospital Readmissions after Continuous-Flow Left Ventricular Assist Device Implantation: An Analysis by Device Type

N. A. Haglund,1 M. E. Davis,2 S. K. Zalawadiya,1 M. Djunaidi,1 M. E. Keebler,1 Y. Song,1 M. R. Danter,1 S. Maltais,1 1Vanderbilt University, Nashville, TN; 2Cardiac Surgery, Vanderbilt University, Nashville, TN.

Study: Readmissions after continuous flow left ventricular assist device (CF-LVAD) for patients bridged to transplantation (BTT) remain poorly characterized. We compared readmission data between HeartMate-II and Heartware devices to determine device related differences.

Methods: We retrospectively assessed readmission data in 122 patients (HMII n=44, 36%; HVAD n=78, 64%) who underwent implant for BTT indications from April 2009 to September 2014. Overall and temporal readmission rates were collected beginning after discharge from index implant. Multivariable regression analysis using pre-specified variables was performed to assess the effects of device type as a predictor of readmission.

Results: Baseline characteristics (age 53 ± 12 years, 80% male, 50% ischemic) were comparable between groups (p>0.05). Overall 317 readmissions were observed during a mean follow-up time of 330 ± 307 days and 110 patient-years data. Cardiac readmission (heart failure or arrhythmia) occurred in 89 (28%) admissions and was comparable among device type (HMII 0.80 ± 1.17; HVAD 0.69 ± 1.36, p=0.28), whereas non-cardiac readmission (all other readmission types) occurred in 228 (72%) admissions and was more frequent among HMII recipients (HMII 2.8 ± 3.3; HVAD1.4 ± 1.7, p=0.001). Readmission rates and length of stay during readmissions based on device type and time interval are presented in Table 1. Multivariable analysis did not show significant differences in readmission rates between device types (RR 1.2, 95% CI 0.69 - 1.97; p=0.55) for each time interval. Analysis of participants with at least 6 months of follow-up (n=103; 179 readmissions) did not identify predictors of readmission (all p>0.05). Readmission rate and hospital length of stay were greatest during the first 6 months after implant and were comparable among device types at all-time points after implant. Predictors of readmission were not identified in this analysis and suggest a complex, multifactorial etiology.

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>HMII</th>
<th>HVAD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6 month</td>
<td>4.22(3.44, 5.17)</td>
<td>3.98(2.9, 5.47)</td>
<td>4.19(3.38, 5.7)</td>
<td>0.63</td>
</tr>
<tr>
<td>6-12 month</td>
<td>0.91(0.59, 1.36)</td>
<td>0.88(0.46, 1.58)</td>
<td>0.940(0.51, 1.63)</td>
<td>0.88</td>
</tr>
<tr>
<td>12+ month</td>
<td>0.690(0.44, 1.08)</td>
<td>0.940(0.56, 1.57)</td>
<td>0.350(0.14, 0.79)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Readmission average hospital length of stay (day/year/person)

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>HMII</th>
<th>HVAD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6 month</td>
<td>31.75(21.44, 41.93)</td>
<td>29.5(19.52, 42.47)</td>
<td>32.95(23.68, 46.98)</td>
<td>0.73</td>
</tr>
<tr>
<td>6-12 month</td>
<td>4.560(2.57, 8.4)</td>
<td>3.481(1.57, 8.13)</td>
<td>5.520(2.78, 11.71)</td>
<td>0.41</td>
</tr>
<tr>
<td>12+ month</td>
<td>2.22(1.45, 3.45)</td>
<td>2.25(1.29, 4.4)</td>
<td>2.19(1.16, 4.22)</td>
<td>0.95</td>
</tr>
</tbody>
</table>
Can We Predict a Complicated Intensive Care Unit stay after Left Ventricular Assist Device Implantation?

N. A. Haglund,1 C. E. Wagner,1 M. E. Davis,1 M. Djunaidi,1 M. Xu,1 S. Maltais.1 1Vanderbilt University, Nashville, TN; 2Cardiac Surgery, Vanderbilt University, Nashville, TN.

Study: Intensive care unit (ICU) length of stay (LOS) varies among patients implanted with a left ventricular assist device (LVAD). We sought to determine if perioperative variables after LVAD implant predicts a complicated ICU stay.

Methods: We retrospectively collected data on 127 patients (HeartMate-II 66, 52%; HeartWare 61, 48%) from January 2012 to October 2014. We defined a complicated ICU stay as a patient who met any or multiple of the following outcomes, ranked by severity of outcome (5=worst): reoperation for bleeding (1), ICU LOS > 14 days (2), mechanical ventilation > 7 days (3), renal replacement therapy (4) or index hospital death (5). Ordinal cumulative probability modeling was used to assess the association of covariates (right ventricular stroke work index (RVSWI), lactate, cardiopulmonary bypass (CPB) time, intra-operative blood product (BP) utilization, LVAD type and device speed) with outcome severity scores.

Results: Preoperative characteristics included mean age (53 ± 12), INTERMACS profile (3.0 ± 1.1), diabetes (42%) and BMI (29.4 ± 5.9). Thirty-four (27%) patients were characterized as having a complicated ICU stay. Median ICU stay was 7 (4, 11) days (range 2–57) and 11 (9%) died during index hospitalization. ICU and operative variables and ICU outcomes after implant are presented in Table 1. Multivariable analysis showed that only increased intra-operative BP utilization (range 1 -11 units) was associated with a complicated ICU stay (OR 2.28, 95% CI 1.33–3.88; p=0.003). Elevation in lactate obtained immediately upon arrival to ICU (range 2.5–6.85) near a statistical significance (OR 2.05, 95% CI 0.98–4.31; p=0.057). Device type and speed, RVSWI and CPB time were not associated with complicated ICU stay (all p>0.05). Complicated ICU stay after LVAD implantation is common. Increased intra-operative blood product utilization independently predicted a complicated stay. Future development of an ICU scoring model may predict post-LVAD ICU complications.

Risk Factors Associated with Delirium in Patients After Left Ventricular Assist Device Placement

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Study: Delirium is associated with increased ICU length of stay, cognitive impairment and mortality in critically ill patients. The prevalence and risk factors for delirium among patients implanted with a left ventricular assist device (LVAD) have not been defined.

Methods: We retrospectively collected data on 127 LVAD patients (HeartMate-II 66, 52%; HeartWare 61, 48%) from January 2012 to October 2014. All patients were assessed for delirium daily with the CAM-ICU by the bedside nurse. We used logistic and ordinal logistic regression to assess the association of either occurrence of delirium or duration of delirium with potential risk factors including-operative benzodiazepine dose, right ventricular stroke work index (RVSWI), INTERMACS score, cardiopulmonary bypass (CPB) time, and revolutions per minute (RPM) of LVAD on arrival in the ICU, all obtained from the medical record.

Results: Delirium occurred in 56 out of 127 patients (44%), with an average duration of 21 hours (1 to 203 hours). Logistic regression analysis (table 1), found that higher INTERMACS score (4 vs. 2.6) lowered the odds of developing delirium by 48% and increased CPB time (107 vs. 57 minutes) increased the odds of developing delirium by 78%. RVSWI, benzodiazepine dose and RPM of LVAD pump had no statistically significant association with delirium. Ordinal regression analysis revealed similar associations with higher INTERMACS score (p=0.018) and shorter CPB time (p=0.012) associated with decreased odds of a greater duration of delirium. Delirium in patients post LVAD is common. Longer CPB time and lower INTERMACS score were associated with increased odds of developing delirium. Interestingly, dose of benzodiazepines intra-operatively had no association with postoperative delirium or duration. Further evaluation of our data needs to assess these risk factors of delirium with increased length of stay and mortality.
Does Indication of Continuous Flow Left Ventricular Assist Device Implantation Influence Hospital Readmission Rate?
S. K. Zalawadiya,1 M. E. Davis,2 M. Djunaidi,1 M. E. Keebler,1 Y. Song,2 S. Maltais,2 N. A. Haglund.1
1 Vanderbilt University, Nashville, TN; 2Cardiac Surgery, Vanderbilt University, Nashville, TN.

Study: Readmissions after continuous flow left ventricular assist device (CF-LVAD) are frequent but remain poorly understood. We sought to assess whether indication (bridge to transplant (BTT) vs destination therapy (DT)) for CF-LVAD implantation influences hospital readmission rates.

Methods: We retrospectively assessed readmission data in 85 consecutive patients who underwent HeartMate-II (HMII) implantation for BTT (n=42) and DT (n=43) indications from April 2009 to September 2014. Overall and temporal readmission rates beginning after discharge from index CF-LVAD implant were determined. Multivariable regression analysis using pre-specified variables was performed to assess the effects of indication type as a predictor of readmission.

Results: Baseline characteristics (age 52 ± 12 years, 85% male, 53% ischemic) were comparable between groups (all p>0.05). Overall, 246 readmissions were observed during a mean follow-up time of 404 ± 386 days and 94 patient-years data. Readmission rates per patient year based on device indication and time interval after CF-LVAD implant are presented in Table 1. Multivariable analysis did not show significant differences in readmission rates between BTT and DT indications (risk ratio (RR) of 1.1, 95% confidence interval (CI): 0.69 - 1.75, p=0.67) for each time interval. Interestingly, subgroup analysis of participants with at least 6 months of follow-up (n=63) showed that only increased perioperative blood product utilization during device implantation (Hazard ratio (HR): 1.3, 95% CI: 1.06 - 1.58, p=0.007) was independently associated with future readmission. Readmissions are common for each device indication. HMII CF-LVAD readmission rates were comparable between BTT and DT indications at all-time points after implant, and occurred most frequently during the first 6 months after implant for both groups. Increased blood product utilization during index implant may be a marker of subsequent readmission risk.

Preoperative Creatinine is the Strongest Predictor of Early Renal Dysfunction after Continuous-Flow LVAD Implantation
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1Vanderbilt University, Nashville, TN; 2Cardiac Surgery, Vanderbilt University, Nashville, TN.

Study: Predictors of early post-operative renal failure (RF) in patients who receive continuous-flow left ventricular assist devices (CF-LVADs) are unclear.

Methods: From 2009–2014, we retrospectively assessed 126 patients who underwent bridge to transplant CF-LVAD implantation (HeartMate-II 45, 36%; HeartWare 81, 64%). Preoperative and 4 week (4w) creatinine (Cr) levels were evaluated. RF was defined as Cr>2.0 mg/dL or the need for renal replacement therapy (RRT). Cr was treated as an ordinal variable and patients receiving RRT were scored as having a Cr greater than the largest observed value for non-RRT patients. Multivariable proportional odds logistic regression was used to assess the effects of preoperative and intraoperative variables on 4w postoperative renal function.

Results: Median age at implantation was 56 years, 79% were male, mean INTERMACS category=3.0, median preoperative Cr 1.22 mg/dL, mean Kormos score=0.50, redo sternotomy 31%, median intraoperative blood product utilization (IBP) 2.0 units, and median CPB 66 minutes. At 4w, median Cr was 1.18 mg/dl (quartiles 0.96, 1.48) with an average increase of 0.03 (-0.21, 0.18) mg/dl. 17 patients (14%) had Cr>2.0 or RRT (9 Cr>2.0 mg/dl; 8 RRT). Multivariable analysis revealed increased preoperative Cr, low albumin, increased CBP duration and increased IBP independently predicted RF 4w after CF-LVAD implantation (all p<0.001). Preoperative Cr explained the largest variation of renal function 4w after implant (Figure 1). Age, INTERMACS score, Kormos score, and redo sternotomy were not predictive of RF after CF-LVAD implantation (all p>0.05). The development of early renal failure after CF-LVAD implantation is common and likely multifactorial. Preoperative renal function explains the largest variation of 4w renal function. Optimizing preoperative renal function prior to CF-LVAD implantation may be useful in minimizing post-operative need for RRT and improving patient outcomes.

Figure 1. Preoperative renal function explains the largest portion of variation of 4w renal function, followed by CBP time, IBP utilization and albumin.
Efficacy of a Bivalirudin-based Treatment Regimen for Suspected LVAD Thrombosis Compared to Epifibatide

D. B. Goffman, M. Bradbury, K. Poppiti, R. Connolly, S. S. Desai, N. A. Burton, P. Shah. Pharmacy, Inova Fairfax Hospital, Falls Church, VA.

Study: Device thrombosis subjects patients to the risk of stroke, pump exchange and increases mortality in LVAD patients. Various treatment strategies exist but there is little data to support drug selection. Bivalirudin binds to thrombin within a clot which may be advantageous over other agents that prevent thrombus propagation. Our goal was to compare the efficacy of a bivalirudin-based regimen (BVL) to epifibatide (EPT) for treatment of LVAD thrombosis.

Methods: Using our institutional LVAD registry, we identified patients treated for hemolysis from 5/2010 to 9/2014. Outcomes were compared after treatment with BVL or EPT. The primary outcome was 180 day freedom from recurrent hemolysis, pump exchange, urgent transplant, stroke, or death. Normalization of lactate dehydrogenase (LDH) values and event rates at 30-days were also evaluated.

Results: During the study period, 137 patients received a LVAD and 22 patients (16%) had 34 hemolysis events. Eight events were not treated with BVL or EPT and were excluded. Six patients in the BVL group also received EPT. Baseline characteristics were similar between groups. At onset of hemolysis, median LDH was 1029 IU/L (IQR: 1019–1470 IU/L), with no difference between groups. Following treatment, 50% in BVL and 69% in EPT group were free of events at 30 days (p=0.43). At 180 days, freedom from events was 50% in both groups (Figure 1). Despite the theoretical benefits of a BVL regimen for treatment of device thrombosis, we found no difference in clinical outcomes. Medical treatment was associated with a 50% survival free of stroke, recurrent hemolysis, pump exchange or death at 180 days. BVL with or without EPT did not seem to modify clinical outcomes compared to EPT alone.

In Vivo Evaluation of Newly Developed Hemocompatible Surface-coating Material for ECMO Device

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Study: ECMO is potent therapeutic option in treating patients with circulatory and respiratory failure. However, ECMO is limited in its use for long-term application. Improving the hemocompatibility of blood contacting material used for ECMO procedures may ameliorate various post-purification syndromes characterized by multi organ dysfunction and cytokine storm. We developed new hemocompatible and low-immunoresponsive coating (MDM polymer) for the medical device with direct contacting to blood circulation. Our newly developed coating was synthesized to amphiphilic block copolymer composed of hydrophobic poly(2-methoxyethyl acrylate) and hydrophilic poly(N,N-dimethylacrylamide) segments. In this study, hemocompatible performance of newly developed MDM polymer was evaluated by large animal model installed venoarterial ECMO device.

Methods: Two healthy goats (BW: 59, 63 kg) were subjected to experimental venoarterial ECMO for up to 24 hours under general anesthesia. These whole ECMO circuits were coated by MDM polymer. In the experiments, systemic anticoagulation was not conducted, except first heparin injection at cannulation (100 IU/kg). ACT recovered to normal range (98–130 s) 3 hours later, and maintained to 24 hours later in post operation term. Bypass flow was set at 3 L/min.

Results: In the result, ECMO could run for 24 hours without major adverse event. In both cases, O2, CO2 transfer rates and pressure drops in the oxygenator were kept at sufficient levels, and there were no significant changes in blood chemistry and serum free hemoglobin levels. However, platelets slightly decreased immediately after pump on (6 to 3 x10^5/dL). After experiments, a small amount of thrombi was found on the bundle of hollow fiber membranes in each oxygenator. No gross finding was observed in major organs at the autopsy. Our ECMO devise coated by MDM polymer demonstrated sufficient performance of thrombo-resistance and hemocompatibility in the condition of normal ACT under in vivo evaluation.
ASAIO Cardiac Abstracts

Feasibility Of Daily Smartphone Assessments Of Quality Of Life And Functional Capacity In Left Ventricular Assist Device Patients

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Study: While previous studies have evaluated overall health related quality of life (HRQOL) in patients (pts) supported with left ventricular assist devices (VAD), surprisingly little is known about their “day-to-day” physical, mental, and social health. We sought to obtain daily HRQOL assessments via a novel smartphone computer adaptive testing (CAT) app measuring HRQOL from the Pt Reported-Outcomes Measurement Information System (PROMIS®).

Methods: Adult pts at least 3 months post-VAD implant were enrolled in this prospective study for 90 days. CATs were administered across 12 domains of physical, mental, and social health. Standardized T-scores were measured (a score of 50 represents the mean). We measured activity via a wireless Fitbit® device including maximum step count recorded during any six minute interval throughout a day (6MSC). Baseline six minute walk distance (6MWD) was also collected.

Results: We enrolled 25 pts of median age 55 yrs (range 21 - 84). CAT app engagement was excellent, with an average of 1.2 HRQOL assessments per day and a mean T-score of 48 ± 9.6. Fitbit data were captured on 74% of pt days with a median of 2864 (IQR 2765) steps per day and a median 6MSC of 288 (IQR 371) steps. Baseline mean 6MWD was 330 ± 73m, which correlated with average Fitbit 6MWS (r= 0.92, p<0.001) and daily steps (r = 0.87, p<0.001). HRQOL including physical function, dyspnea, sleep, and social domains were linearly related to average daily steps (p<0.01). This pilot study supports the feasibility of using a mobile CAT-based survey app and activity tracker to monitor HRQOL in VAD pts on a daily basis. This study also provides valuable, preliminary insights into the day-to-day physical, mental, and social health of VAD pts, including the variability in HRQOL that exists among individual VAD pts. Further research leveraging these technologies to monitor HRQOL is needed in order to guide clinicians in maximizing HRQOL in individual VAD pts.

Pathophysiology of the Long-term Survived Goats with the Helical Flow Total Artificial Heart and Physiological Control

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Study: To realize a total artificial heart (TAH) with high performance, high durability, good anatomical fitting, and good blood compatibility, we have been developing the helical flow TAH (HFTAH) with two helical flow pumps having hydrodynamic levitation impeller.

Methods: The HFTAH was implanted in 13 adult female goats weighting from 45.0 to 64.0 kg. The HFTAH was driven with a quasi-pulsatile mode. As physiological control, 1/R control or ΔP control that is a new physiological control method using simplified equation of the 1/R control was applied.

Results: Two goats survived for 100 and 68 days. In the 100-days survived goat, 1/R control was applied and stable control could be possible until hemolysis occurred on postoperative day (POD) 88. After then, pump outputs and right atrial pressure increased gradually. The hemolysis continued until termination. In the 68-days survived goat, ΔP control was applied and stable control could be possible until termination. In this goat, hemolysis also occurred on POD 44 and continued until termination. In spite of the hemolysis, control condition kept stable and right atrial pressure was within normal range. In both goats, general condition was very good, liver and kidney functions were kept almost normal, and total protein recovered two weeks after surgery. In both goats, experiments were terminated with bearing trouble to which hemolysis was considered to be relevant. Thrombus formation was found in the pump of the 100-days survived goat at the broken right bearing. No thrombus was found in the pump of the 68-days survived goat. Despite that the stability of the hydrodynamic bearing should be improved, promising prospect of the HFTAH with physiological control could be demonstrated.
Renal Function Recovery with Total Artificial Heart Support
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Study: End-stage heart failure patients requiring total artificial heart (TAH) support often have concomitant renal insufficiency (RI). TAH should promote renal recovery (RR) in these patients by improving end-organ perfusion; however, this has not been quantified before. We sought to quantify RR in patients supported with TAH at our institution.

Methods: RR data at 30, 90 and 180 days after TAH implantation were analyzed for patients with RI at the time of surgery. Significant RI was defined as either the use of hemodialysis (HD) or a glomerular filtration rate (GFR) less than 60ml/min/1.73m². GFR measurements excluded those patients on HD.

Results: Between Jan 2008 and Dec 2013, 20 of the 46 (43.5%) TAH recipients (age 51 ± 9yrs, 85% men) had RI at the time of surgery. All procedures were urgent (85%) or emergent (15%). Temporary circulatory support was required in 15% of patients and inotropic support in 90%. Postoperative 30-day mortality was 5%. The mean pre-operative creatinine and GFR were 2.2 ± 1mg/dl and 48 ± 7 ml/min/1.73m², respectively. Renal function recovery was noted at each follow-up interval: increment in mean GFR at 30, 90 and 180 days was 21 ± 35 (p = 0.1), 16.5 ± 18 (p = 0.05) and 10 ± 9 (p = 0.1) respectively. Six of the 20 (30%) patients required pre-operative dialysis. Of these, 4 recovered renal function (3 by day 30, 1 by day 180), 1 remained on HD and 1 died prior to 30-day follow-up. Five of the 20 (25%) patients’ RI progressed after TAH implantation requiring HD. Of these, 2 recovered renal function and were off HD by 90 days. The remaining 3 patients died during the study period while on HD. Overall 75% (15/20) of patients’ RI improved after TAH implantation, including 66% (4/6) of patients who were on dialysis at the time of surgery.

Conclusion: TAH support improved renal function in 75% of patients with preexisting significant renal insufficiency, including those who required dialysis prior to surgery. Worsening RI after TAH implantation, requiring new onset dialysis carries poor prognosis.
Effects of Apical Torsion Angle on Global Hemodynamics during Heart Failure


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Study: To investigate the effects of applied apical torsion as an alternative left ventricular-assist device (LVAD) for heart failure (HF) therapy that avoids blood-contacting surfaces. In this study, we analyzed how the angle of applied rotation affects cardiac function in terms of global hemodynamics, i.e., ejection fraction (EF) and stroke work (SW).

Methods: An 18-element, high-order computational model of a beating left ventricle (LV) attached to a closed-loop circulatory model was created in ContinuityPRO (Insilicomed, Inc.). The model was based on clinical measurements from one patient with severe HF. The apical region was rotated counterclockwise (viewpoint: apex towards base) during early systole, and rotated back during the remainder of systole and diastole. We investigated the effects of varying the degree of rotation on global hemodynamics. First, the HF simulation was performed to obtain baseline values of EF and SW (No LVAD). Three additional simulations were performed in which the angles of maximum systolic rotation were 60, 75 and 90 degrees. Then, changes in EF and SW from baseline were collated. Steady-state, fully-converged solutions were obtained as each simulation ran for 4 cardiac cycles with concurrent contraction of the heart.

Results: Applied apical torsion resulted in substantial increases in EF and SW when compared to the No LVAD model. As the angle of rotation was increased in the range studied, EF and SW also increased (Table 1). This is also indicated by a greater leftward shift in isovolumic relaxation volumes than any changes in isovolumic contraction volumes with increasing rotation angle (Figure 1). These results indicate that applied apical torsion at appropriate rotation angles may be an effective means of improving cardiac function in heart failure.

<table>
<thead>
<tr>
<th>Rotation Angle</th>
<th>EF (%)</th>
<th>SW (mmHg*mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No LVAD</td>
<td>14.8</td>
<td>3870</td>
</tr>
<tr>
<td>60° Rotation</td>
<td>15.6</td>
<td>5658</td>
</tr>
<tr>
<td>75° Rotation</td>
<td>18.1</td>
<td>6602</td>
</tr>
<tr>
<td>90° Rotation</td>
<td>22.3</td>
<td>7363</td>
</tr>
</tbody>
</table>

Table 1: Ejection fraction and stroke work of LV simulations
Impact of Continuous-flow Left Ventricular Assist Device Support on Right Ventricular Geometry and Function

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Study: We evaluated the incidence of right ventricle (RV) failure and long-term effects on RV geometry and function, severity of tricuspid regurgitation (TR), and cardiac hemodynamics after continuous-flow left ventricular assist device (CF-LVAD) implantation.

Methods: Fifty-four patients with chronic heart failure (46 men; mean age 56.8 ± 9.9 years, range: 31–76 years) who underwent implantation of a CF-LVAD (40 HeartMate II, 10 HeartWare, 3 Jarvik 2000 and 1 Berlin Heart InCor devices) as a bridge to transplant (n=39) or as destination therapy (n=15), between January 2002 and July 2014 at our institutions, were investigated. Echocardiography and right heart catheterization data collected from all patients before CF-LVAD implantation were tested for relationship with postoperative RV function (before and after 3 to 6 months of CF-LVAD support).

Results: Overall, RV failure requiring temporary right-sided mechanical circulatory support (RVAD) after CF-LVAD implantation occurred in 16 patients (29.6%). Significant improvements occurred by time in cardiac index after CF-LVAD support with reductions in right atrial pressure, RV stroke work index (RVSWI), tricuspid annular plane systolic excursion (TAPSE), tricuspid annulus peak systolic wall motion velocity (TAPSm), mean pulmonary artery pressure, pulmonary vascular resistance, right-to-left ventricular diameter ratio (R/L ratio) and RV end-diastolic short-/long-axis ratio. There was also a trend towards reduction in TR after CF-LVAD support (p=0.002).

Conclusions: The favorable effects of the CF-LVAD on cardiac hemodynamics result in improved RV function and geometry, improved right- and left-sided hemodynamic profiles, and a reduction in TR severity, suggesting a lusitropic effect on the RV. These findings may have important implications for CF-LVAD patients with moderate degrees of RV dysfunction needing longer-term support.

Extracorporeal Cardiopulmonary Resuscitation: Development of a Prolonged Cardiac Arrest Animal Model

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Study: Sudden cardiac arrest (CA) is responsible for 20% of US deaths; extracorporeal cardiopulmonary resuscitation (ECPR) is an emerging strategy when conventional resuscitative efforts fail. We sought to develop a swine model of prolonged CA to study ECPR strategies that may improve cardiac and neurological recovery.

Methods: Institutional guidelines for animal research were followed. Anesthetized pigs were instrumented for hemodynamic monitoring. CA was induced with electrical induction of ventricular fibrillation. After 30 minutes of untreated CA, hypothermic (32°C) arteriovenous ECPR support was initiated. Return of cardiac function, defined as supraventricular ECG rhythm and cardiac contraction on echocardiogram, was monitored. Defibrillation was performed after 30 minutes of ECPR, if required.

Results: Three experiments have been completed. ECPR provided 50–80 mL/kg of flow, and vasopressors were required initially to keep mean arterial pressures greater than 70 mmHg. Defibrillation was required on all animals. Two animals had return of cardiac function at 1 hour and showed improved contractility as the experiment continued. These 2 animals remained on support for 12 hours, had down-trending serum lactate, and no evidence of end-organ failure. The animal without return of cardiac function developed hemodynamic collapse at 8 hours despite ECPR.

Conclusions: We have created a swine model to simulate prolonged CA followed by ECPR. ECPR resulted in return of cardiac function in 2 out of 3 experiments, which was sustained for 12 hours. Cardiac contractility appeared to increase while on ECPR, suggesting recovery of cardiac function when properly supported in our model.
Computational Optimization of LVAD Outflow Graft Configuration

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Study: To investigate hemodynamic impact of VAD outflow graft configuration on the ascending aorta and aortic valve. The flow induced by the combination of VAD output through the graft anastomosed to the aorta and the limited cardiac output through intermittent opening of the aortic valve is studied to determine the nature of thrombogenic patterns

Methods: In this report we review our use of the Impella 5.0 placed via an axillary cutdown for support of a heterogeneous group of patients with the underlying diagnosis of cardiogenic shock treated from 6/2013 to 6/2014

Results: The 12 patients are comprised of 7 dilated cardiomyopathy patients and 5 ischemic. There was one death in each group. The overall survival to hospital discharge was 84%. Almost all patients exhibited an improvement in LV function and PA pressures post implantation as well as improvement in end organ function and decrease need for pressors and inotropes. The use of the Impella 5.0 allows for decrease in LVEDP and wall stress which is not attainable with IABP or peripheral ECMO (unless direct LV venting is performed. This unloading of the LV limits infarct size and stops ongoing ischemia allowing LV recovery. This can also be accomplished with central ECMO or BIVADS but usually requires a sternotomy and the difficulties attendant to chest closure and ongoing hemorrhage with the need for post op anticoagulation. The ability to generate 5 liters of flow through an axillary cutdown allows patients to be extubated and mobilized permitting longer term support to recovery or safer durable LVAD placement. It also avoids the myriad complications of urgent or emergent sternotomy and, as is often the case, redo sternotomy in this high risk patient population. We believe that early intervention to decompress the LV, along with revascularization where appropriate, significantly improves survival in the cardiogenic shock patient.
Influence of LVAD Inflow Cannula Placement Location on the Flow Stresses and Residence Time in the Left Ventricle

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Study: Though definitive treatment for end-stage heart failure is cardiac transplantation, lack of organ donors limits availability to ~2500 per year. Ventricular assist devices (VAD) are proven as an effective interceding strategy. Advances in VAD technology have resulted in greatly increased clinical use. Two potential locations are feasible for surgical implantation of the inflow cannula into the left ventricle: the apical or diaphragmatic surface. No study has yet provided a scientific basis for optimal VAD inflow cannula configuration, leaving placement to surgeon preference. High spatial and temporal inhomogeneity, induced by the VAD inside the left ventricle, create unfavorable hemodynamics that can increase risk of thrombus formation, via high residence times, low wall shear stress and high shear stress gradients. We compare ventricular flow in apical VAD implantation versus diaphragmatic cannulation, to provide evidence of physical differences related to clinical outcomes.

Methods: Cardiac CT images of an end-stage heart failure patient were obtained prior to VAD implantation. 3D models of the left ventricle were developed and both apical and diaphragmatic configurations of VAD inflow cannula were virtually added. Computational Fluid Dynamics simulated ventricular flow in both configurations. Precursors of thrombosis were evaluated.

Results: We quantify prothrombotic flow variables, as well as metrics of the energetic efficiency of the VAD, such as turbulent kinetic energy and dissipation. Left ventricle pressure distribution is analyzed to correlate flow features with the relative position of ventricular walls and inflow cannula. We show that surgical configuration of VAD implantation determines hemodynamic features, such as residence times, shear stress and vorticity, via cannula/wall distance and suction. Implantation method contributes significantly to thrombus formation and supports evidence-based optimization.

Design Approach and Pre-Clinical Evaluation of the HeartMate III LVAS for Hemocompatibility


Study: The HeartMate III™ Left Ventricular Assist System (HM III) is an investigational platform designed to advance long-term mechanical circulatory support for a broad range of advanced stage heart failure patients. Its basis is a centrifugal pump with a magnetically levitated rotor that produces an artificial pulse, designed for enhanced hemocompatibility via optimized blood-contacting surfaces, fluid dynamics, and low shear stresses. Pre-clinical analyses and tests were conducted to evaluate the large gaps around the rotor to assess potential clinical advantages and establish safety for initiating clinical trials.

Conclusion: HM III has demonstrated promising hemocompatibility, to be confirmed in clinical trials. Magnetic levitation enables relatively large gaps around the rotor, with sufficient washing and low shear stresses.

Methods: A steady-state Computational Fluid Dynamics (CFD) model was created to analyze blood flow to guide design towards sufficient washing in recirculation paths and low shear stresses. Plasma-free hemoglobin (pfHb) and Modified Index of Hemolysis (MIH) in 6 HM III pumps running in artificial pulse mode was compared to that in predicate devices running at a constant speed to assess hemolytic potential per ASTM F1841-97. The test was repeated at 2, 5, and 10 L/min to encompass the clinical operating range.

Results: CFD results showed 232 to 720 mL/min flow above the rotor and 40 to 100 mL/min below the rotor across the operating range. The maximum wall shear stress was 250 Pa at 8300 rpm, 10 L/min. At 2, 5, and 10 L/min, average pfHb 6 hours after test initiation was 86, 94, and 161 mg/dL (n=6) for HM III, and 116, 134, and 352 mg/dL (n=6) for the predicate device. The ratios of average MIH values for HM III and the predicate device at 2, 5, and 10 L/min were 0.65, 0.63, and 0.33.
Cavo-arterial pump (CAP): A Catheter-deliverable Right Ventricular Assist Device for Right Ventricular Dysfunction
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Study: Mechanical circulatory support (MCS) options for patients with right heart dysfunction are limited. Clinical experience suggests that, in most cases, partial circulatory support is sufficient to achieve optimal hemodynamics for this population. The development of a percutaneously deployable pump positioned in the venous circulation that provides partial MCS for the right ventricle (RV) is presented.

Methods: We designed a catheter-deliverable cavo-arterial pump that unloads the RV by routing inferior vena cava (IVC) flow directly to the main pulmonary artery (Fig 1A). Design considerations include providing a 2-pole axial magnetic coupling to drive an 8 mm diameter impeller, ensuring flow for partial RV support, and designing a method to anchor the device in the IVC. A finite element magnetostatic model (COMSOL Multiphysics) was used to predict the torque transmission from the motor magnetic coupling to the impeller. A computational fluid dynamic model (ANSYS FLUENT) was used to predict the pump performance curves. A prototype was printed on an Objet30 Pro 3D printer to show IVC mounting feasibility. Mounting struts were formed from 0.5 mm self-deploying nitinol frame (Fig 1B).

Results: The magnetic coupling provides excellent torque transmission during rotation. When separated by a 2.5 mm gap, the coupling magnets provide up to 6mNm of torque (the motor outputs a maximum of 3 mNm). In addition, CFD simulations show that the pump can provide 1.4–3 L/min of flow at venous pressures (0–30 mmHg) when the impeller is spun between 10 kRPM and 22 kRPM (Fig 1C, D). Lastly, the prototype developed is 10 mm in diameter and 65 mm in length with nitinol frame placed concentric to the pump housing and an 18 Fr cannula attached to the outlet.

Conclusion: We have demonstrated that a percutaneously deployable, partial support platform can be implanted with minimal invasive procedures and can potentially support the right ventricle in various clinical scenarios.

User Studies and the Design of a Completely Implantable VAD System
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Study: Totally implantable systems can eliminate the percutaneous cable and infection risk associated with currently available continuous flow ventricular assist devices (VAD). Such a system must be designed for ease of implantation and minimal tissue damage due to heat or material interactions.

Methods: User studies were completed to determine the features and layout of components. Eight physicians and three VAD coordinators were interviewed providing feedback on the need for small thin components with connectors to support replacement. Thus, the transcutaneous energy transmission system (TET) coils were designed for subcutaneous placement below the clavicle and the controller was designed for placement in the abdomen. Inline connectors were designed for the cables to ease tunneling. Materials were chosen to minimize tissue reactions and the electronics were designed to minimize heat generation.

Results: The LVAD pump cable, TETS cable, and connectors are only 6mm (18F) and 12 mm (36F) in diameter and use reliable IS-1/DF-4 style connectors which are also embedded in the controller’s poured epoxy header. The silicone molded implant coil is 0.74 cm thick with a diameter of 5.5 cm supporting implant depth of up to 1 cm. The flexible external coil is designed with an inner and outer diameter of 5.8 cm and 9.5 cm to avoid overlap and reduce skin compression. The implant controller, with backup battery for untethered operation, is 245 cc in volume, with plans for further size reduction. In-vitro testing demonstrated power transfer up to 20 W and pump support of up to 10 L/min with the Heartmate II VAD and coil to coil spacing of 3 cm. Component heat flux is limited to proven safe levels of 40 mW/cm2 on the controller and 15 mW/cm2 on the TETS coil. A completely implantable system was designed for continuous flow VADs. Component sizes are comparable to conventional and historical pacemakers. The system uses proven technologies to ease implantation and minimize adverse tissue effects.
Polyethylene Barrier Layers to Reduce Water Transmission Through Dynamically Loaded Membranes in a Total Artificial Heart

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Study: Water transmission through polymer membranes is a problem in medical devices, especially if the membrane separates blood from electrical components as it is done in total artificial hearts (TAH). Applying common barrier coatings to a TAH membrane is disadvantages, since it affects hemocompatibility and durability. Therefore, a sandwich construction was chosen as typical used in the food industry as fluid barriers.

Methods: The original membrane of the ReinHeart TAH is made of three 0.2 mm polyurethane layers (PU). It has been replaced by a sandwich construction in which the intermediate layer was changed to polyethylene (PE) layer. So the hemocompatibility of the membrane could be preserved. PE layers of different thicknesses and different degrees of cross-linking density were used to compare the water barrier properties and the mechanical behavior under dynamic conditions. Further modified membranes have been tested in an accelerated dynamic durability tester. The membranes have been loaded under physiological pressure conditions with a frequency of 8 Hz over 28 million pumping cycles. Water transmission has been determined by long term tests. The results were evaluated against the untreated membranes and those with barrier coatings.

Results: Water transmission was reduced by up to 75 % compared to original membranes and by up to 35 % compared to coated membranes respectively. Further the results suggest, that sandwich designed membranes are more robust with respect to the coated ones.

Control of Mitral Regurgitation by a Continuous-flow Left Ventricular Assist Device With a Native Heart Load Control System.

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Study: We have previously developed a Native Heart Load Control System (NHLCS) for a continuous-flow left ventricular assist device (LVAD) and demonstrated that rotational speed modulation in synchronization with the cardiac cycle can alter left ventricular (LV) load. On the other hand, excessive volume underloading of the LV can affect the right ventricular (RV) function by causing shift of a ventricular septum during LVAD support in patients with mitral regurgitation (MR). Optimal settings of LVAD that control MR without RV dysfunction are required. We assessed NHLCS in a goat model of MR.

Methods: We installed implantable centrifugal continuous-flow LVADs (EVAHEART) via left thoracotomy in two goats with an average weight of 69.5 kg. After implantation of the device, MR (mild, moderate and severe) was induced with a temporary inferior vena cava filter that was placed in the mitral valve. The severity of MR was defined by left ventriculography and echocardiography. We evaluated total flow (TF: the sum of aortic flow and pump flow), pulmonary artery pressure (PAP), left atrial pressure (LAP), LV end-diastolic pressure (LVEDP) and LV end-diastolic volume (LVEDV) in each severity of MR with bypass rates (pump flow divided by TF) of 100%, 75% and 50% under four conditions: circuit clamp, continuous mode, co-pulse mode and counter-pulse mode.

Results: Counter-pulse mode provided higher TF and lower PAP, LAP, LVEDP and LVEDV in every severity of MR with every bypass rate compared to the other driving modes. Average TFs with 100% bypass rate in severe MR were 2.76, 3.33, 3.13 and 3.42 L/min, under circuit clamp, continuous mode, co-pulse mode and counter-pulse mode, respectively. Average LAPs were 12.37, 7.97, 8.27 and 7.56 mmHg, and average LVEDPs were12.71, 5.51, 7.83 and 5.05 mmHg, respectively.

Conclusions: Considering higher TF and lower PAP, LAP, LVEDP and LVEDV in counter-pulse mode, the mode may achieve a favorable control of MR without causing RV dysfunction.
Development of an Anti-Interference Control System for a Miniaturized Maglev Blood Pump

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Study: We are developing a miniaturized magnetically levitated (maglev) rotary blood pump. The Maglev pump enhances the blood compatibility compared to the pumps with contact bearings and its compact size allows less invasive implantation. However, magnetic interferences generated by actuator coils on the nearby eddy current position sensor coils usually harms stability of maglev system. This work presents development of a control system with anti-interference methods for the miniaturized maglev pump.

Methods: A maglev control system was initially built with commercially available self-exciting eddy current position sensors. Transfer function from actuator to sensor coils was measured to identify unwanted magnetic interferences. Several special anti-interference techniques were adopted. 1) A new type eddy current signal conditioning circuit with modulation and demodulation method was developed with implemented anti-aliasing filters to remove actuator’s harmonics. 2) High power filters in actuator’s switch amplifier were designed to suppress harmonics. 3) All clocks, especially actuator’s switch clock and eddy current sensor’s clock, were synthesized from a single oscillation source and were phase locked with each other. 4) The frequencies of actuator’s switch clock and eddy current sensor’s clock were chosen to demodulate the actuator’s harmonics by eddy current conditioning circuit to zero or far above circuit’s bandwidth.

Results: The total power loss in maglev coils was less than 400 mW and the sensitivity of the proposed anti-interference control system was lower than 8 dB which satisfied ISO 14839, demonstrating the stability and freedom from interference. Magnetic interferences in miniaturized blood pumps are so significant that common eddy current conditioning methods would fail. This work has demonstrated the employment of special techniques can successfully remove the interference to guarantee a smooth operation of the maglev pump.

Multimodal Anatomical Fitting of an Artificial Heart by Adaptation of Vascular Prostheses

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Study: Anatomical fitting of a total artificial heart (TAH) within the pericardial space is one of the biggest challenges in its design. The vascular prostheses can be used to adapt mechanical requirements of the pump unit to anatomical requirements of the vascular system. An anatomical fitting of these grafts is crucial for a successful implantation and function of the TAH. This study presents the design optimization process with regard to the best anatomical fitting of the grafts and cuffs manufactured in a customized spraying process allowing easy and individualized geometrical adaptations.

Methods: The anatomy of 6 patients were analyzed with the help of CT data. The position of the atria, the valve plane and surrounding tissue were extracted to evaluate the position of the TAH and the geometries of the prostheses. Different graft designs were developed and tested virtually in the prepared CT files. Thereby the diameter and the bending radius of the grafts and cuffs were adapted. In addition a silicone model of the atria and remnants arterial vessels was developed, based on these CT files. This facilitated in-vitro testing of different manufactured graft designs, giving additional insights on haptic interaction between atria, prostheses and device. The verification of these findings is currently being performed in an anatomy study with human cadavers.

Results: With the help of a multimodal, in-silico, in-vitro and anatomy study, a graft design for improved anatomical fitting of the ReinHeart was performed. This improvement results in a more reliable function even in smaller patient group. The spraying process used for prostheses manufacturing, enabled practical implementation of the specialized geometries.
Numerical Analysis of Newtonian and Non-Newtonian Blood Models in Flow of Spiral Groove Bearings

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Study: A novel spiral groove bearing (SGB) was designed for hydrodynamic centrifugal blood pumps. However, present studies of SGB were based on Newtonian blood model, while blood is a non-Newtonian fluid with shear thinning property. In this study, the impact of different blood models was investigated using numerical analysis method.

Methods: Computational fluid dynamics (CFD) was used to estimate the performance of SGB, e.g. load-carrying capacity. Bearing gap between SGB and the mating surface was fixed at 40μm and the rotating speed of SGB was 3000rpm. Boundary conditions were based on experiments and were set the same for analyses with both models. Casson model was implemented to represent non-Newtonian property of blood. The value of yield stress and limiting viscosity for blood were 0.03752Pa and 0.003025Pa s, respectively, obtained from empirical data. And the viscosity of Newtonian blood model was defined as the limiting viscosity.

Results: The shear rate distribution of the two model were alike, but the load-carrying capacity of SGB implemented with Casson blood model was 0.57336N, significantly larger than that with Newtonian blood model of 0.48405N. The pressure and wall shear stress of SGB with Casson blood model were also higher than that with Newtonian blood model. The shear-thinning character of blood has a remarkable impact on the performance of SGB. Thus it is valid to consider blood as a non-Newtonian fluid in design and optimization of SGB for blood pumps.
Durability Testing of Volumetric Motor Pumps in the Carmat Total Artificial Heart

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Study: The Carmat TAH is designed to provide full cardiac support. It encompasses two cavities, each separated by a membrane into a blood compartment and an actuating-liquid compartment. The silicon actuating-liquid is shuttled in and out the cavities by two volumetric electromotor-pumps (EMP), creating diastolic and systolic phases. We compared predicted wear of the EMP based on Archard’s law with life bench tests.

Methods: The EMP produces a reversible radial flow by inverting the rotation of the shaft, with two concentric gears assembled on eccentrically flat bearings. With acceleration from 0 to 8000 RPM in 125 msec, it can generate a “beat rate” of 150 bpm and replace 40cc, resulting in a pulsatile flow of 6 L/min. Five motor pumps were placed on test benches and subjected to dynamic load equivalent to 160 mbar. Data from tests of early-generation EMPs and samples of gear material were used to build the mathematical model.

Results: 130 bench test results from 3 different gear teeth materials have lead to improved EMP bearing/shafts and provided data for the mathematical model. Applying Archard’s law and tribological test data resulted in a logarithmic curve for EMP wear prediction. The model predicted abrasion of less than 0.1 mm on gear teeth after 5 years. Five motor pumps were tested on the bench after 3.6 years (range 0.5–5 year). The first motor pumps were disassembled after 6 month to validate the test condition and confirmed the absence of wear on shaft. Analysis of gear teeth surface roughness showed some degradation limited to small scratches in the early phase and almost no wear during the remaining test period. Testing will continue to validate the model after 10 years.

Conclusion: A wear-predicting model applying Archard’s law was validated by bench tests. Durability of the volumetric EMP of the Carmat TAH as predicted by the model provides promising information for its potential long-term use. This testing approach might provide an alternative methodology to assess durability of implantable pumps.
Effects of Air and Negative Pressure on Blood Activation During Cardiopulmonary Bypass

Study: Cardiopulmonary bypass causes a systemic inflammatory response (CPB-SIRS) associated with multiorgan failure. Previous preliminary data described a porcine model and suggested blood exposure to air and negative pressure plays a role in stimulating CPB-SIRS.

Methods: 8 pigs were placed under anesthesia. The control group (n=4) consisted of a venovenous shunt. The experimental group (n=4) had ~10% of the cardiac output diverted through a venovenous system which exposed the blood to 100ppm of air and -100mmHg of pressure for 2 hours, after which the cannula was removed. Animals were recovered and monitored for 72 hours. Flow cytometry was used to assess monocyte and granulocyte CD11b expression. Results were analyzed using unpaired student t-tests with a p-value <0.05 considered significant.

Results: This circuit mimics the cardiotomy suction and air exposure of CPB without the invasive thoracotomy and hemodynamic instability. There were no differences in hemodynamics between groups. A significant decrease in platelets was seen in the experimental group (p = 0.005) which returned to baseline at 72 hours. In the experimental group CD11b expression on granulocytes (p=0.05) and on monocytes (p=0.29) showed a trend toward higher values (figures 1 and 2, respectively).

Conclusion: Increased activation of leukocytes in the group exposed to air and negative pressure was suggested by increased expression of CD11b. This persisted for 48 hours with a trend back toward baseline by 72 hours. Future studies will include the addition of NO gas to the reservoir to evaluate its effect on the inflammatory response.

Analysis of Percent Time in Therapeutic INR Range in Left Ventricular Assist Device Patients

Study: Patients with LVADs are on chronic anticoagulation therapy to prevent thrombus which requires constant monitoring of a patient’s INR. A common way to quantify INR is the Rosendaal method calculating percent time in therapeutic range (%TTR). Here we analyze the relationship between %TTR and thrombus/bleeding events, as well as the necessity of maintaining a tight INR range in LVAD patients.

Methods: The Artificial Heart Program’s database was queried from 5/26/2006–11/30/2014 for INR values with %TTR, as well as time above range (%TATR) and below range (%TBTR), calculated using the Rosendaal method. Original patient INR goals were used, as well as ranges expanded by 1 and 2 SDs to determine potential boundaries. Thrombus and bleeding related readmissions were collected and correlated with %TTR values.

Results: 82% of the 60 patients analyzed were male with an average age of 59 yrs. Average %TTR was 41.5 using the original INR ranges and 86.2 using INR ranges expanded by 2 SD. Correlation coefficients between these values and rate of readmission are shown. No correlation was found between readmission and %TTR for original INR ranges and ranges expanded by 1 SD. Moderate correlation was observed in 2 SD expanded ranges.

In our experience, maintaining LVAD patient %TTR using highly specific INR ranges has not proven to reduce or increase thrombus and bleeding events other than in extreme INR cases. Significant time and effort is spent keeping patients within a precise INR range, as well as making alterations to optimize goals. Our data shows expanded ranges are necessary to acquire a correlation, and that INR is unable to fully explain the complex factors involved in bleeding and thrombosis.
Hospital Survival and Financial Metrics in Adults Requiring Veno-Arterial Extra-Corporeal Membrane Oxygenation


Study: Veno-Arterial Extra-Corporeal Membrane Oxygenation (ECMO) is commonly utilized for cardio-vascular support. The therapy, however, consumes a large amount of hospital resources. Further, with the advent of newer technology, ECMO can safely be continued for longer periods of time. We sought to understand the effect of ECMO support for greater than eight days on survival and hospital financial metrics.

Methods: The outcomes from patients > 18 years of age, who were determined to be unsuitable for a ventricular assist device and were therefore supported using VA-ECMO, were reviewed from 2010–2013. Clinical outcomes were determined from in-patient chart review. Hospital expense and contribution margins were determined from data obtained from hospital finance. Total variable expense was the sum of all variable expenses generated during the patient’s hospitalization. Contribution margin was defined as total patient revenue minus total variable expense. Patients were divided into two groups depending upon the duration of ECMO support (Group I: ECMO support for 8 days or less, Group II: ECMO support for greater than 8 days).

Results: A total of 53 adults were supported using ECMO. There was no difference in age or gender between groups. Survival to discharge was not different between groups (Group I: 41% (16/39) Group II: 42% (6/14)). The average total variable expense and contribution margin for ECMO/day was $12,558 ± 9,948 and $58,916 ± 61,355 respectively. Subsequently, the total variable expense was significantly lower within group I ($58,583 ± 59,669 vs. $39,297 ± 63,503; p=0.01), while the contribution margin was significantly greater within group I ($106,493 ± 59,140 vs. $ 51,093 ± 49,459; p=0.01). This suggests that ECMO duration for greater than 8 days does not improve survival, but vastly increases the amount of financial resources required. This becomes more relevant as newer ECMO equipment and techniques have enabled longer duration of support.

Preservation of High Molecular Weight vWF and Low Hemolysis With the Low Shear TORVAD™ Ventricular Assist Device

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Study: The TORVAD™ is a positive displacement ventricular assist device (VAD) that synchronizes with the cardiac cycle to deliver full support to a failing heart with a 30 ml counterpulse ejection. Pumping is achieved by independently moving two pistons within a toroidal chamber. The gap between the piston and torus wall is controlled using ceramic hydrodynamic bearings. Controlled gaps and low rotational speeds (90–180 rpm) result in low shear (10–50 Pa), an order of magnitude less than the shear in continuous flow (CF) VADs. Preliminary in vitro experiments have been conducted to determine the effects of low shear on blood damage.

Methods: Bench top blood damage experiments were conducted with fresh whole human blood in a test circuit. An FDA-approved CF VAD was used as a control. The TORVAD™ was set to operate at 4 L/min, producing a dynamic pressure maximum of 140 mmHg and an average pressure of 60 mmHg. The CF VAD produced a flow rate of 3.8 L/min and pressure of 60 mmHg.

Results: Hemolysis, quantified using the normalized index of hemolysis (NIH), was 0.001 g/100L for the TORVAD™ and 0.013 g/100L for the CF VAD. Von Willebrand Factor (vWF) multimers were analyzed by separation of vWF into its multimeric components using sodium dodecyl sulfate agarose electrophoresis. Densitometry analysis was performed on the multimer band results to determine the ratio of high molecular weight (HMW) multimers (bands > 10 length) with respect to baseline. Shear in a CF VAD was associated with a loss of 70% of the HMW vWF, while the TORVAD lost 1% of the HMW vWF. These initial results demonstrate that blood components experience substantially less trauma with the TORVAD™ as compared to a commercially available CF VAD.
Comparing the Effectiveness of Axial and Centrifugal Left Ventricular Assist Devices in Ventricular Unloading

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Study: Centrifugal (CFG) and axial flow (AX) left ventricular assist devices have different flow characteristics which may impact the effectiveness of left ventricular unloading. We sought to determine if patients implanted with the HeartWare (CFG) and HeartMate II (AX) had a similar degree of hemodynamic support by comparing parameters measured using echocardiography and right heart catheterization.

Methods: Using our prospectively collected database, we identified 257 patients implanted with the HeartMate II and 61 with the HeartWare from 2004 to 2014. Patients that died or were transplanted within three months of device implantation were excluded.

Results: Age, BMI, etiology, and device indication were the same between AX and CFG groups. There were significantly more women implanted with the CFG pump (33% vs 19%, p=0.02). Baseline ventricular dimension (LVIDD), mitral regurgitation (MR) severity, right ventricular systolic pressure (RVSP) and pulmonary vascular resistance (PVR) were similar. Wedge pressure (PCWP) and mean pulmonary artery pressure (mPAP) were higher at baseline in the AX group (28.3 vs 23.0, p<0.01, 39.4 vs 35.0, p=0.01, respectively). There was no difference in perioperative mortality (4.7%). Post implantation there was a greater reduction of PCWP, mPAP, and PVR in the AX cohort (-13.9 vs -6.5, p<0.01, -15.7 vs -8.2, p<0.01, -1.3 vs -0.7, p=0.04, respectively). Post implantation LVIDD, MR severity, RVSP, and degree of aortic valve opening were similar. These results demonstrate that both AX and CFG devices resulted in left ventricular unloading however AX devices may offer advantages in the magnitude of left ventricular unloading, which could have implications in ventricular recovery or reduction in pulmonary vascular resistance prior to transplantation.

Blood Species Differences in Mechanical Hemolysis Testing

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Study: Animal blood is often used in preclinical bench testing to assess the risk of blood damage caused by new medical devices. In this study, we used four different physical models to study how blood species (i.e. human, bovine, porcine, and ovine) and flow-related factors affect mechanical hemolysis levels.

Methods: The test models included rocking a blood-filled test tube containing spherical steel beads, shearing blood in a cone-and-plate rheometer for 5 minutes, a single-pass jet through a 150 µm diameter orifice, and recirculating blood in a flow loop with an in-line nozzle. Each test model produced unique flow characteristics representative of blood-contacting devices (e.g. high shear stresses with msec exposure times, low shear stresses with exposure times on the order of minutes). To make direct comparisons among species and models, specific test parameters [hematocrit (36%), anticoagulation (ACDA), and temperature (25°C)] were held constant.

Results: The hemolysis results showed that blood species sensitivity was dependent on which physical model was used. Except for the rocker bead model, which is probably the least representative model of a medical device, porcine and human blood were the most sensitive blood species to flow-induced shear stress, and bovine and ovine blood were the least sensitive (Figure). This study indicates that blood species, and the type of flow regime created by a medical device, may impact the clinical applicability of the results from in vitro mechanical hemolysis testing.
Usefulness of the Preoperative Six Minute Walk Test to Predict Outcomes After Left Ventricular Assist Device Implantation

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**Study:** Functional capacity as assessed by the six minute walk test (6MWT) has been shown to significantly improve in patients with a left ventricular assist device (LVAD) and has been associated with improved quality of life. However the relationship between the preoperative 6MWT and other postoperative outcomes is not well described. We sought to evaluate the association between the preoperative 6MWT and clinical outcomes after LVAD.

**Methods:** All patients implanted with a continuous flow LVAD from 3/2008 through 12/2012 with a preoperative 6MWT were examined. Patients were stratified into 2 groups according to the preoperative 6MWT: group 1 (n=43) had a 6MWT which was less than the average (168 meters) and group 2 (n=36), had a 6MWT ≥ to 168 meters. Demographic, laboratory, hemodynamic, and outcomes data were analyzed. All cause readmission and survival were assessed out to 2 years.

**Results:** Average age of all patients (n=79) was 60.3 ± 11.3 years. Group 1 was 52.4% male while group 2 was 91.7%, p < 0.001. Length of stay was significantly shorter in patients with an increased preoperative 6MWT. These patients had higher albumin levels, required less inpatient rehabilitation, spent more days out of the hospital after discharge, were readmitted less often up to 180 days and had improved survival rates at 6 months.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 Low 6 MWT (n=43)</th>
<th>Group 2 High 6 MWT (n=36)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 MWT (meters)</td>
<td>102 ± 43</td>
<td>228 ± 58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine(mg/dL)</td>
<td>1.26 ± 0.5</td>
<td>1.4 ± 0.3</td>
<td>0.01</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>2.9 ± 0.5</td>
<td>3.0 ± 0.4</td>
<td>0.04</td>
</tr>
<tr>
<td>Cardiac Output(L/min)</td>
<td>4.3 ± 1.6</td>
<td>5.1 ± 1.2</td>
<td>0.04</td>
</tr>
<tr>
<td>Length of Stay (days)</td>
<td>25.2 ± 13.6</td>
<td>19.0 ± 7.8</td>
<td>0.03</td>
</tr>
<tr>
<td>Days out of Hospital</td>
<td>381.3 ± 343.0</td>
<td>402.5 ± 280.3</td>
<td>0.04</td>
</tr>
<tr>
<td>Inpatient Rehabilitation</td>
<td>14 (33.3%)</td>
<td>5 (13.9%)</td>
<td>0.04</td>
</tr>
<tr>
<td>180 Day Readmit</td>
<td>31 (81.6%)</td>
<td>21 (58.3%)</td>
<td>0.03</td>
</tr>
<tr>
<td>180 Day Survival</td>
<td>34 (82.9%)</td>
<td>35 (97.2%)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Malnourishment has been associated with poor outcomes after LVAD implantation. Preoperative exercise capacity as measured by a 6MWT may also be useful as an indicator of clinical outcomes after LVAD. We suggest that the preoperative 6MWT is a clinically relevant tool that may help identify poor LVAD candidates requiring a longer length of stay and additional rehabilitation after LVAD implantation.
In-vitro Evaluation of an Autonomous Control Algorithm Using Stochastic Method for a Ventricular Assist Device
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Study: Adaptively controlling a ventricular assist device (VAD) in the realistic situation would be difficult because it is necessary to model the whole including the VAD and the cardiovascular dynamics. To solve this problem, we have proposed an autonomous VAD control method based on stochastic model. In this study, we sought to investigate whether a flow control application of our method can be used to adaptively control a continuous flow VAD in a pulsatile mock circulation loop.

Methods: The flow rate control algorithm was constructed on the basis of a stochastically control model, dx(t)/dt=A (-dU(x)/dx)+η (x(t): the parameter of the rotational speed, U(x): temporary objective function, A: evaluation function to indicate the desirability of a current state, η: noise). This algorithm detects desirable rotational speed via random walks; the inappropriate state reduces value of evaluation function, and noise becomes dominant. To evaluate behaviors based on the implemented algorithm, control testing on a mock circulation loop simulated a left heart bypass support and inflow sucking (unexpected event) was performed using a medical centrifugal pump driven by our constructed control system and it was compared with the simple linear flow rate control.

Results: The flow rate of the VAD reached a target value in both methods to various changes of the circuit resistance. The control speed was uniformly late in proposed method by searching behaviors. The behaviors to inflow sucking were found as follows: linear control failed by increasing rotational speed for the low flow state caused by the sucking. On the other hand, the proposed method reduced frequency of the sucking up to 12% by behaviors to searchingly decrease rotational speed. In conclusion, the constructed algorithm realized autonomous bypass flow control in the situation of pulsatile circulation without designing the detailed control rule based on the experience or the model of the control target.

Preoperative Tricuspid Valve Regurgitation in LVAD Patients: Impact on Outcomes
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Study: Tricuspid valve regurgitation (TR) in patients undergoing implantation of continuous left ventricular assist device (CF-LVAD) can result in post-operative right ventricular (RV) dysfunction, leading to renal impairment, right ventricular assist device implantation (RVAD), prolonged ICU and hospital stay, early and in-hospital mortality.

Methods: We reviewed the data of 64 consecutive patients who had HeartMate II or HeartWare CF-LVADs implanted between 2012 and 2014 at our institution, without concomitant tricuspid valve (TV) repair. We compared data of 6 patients who had moderate-to-severe, or severe TR (Group 1) to data of 58 patients who had no TR, or had trivial, mild, mild-to-moderate TR (Group 2). Two groups were comparable in regard to age (53 ± 13 vs. 56 ± 12yrs, p=0.613), gender (100% vs 93% men), median INTERMACS score (2 vs. 2, p=0.260), and bridge-to-transplant therapy (50% vs. 60%), p=0.623. The pre-operative model of end-stage liver disease (MELD) IX was statistically higher in Group 1, 56 (IQR: 35–75) vs 32(28–39) in Group 2, (p=0.023). Median post-LVAD MELD IX score was similar (40 vs.31, p=0.107). No differences (p<0.05) were seen with respect to RVAD implantation, 30-day overall mortality, 30-day cardiovascular (CVS) mortality, post-operative renal failure, and in total hospital length of stay (Table 1).

Results: In our study groups the degree of preoperative tricuspid insufficiency didn’t seem to affect short-term patients’ outcomes. Further, larger prospective studies are needed to evaluate long-term outcomes and long-term effects of TR.
Towards a Prognostic Cost Model for Continuous Flow (CF) LVAD
N. A. Loghmanpour, J. F. Antaki. Biomedical Engineering, Carnegie Mellon University, Pittsburgh, PA.

Study: With the steadily increasing use of CF-LVAD, there is heightened scrutiny on the cost effectiveness of this therapy. This study aimed to evaluate the efficacy of an existing Bayesian-based prognostic model for mortality and adverse events in terms of monetary cost. Specifically, we test the hypothesis that accurate prediction of 1-year mortality on LVAD would provide a financial savings by sparing those patients of the incremental financial burden.

Methods: This is a retrospective study using 9,976 CF-LVAD recipients from INTERMACS between 2006–2014. A Bayesian-based model for 1-year survival on an LVAD (previously shown to exhibit 89.0% accuracy and an AUC of 95.3%) was used to stratify patients from this cohort. For each patient predicted to die within one year, the 1-year cost was estimated based on previously published values for initial VAD insertion, outpatient care, end-of-life, re-hospitalization and LVAD replacement if any. We then surmised the comparative cost of optimal medical management (OMM) for these assumed high risk patients.

Results: The Bayesian model predicted 1,833 1-year mortalities (65.4% sensitivity) and 8,143 survivals (93.9% specificity). The combined LVAD-related treatment cost of these high-risk candidates was estimated to be $150M. (This is approximately 4% of the overall cost of all patients in the INTERMACS registry.) By surmising that these same patients would/should have been continued on OMM, the aggregate cost was reduced to $105M (Figure 1). 83.1% of the OMM cost was attributed to estimated end-of-life cost. Prognostic models for LVAD therapy currently concentrate on survival and adverse events. Inaccuracy of these models may yield significant costs in terms of duration and quality of life. Although there is a financial price to pay for over-estimating the 1-year survival, it is arguably overshadowed by the humanitarian cost of denying a patient who might benefit or implanting an LVAD into a high-risk patient who will die early.

Alarms From the Total Artificial Heart Discharge Driver Requiring Changeout
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Study: Background: End stage biventricular heart failure has limited treatment options. In May 2010 Syncardia introduced the investigational portable freedom driver allowing patients to be discharged from hospital. The freedom driver was FDA approved in June 2014. While the freedom driver does allow freedom, there is risk associated with changeouts. We sought to describe our centers experience managing TAH freedom alarms and emergencies both in the hospital and in the community.

Methods: This is a retrospective study using 9,976 CF-LVAD recipients from INTERMACS between 2006–2014. A Bayesian-based model for 1-year survival on an LVAD (previously shown to exhibit 89.0% accuracy and an AUC of 95.3%) was used to stratify patients from this cohort. For each patient predicted to die within one year, the 1-year cost was estimated based on previously published values for initial VAD insertion, outpatient care, end-of-life, re-hospitalization and LVAD replacement if any. We then surmised the comparative cost of optimal medical management (OMM) for these assumed high risk patients.

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Conclusions: The need for staff and companions to respond to alarms requiring driver changeout may be higher than seen in the LVAD population. Broken and misaligned CPC springs may pose increased difficulty with freedom driver changeouts. Further investigation should focus on increasing the robustness of the CPC connector to avoid this malfunction.
Post-Explant Visualization of Continuous-Flow Total Artificial Heart and Outflow Grafts Using a Miniaturized Camera
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Study: In preclinical studies, the post-explant evaluation of the continuous-flow total artificial heart (CFTAH) for tissue regeneration, neointima formation, and thrombus can be challenging due to narrow device architecture. The outflow grafts and their junctions need to be explored before full pump disassembly to avoid disruption of any biomaterial buildup inside. This work aimed to visualize the CFTAH using a custom-made high-definition miniature camera.

Methods: A custom-made miniature imaging catheter provided by Karl Storz Endoscopy-America, Inc. (El Segundo, California, USA) had a resolution as 12.5 LP/mm @ 4 mm and 1.0 LP/mm @ 50 mm (field of view - 90°; depth of field - 4–50 mm). At a necropsy of a calf after 90-day of the CFTAH implantation, a small window was cut into the pulmonary and aortic outflow grafts wall in the silicone portion to introduce the flexible camera tip. The camera tip was steered toward the pump and the outflow ports.

Results: The CFTAH from inside showed no signs of thrombus or tissue buildup. Right outflow analysis showed significant thrombus inside the Dacron portion of the graft, expanding distally and proximally toward the CFTAH connection. Thrombus formation was observed at the Dacron portion, extending toward the metallic outflow port connection of CFTAH to the pulmonary conduit. The analysis of left outflow graft showed smaller thrombus formation in the shape of cords. The left metallic outflow port was clean. The right and left outflow graft lumens were both patent; however, the right outflow graft had significant tissue buildup. The camera tip maneuverability within CFTAH was optimal; visualization of structures beyond the impeller was not attempted to prevent camera damage by sharp blades and narrow device architecture.

Conclusions: Miniature steerable cameras are an easy and reliable solution to evidence the internal conditions of CFTAH before full disassembly post-explant.

Effect of Pulsed Operation of a Continuous Flow Left Ventricular Device on the Right Ventricle during Increased Afterload and Preload Conditions
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Study: The holy grail of mechanical circulatory support remains a physiologically responsive continuous flow left ventricular assist device (cfLVAD). To meet this goal, reciprocal right-sided volume and pressure perturbations are necessary. In this experiment we measured the response of the right ventricle (RV) to pulsed operation of a cfLVAD. We hypothesized that pulsed operation causes the RV to become more energetic and we tested this by assessing RV function with wave intensity analysis.

Methods: In vivo experiments were conducted using anesthetized pigs supported with a cfLVAD. Pressure was measured in the RV, and pressure and flow were measured in the pulmonary artery. cfLVAD speed was changed dynamically to mimic a cardiac cycle (systole:diastole) and the pump rate set to 10% of the intrinsic heart rate. Pulsed cfLVAD operation was tested during baseline, norepinephrine, and acute volume loading conditions.

Results: Figure 1 shows an example of pulmonary artery pressure, velocity, and net wave intensity during a cardiac cycle. RV contraction creates a forward compression wave (FCW) and relaxation creates a forward decompression wave (FDW). Figure 2 shows the wave intensity during pulsed operation during each intervention. Comparing continuous to pulsed operation, net positive wave energy (J/m²) increased during baseline (0.48 to 0.52, p < 0.001), increased marginally during norepinephrine (0.71 to 0.72, p = 0.046), and did not change during volume loading (0.56 to 0.58, p = 0.08). These results demonstrate the normal response to pre- and after-load conditions during pulsed cfLVAD operation.

Conclusions: Optimum pulsed operation of the cfLVAD results in physiologically responsive RV function, which is maintained at baseline, increased preload, and increased afterload conditions. These observations may have a role to play in the pathogenesis of RV failure in left-sided continuous flow states.
INTERMACS 1 Patients: Can They Be Rescued with Left Ventricular Assist Devices or Are They Beyond Salvageable
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Study: Left ventricular assist devices (LVADs) are increasingly used to support critically ill patients who have failed medical therapy for either bridge to transplant or destination therapy. This study investigated outcomes of LVAD implant in the critically ill, crash and burn - INTERMACS 1 patient cohort

Methods: A retrospective review of the LVAD registry at a single institution from 2006 to 2014 was conducted (n=311). Only patients with primary LVAD implantation were included. Patient demographics, comorbidities, and peri-operative outcomes were evaluated. Primary outcome was mortality with secondary outcomes of length of stay and complications.

Results: Of the total LVADs placed, 18% of patients were classified as INTERMACS 1 (n=55). The mean age for INTERMACS 1 patients was 51.1 + 13.1 years, 62% were men, and 52% had an ischemic etiology for heart failure. Prior to LVAD implant, 33% of the patients were on extracorporeal membrane oxygenation and 53% had an intra-aortic balloon. The cardiac index at the time of implant was 2.1 + 0.5 L/min/BSA2. LVAD implantation was classified as emergent in 74% of the cases. The overall median duration of LVAD support was 15 days (IQR=35). The rate of complications was low with 18% having acute kidney injury that required temporary dialysis, 11% with sepsis, and 4% with new onset of arrhythmia. The median time to extubation was 4 days (IQR=18) and overall hospital length of stay 31 days (IQR=24). 32% of patients were transplanted. The survival at 10 days, 30 days, and 90 days by Kaplan-Meir analysis was 86%, 68%, and 56%, respectively. As a stabilization strategy for high risk INTERMACS 1 patients, LVADs provide a viable means for hemodynamic stabilization with excellent short and mid-term results. Though outcomes are compromised compared to more stable patients, LVAD implant should be strongly considered in INTERMACS 1 patients.

Magnesium Handling in Patients with Impaired Renal Function Supported with a Continuous Flow Left Ventricular Assist Device
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Study: Continuous flow left ventricular assist devices (CF-LVAD) have become accepted therapy for treatment of end-stage heart failure. Improved survival and quality of life when compared to traditional medical therapy has been demonstrated. However effects of CF-LVAD on renal tubule function are not well defined. Magnesium depletion and hypomagnesemia (≤2.0 mg/dL) with high magnesium (Mg) requirements is common in CF-LVAD patients. Hypothesis: Patients with impaired renal function (Cr >1.5) receiving CF-LVAD therapy have a persistent renal tubular injury resulting in urine magnesium wasting.

Methods: Single center retrospective study of patients undergoing CF-LVAD implantation with HVAD (HeartWare, Miami Lakes, FL) or Heartmate II (Thoratec Corp, Pleasanton, CA) between March and December 2014. Serum and urine creatinine (Cr) and Mg were measured at pre-implantation, discharge (11 ± 4 days), and one-month intervals (30 ± 9 days). Fractional excretion of Mg (FEMg) was calculated (UMg x SCr/[(SMg x UCr)*0.7]) x 100. Student’s t-test analysis was performed.

Results: Twelve patients (9 men) with a mean age 60.2 ± 9.8 y were included in analysis. All patients were receiving Mg supplements. FEMg was elevated in both groups. Serum Cr remained stable in the <1.5 Cr group (0.84 ± 0.3 mg/dL), but decreased from 1.9 ± 0.3 mg/dL to 1.48 ± 0.6 mg/dL at discharge in the >1.5 Cr group. Fractional excretion of Mg (FEMg) was calculated (UMg x SCr/[(SMg x UCr)*0.7]) x 100. Student’s t-test analysis was performed.
Red Cell Distribution and Its Impact on Produced Hemolysis in Rotary Pumps as a Model Study
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Study: Prediction of red blood cells (RBC) destruction caused by different types of medical devices and artificial organs, is still an important issue. It is considered that the shear rate profile has an effect on the redistribution of RBCs. This phenomenon leads to appearance of “local” hematocrit (Hct) values, which is well known as a physiological phenomenon in “macro” and “micro” circulation. Local Hct can lead to different local viscosity and consequently various shear stresses. This investigation is directed to mimic the complex flow patterns established in Rotary Blood Pumps (RBP) by means of low and high shear Couette flow modelling.

Methods: In order to mimic the flow pattern in RBP-types, two different Couette devices are constructed: one with coaxial cylinders with a gap distance of 1mm and another one with an inserted thin blade mounted on the inner cylinder surface allowing thinning the gap distance partially to 200µm. Heparinized pig blood was used and various Hct-values were adjusted using the native plasma.

Results: In the case of normal free gap with lower shear rates up to 2000 1/s the hemolysis index were surprisingly higher than those blood samples which were imposed to shear rate up to 10,000 1/s in the second configuration. This phenomenon leads to appearance of “local” hematocrit (Hct) values, which is well known as a physiological phenomenon in “macro” and “micro” circulation. Local Hct can lead to different local viscosity and consequently various shear stresses. This investigation is directed to mimic the complex flow patterns established in Rotary Blood Pumps (RBP) by means of low and high shear Couette flow modelling.

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Results: In the case of normal free gap with lower shear rates up to 2000 1/s the hemolysis index were surprisingly higher than those blood samples which were imposed to shear rate up to 10,000 1/s in the second configuration. It can be demonstrated in the configuration with the presence of blade leads to redistribution of RBCs in the two different shear regions. The same trend was observed by variation of the Hct also by varying the exposure time as well as the shear rate.

Conclusion: The results suggest that a single critical shear rate is not realistic for the design and semi empirical modeling on the RBC trauma for rotary blood pumps.
Off-Pump Implantation of the HeartWare Left Ventricular Assist Device
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Study: Implantation of left ventricular assist devices avoiding cardiopulmonary bypass (CPB), may decrease the activation of the inflammatory and coagulation cascades, decrease bleeding and improve recovery. We analyzed our experience on implantation of HeartWare LVAD (HVAD) without CPB.

Methods: We reviewed the charts of 30 patients (pts) who underwent HVAD implantation from December 2012 to December 2014 at our center. 16 pts underwent HVAD implantation without use of CPB (OffCPB group) and 14 pts had HVAD implanted with the use of CPB (CPB group). We compared preoperative and postoperative data from the 2 groups, with an emphasis on perioperative outcomes.

Results: Preoperatively, both groups had similar demographic, functional and hemodynamic characteristics. INTERMACS score of 1 or 2 distribution was similar: 11/16 pts (69%) in Off CPB and 10/14 pts (71%) in CPB group. Compared to the CPB group, the OffCPB pts had a shorter intubation time with only 1/16 vs 6/14 pts requiring mechanical ventilation over 3 days; P=0.031. ICU stay 8 ± 5 vs 14 ± 11 days, P=0.084; hospital stay 30 ± 20 vs 48 ± 28 days, P=0.237 as well as returns to the operating room for correction of bleeding problems 0/16 vs 2/14 pts; P=0.209 were not statistically different between OffCPB and CPB pts respectively. During surgery and within the postoperative 48-hour period 7/16 pts in OffCPB group did not receive any blood transfusion while all 14 pts in CPB group did. P=0.007. OffCPB pts received significantly less transfusions than CPB group pts (P=0.012) on average: 1.4 ± 1.9 vs 8.0 ± 8.5 RBC units, 1.4 ± 2.0 vs 6.0 ± 5.8 FFP units, 0.3 ± 0.9 vs 2.7 ± 2.0 platelet doses and 0 vs 0.3 ± 0.6 cryoprecipitate doses. In each group 1 patient died (after 18 and 21 days) of multi-organ failure. Off CPB approach allows HVAD to be implanted quickly, with significantly less perioperative bleeding and transfusion requirements, and facilitates postoperative rehabilitation. Larger prospective studies are needed to evaluate long term benefits of this technique.

Optimally Pulsed Control of a Continuous Flow Left Ventricular Assist Device Results in more Biomimetic Operation
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Study: Pulsed operation of a continuous flow left ventricular assist device (cLVAD) is presumed to be more physiological. However, there is paucity of evidence to demonstrate distinct advantage over continuous flow in terms of positive energy gain. We hypothesized that a pulsed LVAD operation would enable the LV to produce more energy, quantifiable by wave intensity analysis.

Methods: In vivo experiments were conducted using anesthetized open-chest pigs supported with a cLVAD. Pressure was measured in the left ventricle, and pressure and flow were measured in the ascending aorta. LVAD speed was changed dynamically to mimic a cardiac cycle (systole: diastole) and the pump rate set to 10% of the intrinsic heart rate. Pulsed cLVAD operation was tested during baseline, norepinephrine, and acute volume loading conditions.

Results: Figure 1 shows an example of aortic pressure, velocity, and net wave intensity during a cardiac cycle. LV contraction creates a forward compression wave (FCW) and relaxation creates a forward decompression wave (FDW). Figure 2 shows the difference between continuous and pulsed operation during each intervention. Pulsed operation increased net positive wave energy (J/m²) by 233% at baseline (p < 0.001), 152% with norepinephrine (p < 0.001), and 241% with volume loading (p < 0.001) when compared to continuous flow. Conclusion: Pulsed operation of a cLVAD can result in a more biomimetic mechanical circulatory support, which can respond appropriately under physiologically stressful conditions.
Direct Left Atrial Pressure Monitoring in Patient With Total Artificial Heart
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Study: The Millar Mikro-Cath Pressure Catheter is a device for direct left atrial pressure (LAP) monitoring.Syncardia total artificial heart (TAH) as bridge-to-transplant therapy offers benefits to patients with biventricular failure as it avoids complications like RV failure, arrhythmias, valvular regurgitation, clotting in ventricle and low blood flows. We present a unique case of direct LAP monitoring in patient that underwent TAH placement in order to better optimize patients’ early hemodynamics and device operating parameters.
Methods: 65-year-old man, with ischemic cardiomyopathy and INTERMACS profile 1 underwent Syncardia TAH implantation for biventricular failure. During the same procedure the Millar Mikro-Cath was inserted into the left atrium for postoperative optimization of the left artificial ventricle. The central venous catheter was used to optimize right artificial ventricle. The Millar catheter was in place for monitoring for 3 days. The LAP ranged from 23 mmHg to 17 mmHg. During his early post-operative stay in ICU due to elevated right and left sided cardiac pressures, left and right sided vacuum (TAH operating parameters) were changed with decrease in left atrial and right heart filling pressures. Hemodynamics of the patient before and after optimizing of TAH operating parameters (POD1) is shown in Table 1. The patient had improvement in renal function and was extubated on postoperative day 2. We observed no complications (thrombosis, bleeding) associated with use of LA catheter and was removed safely with PTT between 50–60 seconds.
Results: Mikro-Cath Pressure Catheter in patient with TAH appears to be useful in optimizing early hemodynamics.

| Table 1 LAP Guided Optimization of TAH Operating Parameters |
|---------------------------------|-----|-----|
| Parameter                        | 51  | 57  |
| LV flow rate (ml/beat)           | 46  | 53  |
| RV flow rate (ml/beat)           | 23  | 17  |
| LAP (mmHg)                      | 17  | 13  |
| CVP (mmHg)                      |     |     |
| Left drive pressure (mmHg)       | 200 | 200 |
| Right drive pressure (mmHg)      | 90  | 90  |
| HR (bpm)                        | 138 | 138 |
| Vacuum                          | 8/10| 12/12|
| MAP (mmHg)                      | 69  | 73  |

Extending the TETS System for Improved Patient Comfort
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Study: The Penn State/Minnetronix transcutaneous energy transmission system (TETS) was originally designed to support an artificial heart. A TETS system uses a single set of power transfer coils, one external, and the other implanted to eliminate the need for a percutaneous cable. The TETS system has been updated with smaller, flexible coils to power continuous flow VADs and ease implantation beneath the clavicle. The patient still must wear a power controller attached to the external coil. The power transfer coils implement a transformer. By implementing a distributed transformer it is possible to extend the power transfer to other parts of the body and adapt the coil’s shape and size. The power transfer occurs in two locations, the first with fixed size coils at the implant. The second set of coils can be designed to allow the patient freedom to roll during sleeping. With the additional coil set, the power controller does not need to be directly tethered to the patient.
Methods: In this work, a method was developed to allow the patient to wear a distributed transformer in the form of a connected set of coils. One coil, worn over the implant coil, is connected to a second larger coil that forms a belt and is wrapped around the waist. The power transfer occurs in two places, from a power coil in the bed to the coil around the waist, and from there between the coils in the clavicle region as shown in the Figure below.

The belt gives the patient rotational freedom when sleeping on a mattress with a coil array. The power controller is tethered to the array in the mattress rather than to the patient.
Results: In vitro testing demonstrated power transfer for up to 20 W of power delivery sufficient for continuous flow LVADs. Power was transferred over 2 cm separation at each coil set. Coil heating was maintained to safe levels of less than 15 mW/cm². The advantage of this method is that the radiation of power occurs only at the coil pairs rather than across large distances.
Changes in Valve Function with LVAD: Comparison of HeartWare (HW) and Heartmate II (HM)


Study: LVAD therapy has become an established treatment for end-stage heart failure. One complication with LVAD support is development of aortic insufficiency (AI). AI in LVAD patients results in reduced cardiac output and is associated with poor outcomes. Mitral regurgitation (MR) generally decreases with LVAD due to ventricular unloading. Studies have shown that centrifugal and axial pumps exhibit different flow patterns and pulsatility. The purpose of this study is to evaluate whether these differences impact progression of AI and MR between HW and HM patients.

Methods: The Artificial Heart Program’s database was queried for HW and HM implants between Dec. 2004 and Dec. 2013. Echocardiograms were evaluated at pre-implant and 3 m, 6 m, and 12 m post implant. A scaling system was devised to quantify AI and MR over this time (Table 1). Significance was determined by T-Test.

Results: 46 HM and 23 HW patients were included in the study, with mean support times of 519 and 330 days, respectively. At baseline no significance was found in mean AI or MR between groups (p > 0.05). For HM, mean AI scores increased from 0.3 ± 0.4 to 1.3 ± 0.3 in 12 m (p<0.05). For HW, mean AI score increased from 0.3 ± 0.3 to 0.7 ± 0.6 in 12 m (p<0.05). Differences in AI became significant between groups after 6 m (1.2 for HM II vs 0.7 for HW, p<0.05). Furthermore, the number of patients with scores ≥1.5 increased from 1 to 5 in HM and 1 to 2 in HW. Mean MR score decreased from 1.6 ± 0.7 to 0.8 ± 0.4 in HM and 1.6 ± 0.9 to 0.8 ± 0.5 in HW in 3 m (p<0.05). Differences in MR between groups was found with regards to MR. (Fig 1). Our results suggest that though the degree of unloading as measured by change in MR was similar between pumps, the progression of AI differed. This may be a function of the differences in flow and pulsatility between axial HM and the centrifugal HW. Further research should be done in order to confirm these findings.

Quantification of AI/MR

<table>
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<tr>
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<tbody>
<tr>
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</tr>
<tr>
<td>0.5</td>
<td>Trace</td>
</tr>
<tr>
<td>1</td>
<td>Mild</td>
</tr>
<tr>
<td>1.5</td>
<td>Mild to Moderate</td>
</tr>
<tr>
<td>2</td>
<td>Moderate</td>
</tr>
<tr>
<td>2.5</td>
<td>Moderate to Severe</td>
</tr>
<tr>
<td>3</td>
<td>Severe</td>
</tr>
</tbody>
</table>

Simulation of Thrombus Growth in HeartMate II

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Study: Pump thrombosis (PT) is a multi-factorial problem which may be increasing due to changes in clinical practice patterns. This has motivated our group over the past two decades to derive a mathematical model to help predict conditions which promote thrombus deposition. The present study focused on the inflow region of the HeartMate II, which appears to be a vulnerable zone for PT.

Methods: Numerical simulation of the full pump was performed using custom-written mesh generation code and computational fluid dynamics (CFD) solver that incorporates an extended form of the Sorenson thrombosis model, which describes the processes of platelet activation, advection and deposition. High-speed (125-3000fps) video visualization was performed on a transparent replica of the HeartMate II, concentrating on the upstream bearing region. A wide range of pulsatile hemodynamic conditions (mean flow and pulsatility) were studied to explore the boundaries defining the transition from streamlined to disturbed flow.

Results: CFD simulations replicated patterns of thrombus deposition within the inlet stator section of the pump, similar to those reported clinically. High-speed flow visualization under pulsatile conditions revealed the appearance of a large toroidal vortex in the region of the inflow bearing during the diastolic portion of the cardiac cycle. The proportion of time in which the flow was observed to be chaotic was dependent on several factors including: mean flow rate, pulsatility, and deceleration (dQ/dt). Ongoing CFD simulations are investigating additional independent factors (hemodynamics, surface chemistry, biochemical activation) that are most likely to promote thrombus deposition.
Interaction of Mitral and Tricuspid Regurgitation Influences the Survival in Patients with Continuous-flow Left Ventricular Assist Devices

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Study: Mitral (MR) and tricuspid (TR) valvular regurgitation could affect survival in patients with continuous-flow left ventricular assist devices (CF-LVADs). Although isolated effects of severe MR and severe TR have been studied before, their possible interaction and its effect on survival has not been clearly delineated.

Methods: We retrospectively analyzed the prospectively collected Mechanical Circulatory Support Research Network registry in which pre-CF-LVAD MR and TR were graded semiquantitatively from 0 (no regurgitation) to 4 (severe regurgitation). The relationship between valvular regurgitation and overall survival were examined in a continuous nonlinear manner. Effect of MR and TR interaction on survival was further evaluated with Kaplan-Meier analysis.

Results: Between 2007 and 2013, a total of 508 patients underwent CF-LVAD implantation (HeartMate II, n=410, HeartWare HVAD, n=98). Median follow-up length was 337 days (interquartile range [IQR], 127–691), median age at implant was 59 (IQR, 49–66), and 20% were female. Information on both MR and TR was available in 496 patients. While increasing degree of MR had a mildly positive effect (p=0.268), increasing degree of TR was affecting survival negatively (p=0.043). The numerical difference between MR and TR (MR-TR) had a stronger association with overall survival (p=0.036) than MR or TR alone.

Kaplan-Meier analysis demonstrated clear increments in survival related to MR-TR degree (p=0.011).

With several tools currently available for assessing risk and predicting outcomes after CF-LVAD implantation, the MR-TR interaction could be useful adjunct as an additional tool.
Short-term Outcome of Left Ventricular Assist Device Therapy in Patients With End-stage Hypertrophic Cardiomyopathy
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Study: The major etiologies underlining in the patients supported by left ventricular assist device (LVAD) include dilated (DCM) and ischemic cardiomyopathy (ICM). Patients with advanced-stage hypertrophic cardiomyopathy (HCM) have a poor prognosis carrying a high risk of death due to heart failure or arrhythmias. We present outcomes of durable LVADs therapy for HCM patients.

Methods: Since the durable LVADs became clinically available in Japan, we experienced 31 implantations (15HeartMate II, 6 EVAHEART, 8 DuraHeart, 1 HVAD, and 1 Jarvik 2000). Five of them had suffered from dilated phase HCM. Twenty six patients had suffered from other diseases including DCM predominantly and small component of ICM. We analyzed the baseline characteristics and early-term outcomes in 5 patients with HCM in comparison to the remaining 26 patients with DCM and ICM.

Results: Baseline characteristics of two groups were similar except for LV diameter. HCM patients had significantly smaller LV diameter both preoperatively postoperatively. Postoperative echocardiography showed functionally closed aortic valve with regurgitation which was mild but more frequently in HCM patients. Bilirubin and BNP values were significantly higher in HCM patients at 30d postoperatively (p=0.006 and 0.015, respectively). Temporal renal replacement therapy was more frequent in HCM patients (p=0.0001). One HCM patient needed RVAD implantation. The 6-month survival rate was 53% in HCM patients and 95% in DCM and ICM patients (p=0.0001). Durable LVAD can improve hemodynamic status in end-stage HCM patients. However, renal failure due to right ventricular failure was more common in during perioperative course. Intensive care to improve RV function is more necessary in HCM patients.

Feasibility Study of Non-Invasive Ultrasound Assessment in LVAD and TAH for Endothelial Function
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Study: Total artificial heart assist (TAH) and left ventricular assist devices (LVAD) are very effective in cardiogenic shock and end-stage heart failure treatment to save lives. Myocardial function and viability are usually dramatically improved with immediate effects. We investigated flow-mediated dilation of the brachial artery in TAH and LVAD patients to assess immediate vascular endothelial function and compare them for any significant differences between these two different assist devices.

Methods: From June 2014, two (2) patients, one patient with cardiogenic shock and one patient with end-stage heart failure, underwent a SynCardia Total Artificial Heart placement in our center. Another two (2) cardiogenic shock patients were indicated for LVAD and received HeartMate II in the O.R. All the patients (n=4) survived the procedures. Using an Envisor Ultrasound Machine, we measured flow-mediated dilation of the brachial artery in both TAH and LVAD patients. Multiple measurements were taken at baseline, and after occlusion of brachial artery for five minutes. All the data were measured off-line and analyzed using SPSS Inc.

Results: TAH patients (age 56, 47 years) and LVAD patients (age 38, 52 years) were indicated for individual assist devices. In HeartMate II LVAD patients, ultrasound assessment revealed immediate response after cuff release following five minutes occlusion of the brachial artery and peak systolic flow velocity increased by 65%. Compared to LVAD patients, there were no changes of peak systolic flow velocity in artificial heart patients. Images show the “+ve responses” in LV assist devices and “no responses” in artificial heart devices.

Conclusion: There were significant changes of peak flow-mediated dilation of the brachial artery in LV assist device patients whereas there were no responses and changes in artificial heart receiving patients. Loss of both original ventricles in TAH patients may have played a “-ve” role on vascular endothelium.
Prolonged Normothermic Ex-Situ Heart Perfusion with Live Animal Paracorporeal Support

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Study: Normothermic ex-situ heart perfusion (NEHP) has the potential to revolutionize transplant medicine as demonstrated by recent clinical trials. However, preservation >12 hours has yet to be routinely demonstrated. To identify potential factors and perfusate components that may allow long-term ex-situ perfusion, we compared hearts preserved by our NEHP system to hearts continuously cross circulated with a parallel, paracorporeal animal (pPA).

Methods: In the NEHP group (n=3), porcine hearts were attached to a circuit consisting of a reservoir, roller pump, membrane oxygenator, and were perfused via the aortic root for 12 hours. In the pPA group (n=2), hearts were attached to a similar circuit, with the addition of a second pig attached in a parallel veno-venous configuration to the original circuit, such that it continuously replenished the blood perfusate.

Results: Hearts attached to the pPA were more vigorous and approached normal physiologic parameters with higher oxygen consumption (5.65 ± 0.08 vs. 2.91 ± 0.03 mL/min) and lower lactate production (1.99 ± 0.20 vs. 3.54 mmol/hr compared to the NEHP group. Calculated vascular resistance was significantly lower in the NEHP group (0.34 ± 0.07 vs. 0.14 ± 0.03 mmHg/L/min). Discussion: Diminished vascular resistance and metabolism observed in NEHP hearts correlates with the loss of vasomotor tone observed in brain dead patients after 6–12 hours. Since these parameters were maintained in pPA animals, continued optimization of our NEHP system requires that we identify the essential circulating factors provided by the paracorporeal donor. If adding these critical circulating factors to the NEHP system results in hearts with physiologic and metabolic function similar to the pPA experiments, it may be possible to accomplish long term heart preservation, and will allow for continued research into this technology which may greatly impact transplant medicine.
Incidence of Right Ventricular Failure: Single Center Experience
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Study: The purpose of this analysis was to compare our single center experience with Right Ventricular Failure (RVF) in different continuous flow devices.

Methods: From January 2011 to December 2013, 87 patients with chronic heart failure were implanted with a continuous LVAD (77 patients received a HeartMate II, 14 patients received Heartware HVAD and 6 patients received BIVAD/TAH). For the purpose of this study we excluded BIVAD/TAH patients and patients in INTERMACS profile 1. A total of 13 patients where in profile 1, of which 9 received Heartmate II while the remaining 4 received BIVAD support. Patient’s demographic, medical history, baseline hemodynamic and follow-up data were retrospectively reviewed. Incidence and risk of RV failure post-implantation was defined as the need for inotropic support after 14 days of LVAD implantation or temporary RVAD insertion.

Results: As shown in the table below, the patients implanted with a HeartMate II and HVAD are similar in terms of demographic, medical history, lab values, and hemodynamic parameters. There is a trend of higher proportion of male receiving a HeartMate II but the difference was not statistically significant. After LVAD implantation, the incidence of RV failure was 5/68 (7%) in patients implanted with a HeartMate II and 6/14 (43%) in patients implanted with an HVAD. This difference was statistically significant (p-value < 0.0001). The difference remained statistically significant after adjusting for gender. At mean follow up of 12 months, the survival was 59/68 (87%) for the Heartmate II patients and 8/14 (57%) for the HVAD patients.

Conclusion: These results suggest that at our center the HVAD is associated with a higher incidence of post-operative RV failure. These observations are based on retrospective data analysis collected from small number of patients. Further prospective studies are warranted to confirm these findings and understand the cause of this difference in the incidence of RV failure between the HeartMate II and HVAD pumps.

<table>
<thead>
<tr>
<th>Variables</th>
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<th>HVAD (n=14)</th>
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</tr>
<tr>
<td>Mle, no. (%)</td>
<td>50 (73)</td>
<td>6 (43)</td>
<td>0.054</td>
</tr>
<tr>
<td>Creatinine, no. (%)</td>
<td>41 (69)</td>
<td>8 (57)</td>
<td>0.06</td>
</tr>
<tr>
<td>CAD History no. (%)</td>
<td>3 (4)</td>
<td>0 (0)</td>
<td>0.42</td>
</tr>
<tr>
<td>Diabetes, no. (%)</td>
<td>23 (34)</td>
<td>6 (43)</td>
<td>0.51</td>
</tr>
<tr>
<td>Dystrophia, no. (%)</td>
<td>39 (57)</td>
<td>3 (21)</td>
<td>0.13</td>
</tr>
<tr>
<td>Hypertension, no. (%)</td>
<td>43 (66)</td>
<td>10 (71)</td>
<td>0.79</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>33.6 (20.7-51.8)</td>
<td>34.5 (23.9-40.6)</td>
<td>0.38</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>28 (18.37)</td>
<td>28 (21.39)</td>
<td>0.93</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.28 (0.5-5.5)</td>
<td>1.28 (0.7-2.0)</td>
<td>0.99</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>1.1 (0.3-4.7)</td>
<td>0.9 (0.3-3.1)</td>
<td>0.34</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.1 (2.8-4.2)</td>
<td>3.0 (2.2-3.7)</td>
<td>0.48</td>
</tr>
<tr>
<td>DFR</td>
<td>1.34 (0.8-4.1)</td>
<td>1.07 (0.9-1.3)</td>
<td>0.09</td>
</tr>
<tr>
<td>MELD score</td>
<td>12.1 (6-35.0)</td>
<td>10.3 (6.4-16.8)</td>
<td>0.27</td>
</tr>
<tr>
<td>Serum TR</td>
<td>6 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>EF (%)</td>
<td>44.5 (8-30)</td>
<td>57.8 (10-25)</td>
<td>0.55</td>
</tr>
<tr>
<td>LVEBD (mm)</td>
<td>63.0 (23-90)</td>
<td>57.6 (41-81)</td>
<td>0.02</td>
</tr>
<tr>
<td>LV EDCO (mm)</td>
<td>78.6 (28-94)</td>
<td>65.3 (30-83)</td>
<td>0.01</td>
</tr>
<tr>
<td>Systolic PAP (mmHg)</td>
<td>44.8 (10-80)</td>
<td>41.2 (24-28)</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Indications and Outcomes of Adult Congenital Patients Requiring Durable Mechanical Circulatory Support as Bridge to Transplantation.
M. F. Masood,1 K. R. Balsara,1 G. A. Ewald,1 U. Boston,1 S. J. LaRue,1 P. Eghtesady,1 A. Itoh.1 1Department of Surgery / Division of Cardiac Surgery, Washington University in St. Louis / Barnes Jewish Hospital, St. Louis, MO; 2Department of Medicine / Division of Cardiology, Washington University in St. Louis / Barnes Jewish Hospital, St. Louis, MO.

Study: Our data reports indications, and outcomes of adult congenital heart failure patients requiring durable mechanical circulatory support (MCS) as bridge to transplantation.

Methods: Clinical data was collected retrospectively in all patients who underwent MCS at our tertiary care referral center from December 2001 through February 2015.

Results: Adult congenital patients were defined as patients >18 years of age. Primary diagnosis was d- and L- Transposition of Great Arteries (d-TGA) (L-TGA) in 3 (60%) and 2 (33%) patients respectively. 6 / 620 (0.67%) patients received durable MCS all as indication of bridge to transplant (BTT) with mean PVR of 4.68 Woods unit. Mean age at implant was 36 ± 9 years. 1 (17%) patient was male whereas 5 (83%) patients were females. Mean BMI was 28.2 ± 5.9. 3 (50%) patients were INTERMACS level 1 whereas 3 (50%) patients were INTERMACS level 2. Pre-operative ECMO and intra-aortic balloon pump was utilized in 2 (33%) patients. Redo-sternotomy was performed in 100% of patients and 4 (67%) patients underwent delayed sternal closure. Types of durable MCS were Thoratec HeartMate II in 3 (50%) patients, Syncardia Total Artificial Heart (TAH) in 1 (17%) patient and Heartware HVAD in 1 (17%) patient. Postoperative temporary mechanical support was provided by Thotratec Centrimag RVAD support 1 patient (17%) and ECMO in 2 (33%) patients. Morbidity of postoperative cardiogenic shock was noted in 2 (33%) patients, whereas respiratory failure, splenic rupture and ischemic colon was noted in 4 (67%), 1 (17%) and 2 (33%) patients respectively. Mortality was 67% after 95 ± 84 days of support and 2 (33%) patients are discharged home and currently alive on MCS with 1150 and 30 days of support, awaiting transplantation. Average ICU and hospital LOS is 52 ± 80 and 69 ± 82 days respectively.
Temporal Increase in Pre-Discharge Thrombelastogram Maximum Amplitude in HeartMate II Recipients


Study: Pump thrombosis remains a vexing problem in rotary blood pumps (RBPs). Our center employs thrombelastogram maximum amplitude (TEG-MA) to monitor for the need to consider escalating antiplatelet therapy. We analyzed parameters that might aid in identifying patients at higher risk of hemolytic episodes as indicators of pump thrombosis.

Methods: We analyzed pre-implant, post-implant, and pre-discharge activated prothrombin time (PTT), international normalized ratio (INR), TEG-MA, lactate dehydrogenase (LDH), and plasma free hemoglobin (PFH) in 231 HeartMate II (HMII) implants since 2008. We grouped 182 patients with no hemolysis events (NO) vs. 49 patients with hemolysis events (HE), defined as repeated PFH >25 mg/dL. Univariate comparison of means and linear correlations were conducted. There have been minor modifications to our center’s anticoagulation protocol, but all patients receive Coumadin, aspirin, and persantine.

Results: The post-implant (72.5 vs. 69.6) and pre-discharge (74.0 vs. 71.4) TEG-MA were significantly elevated (p<0.04) in HE vs NO groups. The pre-implant mean TEG-MA was HE=65.9 and NO=65.7 (p=N.S.). The normal TEG-MA range is 50–70; thus, on average, all HMII patients have an elevated TEG-MA reflecting increased platelet activity. We then combined the groups and found a significant increase in TEG-MA in all HMII patients, with the mean increasing from 68.9 in 2008–2009 to 73.2 in 2014. Other factors such as INTERMACS category, gender, etiology, etc. have not changed over this time period. In our center’s experience the TEG-MA level following HMII implant has significantly increased in all patients from 2008–2014. Although the cause was not determined, patients with hemolysis events were noted to exhibit higher TEG-MA, which may suggest a need for increased antithrombotic therapy. While this finding may have clinical inference for increasing pump thrombosis, further investigation must be undertaken to confirm a cause and effect relationship.
Outpatient Management of Heartware® Ventricular Assist Device System in Children: A Multi-center Experience

M. Schweigels; C. Vanderpluym; A. Jeewa; C. E. Canter; P. Jansz; P. E. Parrino; O. Miera; J. Schmitto; M. Mehegan; I. Adachi; M. Huebler; D. Zimpfer; Parrino, Berlin, GERMANY; M. Schweiger, Division of Cardiac Surgery, Childrens Hospital, Zurich, SWITZERLAND; Children’s Hospital, Boston, MA; Ochsner Medical Center, New Orleans, LA, USA, New Orleans, LA; Deutsches Herzcentrum, Berlin, GERMANY; Division of Cardiac Surgery, Medizinische Hochschule, Hannover, GERMANY; Childrens Hospital, St. Louis, MO; Department of Cardiac Surgery, Medical University, Vienna, AUSTRIA.

Study: There is growing experience with the use of the Heartware® ventricular assist device (VAD) in children. Little is known about the outcomes of children supported on this device, and the feasibility of outpatient management. We sought to describe the strategies to achieve outpatient management and outcomes for children discharged.

Methods: All centers with paediatric patients discharged from the hospital on the device were identified using Heartware® Inc. database. A total of 14 centers were contacted, with 9 centers, contributing data retrospectively. Only children ≤18 years at time of implantation and who had been discharged were included in the analysis.

Results: From 2011–2013, 12 pediatric patients (7 females), mean aged 11.9 ± 2.3 years (range 8–15), mean weight 43 ± 19 kg (range 18–81), mean body surface area 1.3 ± 0.3 m² (range 0.76–1.96) were identified. Diagnosis included: dilated cardiomyopathy (CMP) (n=5), non-compaction CMP (n=4), toxic CMP (n=2) and viral CMP (n=1), indications for support were permanent support (n=1), bridge to recovery (n=1) and bridge to transplantation (n=10). Prior to HVAD implantation, all patients received intravenous inotropes and 2 patients were on temporary mechanical support (n=1), bridge to recovery (n=1) and bridge to permanent support (n=1). Mean readmission rate was 2.1 (range 0–12). No adverse events involving emergency department occurred. Eight children resumed local schooling.

HeartWare HVAD for biventricular support in children and adolescents: The Stanford Experience

M. L. Stein; J. Yeh; O. Reinhartz; D. N. Rosenthal; B. D. Kaufman; C. S. Almond; S. A. Hollander; K. Maeda; Pediatrics and Anesthesiology, Stanford Hospitals and Clinics, Stanford, CA; Pediatrics, University of California - San Diego School of Medicine, San Diego, CA; Cardiothoracic Surgery, Stanford University, Stanford, CA; Pediatrics, Stanford University School of Medicine, Stanford, CA.

Study: The HeartWare HVAD is designed for left ventricular support, however, use of two HVAD devices for biventricular (BiVAD) support is emerging. We report clinical course and recovery with respect to respiratory support and mobilization in 3 pediatric patients with HVAD biventricular support.

Methods: Records of 3 patients < 21 yrs who received biventricular support with HeartWare HVAD from 6/1/13-12/31/14 were reviewed and compared to 5 patients < 21 yrs with HeartWare HVAD for left ventricular support alone in the same period.

Results: Clinical characteristics are reported in Table 1. All BiVAD patients required cardiac catheterization for optimization of their device settings. High right and left sided filling pressures were common and were addressed with changes in VAD settings. At the end of the study period, all three BiVAD patients had undergone heart transplantation, and 4 of 5 LVAD patients had undergone heart transplantation. None of the BiVAD patients suffered a stroke or serious neurologic event during support. Bleeding requiring surgical exploration occurred in all three BiVAD patients and in 2 of 5 LVAD patients. The BiVAD patients were extubated on POD 4, 5, and 12. Four of five LVAD patients were extubated by POD 3. First mobilization out of bed for BiVAD patients occurred on POD 19, 31, and 33, and one BiVAD patient ambulated during the period of support. Of the 4 LVAD patients supported >2 weeks, all were mobilizing out of bed, and 3 were ambulating by POD 14.

Conclusions: Pediatric patients can be successfully bridged to transplantation with biventricular support via the HeartWare HVAD; however, optimization of hemodynamic support is difficult. Biventricular support is capable of improving patients’ functional status allowing extubation, mobilization, and even ambulation given adequate support duration and stability.

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>LVAD group (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>18</td>
<td>20</td>
<td>14</td>
<td>14.3 (range 6.7–19.5)</td>
</tr>
<tr>
<td>Sex/ Weight (kg)</td>
<td>male 71</td>
<td>male 90</td>
<td>male 31</td>
<td>male (5) 51 (range 21–65.5)</td>
</tr>
<tr>
<td>Cardiac Diagnosis</td>
<td>arrhythmogenic right ventricular cardiomyopathy</td>
<td>post transplant graft vascu-lopethy (s/p OHT 2004)</td>
<td>repaired tetralogy of Fallot</td>
<td></td>
</tr>
<tr>
<td>Prior Mechanical Support</td>
<td>ECMO</td>
<td>LVAD x5 days</td>
<td>ECMO</td>
<td>ECMO (1)</td>
</tr>
<tr>
<td>Duration of support (days)</td>
<td>40</td>
<td>205</td>
<td>22</td>
<td>39 (range 10–155)</td>
</tr>
<tr>
<td>Cardiac catheterization</td>
<td>Support day 4</td>
<td>Support day 18</td>
<td>Support day 13</td>
<td>Support day 2 Support day 7 Tamponade - 2 (Support day 27 - basal ganglia stroke secondary to metabolic disorder)</td>
</tr>
<tr>
<td>Major Complications</td>
<td>Tamponade (Support day 0) Removal of RVAD outflow band (Support day 5)</td>
<td>Tamponade (Support day 8)</td>
<td>Tamponade (Support day 10)</td>
<td>Transplant 4 Death 1</td>
</tr>
<tr>
<td>Outcome</td>
<td>Transplant</td>
<td>Transplant</td>
<td>Transplant</td>
<td>Alive 3 183–398 days post transplant Death 1 362 days post transplant</td>
</tr>
<tr>
<td>Status at last follow up</td>
<td>Alive 446 days post transplant</td>
<td>Alive 53 days post transplant</td>
<td>Alive 187 days post transplant</td>
<td></td>
</tr>
</tbody>
</table>

Patient Characteristics
**Development of an Implantable Pulsatile Pediatric Ventricular Assist Device**

E. Larson,1 J. Gohean,2 R. Longoria,3 M. Kurusz,1 R. Smalling.1 1Windmill Cardiovascular Systems, Austin, TX; 2Department of Mechanical Engineering, The University of Texas at Austin, Austin, TX; 3Division of Cardiovascular Medicine, The University of Texas Health Science Center at Houston, Houston, TX.

**Study:** The TORVAD™ is an implantable ventricular assist device able to deliver low-shear, synchronized, pulsatile flow. The key advantages of the TORVAD™ platform include the ability to synchronize with the heart while exposing the blood to minimal shear, as evidenced by low hemolysis and preservation of high molecular weight von Willebrand factor in a mock loop. Development of the TORVAD™ has previously focused on an adult sized device, and the design principles are now being applied to the development of a child sized version.

**Methods:** Previously established design tools for the adult TORVAD™ are employed to scale the pump for implantation in children with a body surface area between 0.6 to 1.5 m². These design tools include a computational model of the cardiovascular system to predict patient hemodynamics and determine pumping requirements, finite element heat transfer models to minimize heat generation at tissue interfaces, electromagnetic motor design software to maximize motor efficiency, three-dimensional computation fluid dynamics (CFD) to minimize shear and design for thorough washout within the blood pathways of the pump, and finite element magnetostatic simulations to optimize piston/motor magnetic coupling.

**Results:** Computational cardiovascular system model results predict that a 12 to 15 mL stroke volume pump is capable of fully supporting a pediatric patient by synchronizing with the cardiac cycle and preserving native aortic valve flow. The established computational design tools have been employed to modify and miniaturize the adult TORVAD™ for pediatric support. Use of CFD analysis demonstrates that the device achieves high washout and low shear.

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**Venoarterial ECMO Use as a Bridge to Recovery in Beta Blocker Overdose**

C. L. Jenks. Pediatric Critical Care Medicine, University of Texas Southwestern Children’s Medical Center of Dallas, Dallas, TX.

**Study:** 16 year old female who presented after ingestion of an entire 30 day supply of her grandmother’s metoprolol and amitriptyline.

**Methods:** She developed altered mental status and was transported to a local emergency department. She was bradycardic 30-40s, hypotensive 50/20s. Initial resuscitation included 5 Liters of crystalloids, norepinephrine and dopamine infusion. Our transport team arrived, intubated the patient, and started an epinephrine infusion. Upon arrival in our pediatric intensive care unit, her pupils were 7-8s and sluggish, persistent bradycardia 30-40s and hypotensive as before, pulses were weak, a vasopressin infusion was initiated, started on calcium, glucagon, and bicarb infusions. Atropine was ineffective. Her initial complete blood count and electrolytes were normal, creatinine was noted to be increased to 2.7 mg / dL, Tylenol, aspirin and alcohol levels were undetectable. Transaminases were normal. Initial arterial blood gas pH 7.18 / PaCO2 of 35 / PaO2 of 129 / bicarb 13, base deficit 15, lactate of 5 mmol / L. Continuous venovenous hemofiltration was initiated. As she was refractory to current beta blockade overdose treatment and was persistently bradycardic / hypotensive as before, pulses were weak, a vasopressin infusion was initiated, started on calcium, glucagon, and bicarb infusions. ECMO support is a viable option for toxic overdose not responding to conventional treatment.

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**Development of an Implantable Pulsatile Pediatric Ventricular Assist Device**

E. Larson,1 J. Gohean,2 R. Longoria,3 M. Kurusz,1 R. Smalling.1 1Windmill Cardiovascular Systems, Austin, TX; 2Department of Mechanical Engineering, The University of Texas at Austin, Austin, TX; 3Division of Cardiovascular Medicine, The University of Texas Health Science Center at Houston, Houston, TX.

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Single Ventricle Model for Clinical Simulation Training
G. M. Pantalos, L. Pyles, B. Ngha, K. Hughes, K. Martin, C. Ziegler, J. Sparks, A. Calhoun. Cardiovascular and Thoracic Surgery, University of Louisville, Louisville, KY; Physiology and Biophysics, University of Louisville, Louisville, KY; Medical Education, University of Louisville, Louisville, KY; Pediatrics, University of Louisville, Louisville, KY.

Study: Effective, safe, and efficient delivery of pediatric critical care requires all staff be trained in essential technical and communication skills. The need for optimal team performance is heightened when congenital defects exist and life support technology is used. High fidelity simulation of clinical scenarios of complex pediatric patients can maximize the performance of the medical team, minimize threats to patient safety, and improve patient outcomes. A current limitation to training is that critical care simulations use either computer-based algorithms to simulate physiologic waveforms on a monitor or a simple fluid loop in a “wet lab” to teach fundamentals of device operation as the critical care team runs through an exercise. While technically correct, these simulators lack clinical fidelity.

Methods: Our team has created a physical model of single ventricle physiology for use with a pediatric scale circulation simulator that approximates key anatomic structures of the cardiovascular system. Pulsatile, physiologic pressures and flows are created by pumping a blood analog fluid through the modeled vasculature. The single ventricle was simulated using a pediatric ventricular assist device by relocating the outflow port to the center of the ventricular housing and placing the inflow port from a second ventricle where the original outflow port was located (two inlets + one outlet), like a patient with truncus arteriosis. Additional options include adding a Sano Shunt, a Blalock-Taussig Shunt, outflow valve incompetence, an intra-atrial shunt, and ECMO support. Adjustable systemic and pulmonary vascular resistance elements can be used to establish an acceptable balance between pulmonary and systemic circulation flow distribution (Qp/Qs).

Results: The goals of this improved simulator are to raise overall staff competence in dealing with complex situations and life support equipment by refining the training experience and to provide a more realistic tool to support root cause analysis for quality improvement.

Impella Use for Left Ventricle Decompression in a 6-Year-Old on ECMO Support: The Youngest Pediatric Patient Reported.
J. Goldman, S. Tume, A. Jeewa, D. Parekh, H. Justino, I. Adachi. Pediatrics, Baylor College of Medicine, Houston, TX.

Study: Decompression of the left ventricle (LV) is often necessary while on ECMO support to avoid lung edema. Previous studies have shown that LV decompression is necessary in 22% to 50% of children undergoing venoarterial (VA) ECMO support. In the pediatric population, LV decompression while on peripheral ECMO cannulation is typically achieved using atrial septostomy or left atrial vent. This approach creates a large intra-atrial communication, which can persist after discontinuation of ECMO support. Residual intra atrial shunt predisposes recovering myocardium to volume overload, and requires surgical or catheter device closure of the defect. In the adult population the Impella® (Abiomed, Danvers, MA) catheter-based micro axial ventricular assist device, has emerged as an option for LV decompression in conjunction with ECMO support. It is unclear if this catheter-based technology is applicable in children due to vessel and cardiac chamber size limitations.

Methods: We describe our experience with Impella 2.5 support in a 6-year-old child undergoing VA ECMO support for viral myocarditis.

Results: A 6-year-old female (weight 22 kg, BSA 0.85 m2) with a remote history of heart transplantation presented with acute congestive heart failure and end-organ dysfunction. She was diagnosed with Epstein-Barr virus myocarditis. Her hemodynamic decline required venoarterial (VA) ECMO support. While on ECMO support she developed progressive lung edema, and required surgical or catheter device closure of the defect. In the adult population the Impella® (Abiomed, Danvers, MA) catheter-based micro axial ventricular assist device, has emerged as an option for LV decompression in conjunction with ECMO support. It is unclear if this catheter-based technology is applicable in children due to vessel and cardiac chamber size limitations.
Explantation of a HeartWare Ventricular Assist Device with a Titanium Plug: The First US Experience

D. A. Lara,1 A. Jeewa,2 B. A. Elias,2 E. O. McCullum,1 I. Adachi.1
1Pediatrics, Baylor College of Medicine, Houston, TX; 2Congenital Heart Service, Texas Children’s Hospital, Houston, TX.

Study: There has been steady increase in the number of children with end-stage heart failure while the number of organs available for heart transplantation has been stagnant. This reality makes the use of ventricular assist device (VAD) for ‘bridge-to-recovery’ a valuable option. Here we describe a 14-year-old female with anthracycline-induced cardiomyopathy who received a Heartware VAD and had successful explantation of VAD following cardiac recovery.

Methods: Over one year of VAD support, the patient’s cardiac function returned to normal. She had two “off-pump” tests which confirmed good cardiac output without VAD support. She was brought to the operating room 1 year post-implantation. Via repeat median sternotomy with cardiopulmonary bypass support, the VAD was explanted. A titanium plug (manufactured by Steffan Fittkau GmbH, Berlin, Germany) was used to close the hole in the LV apex and preserve the sewing ring for potential need of future VAD support. Because the titanium plug is not a currently approved device by the US Food and Drug Administration, we had multiple lengthy discussions with the FDA before its clinical use. This is the first use of the plug in the United States.

Results: The patient did well post operatively and was discharged home on post-operative day 11. Postoperative echocardiography showed normal cardiac function. LV biopsy at explantation showed similar findings to those obtained at implantation (mild to moderate interstitial and endocardial fibrosis with myocyte hypertrophy). Myocardial recovery during long-term VAD support is a rare finding in children. Although the patient has been doing very well clinically, unfavorable myocardial histology is a concern for future deterioration of cardiac function. The use of the titanium plug and preservation of the LV sewing ring will allow us to more easily replace a VAD if her function declines again.

Supporting Children with Congenital Heart Disease with the HeartWare HVAD®

A. Jeewa,1 S. Denfield,2 E. D. McKenzie,2 J. Price,1 W. J. Dreyer,1 A. Cabrera,1 B. Elias,2 J. Heinle,1 I. Adachi.1
1Pediatrics, Baylor College of Medicine, Houston, TX; 2Texas Children’s Hospital, Houston, TX.

Study: Ventricular assist device (VAD) use in children has increased in recent years. The experience with continuous flow VADs in children with congenital heart disease (CHD) is limited. Our aim is to present the institutional outcomes of children with CHD who were supported with a HeartWare HVAD®.

Methods: Since 2013, all cases with CHD that were implanted with an HVAD® at our institution were reviewed. All patients met institutional criteria for VAD support. Institutional review board approval was obtained. Clinical outcomes were obtained from the medical record. Description of baseline characteristics was obtained in addition to support duration and associated complications.

Results: Three patients with CHD and severe ventricular dysfunction, all with a body surface area (BSA) < 1 m², underwent HVAD® placement. See Table 1 for cardiac diagnosis and post implant data. Each patient exhibited technical challenges of device implant. Patient 1 had multiple surgeries including coarctation repair, sub-aortic resection, and aortic root homograft replacement. The left ventricle (LV) inflow cannulation was complicated due to the small LV cavity with closely spaced mitral valve papillary muscles. Patient 2 had right hand topology (LV on the right side) due to his diagnosis of congenitally corrected transposition of the great arteries and required placement of the HVAD® more anterior and rightward than usual. Patient 3 was transitioned from ECMO to an HVAD®. Her heavily trabeculated systemic ventricle precluded insertion of HVAD® inflow into the ventricular cavity. Instead, cannulation was performed to the common atrium. In conclusion, this small subset of patients demonstrates the successful use of the HVAD® in children with CHD, although lengths of stay after implant were long. Children with CHD and a BSA < 1 m² can be successfully supported with an HVAD® but may require innovative implant methods of the inflow cannula.

Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Cardiac diagnosis</th>
<th>Age at implant (years)</th>
<th>BSA (m²)</th>
<th>Complications</th>
<th>LOS (days)</th>
<th>Current status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Shone’s complex (Sub-aortic stenosis and Coarctation)</td>
<td>9.9</td>
<td>0.86</td>
<td>Driveline infection</td>
<td>14 months on support</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>CCTGA v/p atrial switch and Rastelli repair</td>
<td>4.69</td>
<td>0.9</td>
<td>Chylothorax</td>
<td>9 months on support</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Dextrocardia, heterotaxy syndrome, total anomalous pulmonary venous return, unbalanced AVSD</td>
<td>10</td>
<td>0.9</td>
<td>GI bleed with over-coagulation</td>
<td>73</td>
<td>Transplanted after 150 days of support</td>
</tr>
</tbody>
</table>

BSA: body surface area; LOS: length of stay; CCTGA: congenitally corrected transposition of the great arteries; AVSD: atrioventricular septal defect; BCPS: bidirectional cavopulmonary shunt.
Full Liquid Ventilation in a Pediatric ECMO Patient
G. Fischer. University of Minnesota, Minneapolis, MN.

Study: While partial liquid ventilation has been studied in the adult and pediatric patient population, full liquid ventilation has rarely been investigated due to the challenges of this therapy with commercially available ventilators.

Methods: We describe the use of full liquid ventilation with Perflubron for an infant with refractory acute lung injury on ECMO. First instillation of Perflubron in this patient is shown on x-ray in figure 1.

Results: Use of full liquid ventilation correlated with improvement of lung compliance and eventual decannulation from ECMO.

Can Small Children Be Safely Supported to Transplant on Adult Continuous-flow Ventricular Assist Devices?
C. Villa. Cincinnati Children’s, Cincinnati, OH.

Study: Pediatric VAD programs are using adult continuous flow VADS (CF-VADs) that were engineered to meet the cardiac output needs of adults. Anecdotal evidence suggest pediatric centers are accommodating size differences by decreasing pump speed to avoid complications of supranormal cardiac output such as right ventricular (RV) failure. It remains unclear if these changes are effective at reducing the risk of RV failure without compromising device reliability and increasing the risk of complications. We sought to address the concerns for increased morbidity and mortality in small children bridged to transplant with CF-VADs.

Methods: The UNOS database was used to identify pediatric patients that were listed for transplant and had a CF-VAD from 2003 to 2013. Patients were stratified into 2 groups based on body surface area (1.5m2).

Results: A total of 152 patients were identified, 23 (15%) were <1.5 m2. The median age at listing was 11 yr (1.5m2). The smallest listed VAD patient was 0.6 m2; the smallest patient transplanted was 0.8 m2. No patients < 1.5 m2 were ventilated at the time of transplant. There were no significant differences in end organ function, inotrope use at transplant, waitlist mortality or 1 year survival between groups (Table 1).

Conclusions: This data shows no significant increases in right heart failure (via surrogates such as inotrope use, bilirubin), ventilator use, cerebrovascular disease or waitlist mortality in patients < 1.5 m2 that are supported with a CF-VAD. Thus, despite being engineered for adults, CF-VADs can be used to bridge children <1.5 m2 without significant morbidity and mortality. Further study is needed to establish the point where patient size compromises device reliability and patient outcomes.

<table>
<thead>
<tr>
<th>Variable</th>
<th>BSA Group &lt; 1.5 m² (25 patients)</th>
<th>BSA Group ≥ 1.5 m² (127 patients)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
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<td>BSA range (m²)</td>
<td>0.6-1.4</td>
<td>1.5-2.7</td>
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<tr>
<td>Number of days on waitlist</td>
<td>72 (44-110)</td>
<td>65 (29-180)</td>
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<tr>
<td>Patients with inotrope use at listing</td>
<td>16 (33%)</td>
<td>66 (33%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Patients with inotrope use at transplant</td>
<td>6 (27%)</td>
<td>25 (20%)</td>
<td>0.39</td>
</tr>
<tr>
<td>Ventilator at listing</td>
<td>3 (15%)</td>
<td>19 (15%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Ventilator at transplant</td>
<td>0 (0%)</td>
<td>3 (2%)</td>
<td>1.0</td>
</tr>
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<td>Creatinine at transplant (mg/dL)</td>
<td>0.8</td>
<td>0.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Bilirubin at transplant (mg/dL)</td>
<td>0.6</td>
<td>0.9</td>
<td>0.1</td>
</tr>
<tr>
<td>Deaths on waitlist (%)</td>
<td>1 (4%)</td>
<td>5 (4%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Post-transplant mortality</td>
<td>1 (5%)</td>
<td>24 (19%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Death &lt; 1 month</td>
<td>0 (0%)</td>
<td>2 (1%)</td>
<td>1.0</td>
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<tr>
<td>Death 1 month-1year</td>
<td>1 (5%)</td>
<td>4 (3%)</td>
<td>0.49</td>
</tr>
</tbody>
</table>
**Thrombosis in Pediatric ECMO: Comparison Centrifugal and Roller Pumps**

S. Hastings. Georgia Institute of Technology, Atlanta, GA.

**Study:** Thrombosis in pediatric extracorporeal membrane oxygenation (ECMO) is a frequent complication. The balance of anticoagulation to prevent thrombosis while avoiding hemorrhage remains challenging. It is unknown if there are differences in the risk of thrombosis with the type of ECMO circuit pump used, most commonly the roller head (RP) or the centrifugal pump (CP).

**Methods:** Fifty pediatric ECMO circuits were obtained following removal from extracorporeal support. Circuits were inspected for thrombi, and some samples of thrombi were preserved and histologically studied. CP and RP circuits are divided into two segments, the pump and the loop. For roller pumps, the length of tubing that passes through the roller head is considered as the pump segment. Of the 50 circuits studied, 34 were RP, and 16 were CP. Better Bladders® were used in 39 cases, 11 used silicone bladders.

**Results:** All CP (16/16) exhibited clot at the top of the shaft with some cases having large thrombi present (Fig 1). In contrast, none of the RP pump segments had clot (0/34, p<0.001). In addition, CP loop segments had more adherent thrombosis than RP circuit segments, with incidence of clot of 41% vs. 25%, respectively (p<<0.01). The “Better Bladder” had no thrombi (0/39), whereas all the silicone bladders (11/11) exhibited thrombi at both entrance and exit. These results show a wide disparity in the development of clots in ECMO circuits powered by RP versus CP, as well as by type of bladder. Further refinement in anticoagulation strategies for ECMO patients will have to take into account the components of the circuit, and may necessitate changes in anticoagulation based on the equipment used.

Fig 1. CP samples. A: Minimal thrombus formation at the top of the shaft. B: Large thrombus at the pump inlet.

**Characterizing Magnetically Levitated Pediatric VAD and Further Miniaturization of Magnetic System**

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**Study:** A magnetically levitated rotary blood pump which consists of a double stator type maglev motor and centrifugal pump is undergoing development for heart disease treatment of pediatric patients including both infants and small children. A newly developed magnetic levitation theory which can completely levitate a rotating impeller has significant advantages of miniature device size, long life expectancy and high blood compatibility. This research investigated pump performances of the developed maglev pediatric VAD. And miniaturization of the magnetic system was carried out to achieve fully implantable device.

**Methods:** The maglev pediatric VAD has two stators which have an identical structure and a levitated impeller axially sandwiched by the stators. Dimensions of the developed VAD is 28 mm in outer diameter, 41 mm in length and 25 ml in volume. Head pressure and flow rate characteristics of the developed VAD were demonstrated in a closed circulation loop. Toward further miniaturization of the pediatric VAD, detailed geometries of magnetic system were determined based on three-dimensional magnetic field FEM analysis. The magnetic suspension forces and rotating torque characteristics of the designed motor were then evaluated.

**Results:** The developed pediatric VAD achieved wide flow rate range of 0.1~5.0 L/min against a head pressure of 100 mmHg by changing a rotating impeller speed from 2000 rpm to 5000 rpm. It indicates a sufficient potential of long term circulation of pediatric patients growing up. A hemocompatibility of the developed pediatric VAD is being evaluated. The newly designed motor was significantly miniaturized up to 22 mm in outer diameter and 34 mm in total height. The volume of the designed motor was decreased by half of the developed prototype, maintaining sufficient magnetic suspension force and rotating torque capacity required for the pediatric VAD operation. Actual magnetic suspension and rotation performances of the maglev motor are being evaluated.
Pulmonary Artery Band Reduces Left Atrial Pressure in Dilated Cardiomyopathy

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Study: A 6 week old female presented with cardiogenic shock and acute kidney injury. She was intubated and commenced on high-dose inotropic support before transfer to our institution. Echocardiography demonstrated severely depressed LV function with moderate mitral regurgitation. Despite optimal medical therapy over the next 3 weeks, she remained TPN dependent and required inotropic and ventilatory support. Due to progressive decline in her clinical status, ventricular assist device (VAD) support was deemed necessary. However, given the higher risk profile of VAD support in small children, a decision was made to attempt pulmonary artery band (PAB), with VAD as a backup option. The procedure was performed via median sternotomy. Left atrial pressure (LAP) and right ventricular pressure (RVP) were monitored, in addition to CVP and systemic arterial pressure. With gradual tightening of PAB, there was an incremental decrease in LAP with only minimal change in CVP. As a result, the pressure difference between LAP and CVP decreased with PAB tightening. At the end of the operation, LAP and CVP became equivalent when RVP reached 65% systemic. Simultaneous transesophageal echocardiogram showed subtle shift of the interventricular septum leftward, resulting in modest increase in RV volume. She tolerated the procedure and was extubated on day 5. Serial echocardiograms failed to demonstrate any obvious improvement; LV function remained severely depressed with an ejection fraction of approximately 30% with continued moderate mitral regurgitation. Her clinical status was, however, completely changed. The most notable difference was tolerance of full enteral feeding and accompanying somatic growth. She has been stable on milrinone since the PAB placement, currently awaiting heart transplantation on the general inpatient unit. With appropriate patient selection, PAB may help to delay or avoid VAD placement in small children, who are high-risk candidates for VAD support.

Methods: Case report

Results: Case report

Family of New Polish Moll Type Tilting Disc Valves for Application in Pediatric Pneumatic VAD - Functional and Performance In-vitro and In-vivo Studies.

M. Glowacki, M. Gawlikowski, M. Jaworek, R. Kustosz, M. Koscielniak-Ziemniak. Artificial Heart Laboratory, Profesor Zbigniew Religa Foundation of Cardiac Surgery Development, Zabrze, POLAND.

Study: Due to lack of satisfactory solution on the market, the specialists from Foundation of Cardiac Surgery Development and Łódź University of Technology designed a unique valve dedicated to pediatric VADs. Construction of the valves was designed to lower the risk of thrombogenicity, providing low pressure drop and back flows. Moll type tilting disc pediatric valves come in four sizes: 14, 16, 18 and 20mm diameter. They are designed to be mounted in extracorporeal, pneumatic ReligaHeart PED VAD. The purpose of this research is to validate good hemodynamic and athrombogenic features of developed valves in physical, in-vitro and in-vivo studies. The results have to provide an answer if the valves can be qualified to be applied in pediatric VAD.

Methods: The first phase of development studies involves physical examination performed in compliance with ISO 5840 guidance, and long term fatigue tests. Next stage includes in-vitro studies conducted in accordance with acute thrombogenicity method. The final phase consists of early pre-clinical stage which involves acute in-vivo experiments. In-vivo experiments include implantations of two sizes of pediatric VADs: 45ml stroke volume (SV) equipped with 18 and 20mm size valves and 30ml SV equipped with 14 and 16mm size valves to domestic pigs. Total in-vivo experiment time was 68 hours. The following data was collected during experiment: blood flow, driving pressure, micro and macro biological material received after deplantation. The procedure was performed via median sternotomy. Left atrial pressure (LAP) and right ventricular pressure (RVP) were monitored, in addition to CVP and systemic arterial pressure. With gradual tightening of PAB, there was an incremental decrease in LAP with only minimal change in CVP. As a result, the pressure difference between LAP and CVP decreased with PAB tightening. At the end of the operation, LAP and CVP became equivalent when RVP reached 65% systemic. Simultaneous transesophageal echocardiogram showed subtle shift of the interventricular septum leftward, resulting in modest increase in RV volume. She tolerated the procedure and was extubated on day 5. Serial echocardiograms failed to demonstrate any obvious improvement; LV function remained severely depressed with an ejection fraction of approximately 30% with continued moderate mitral regurgitation. Her clinical status was, however, completely changed. The most notable difference was tolerance of full enteral feeding and accompanying somatic growth. She has been stable on milrinone since the PAB placement, currently awaiting heart transplantation on the general inpatient unit. With appropriate patient selection, PAB may help to delay or avoid VAD placement in small children, who are high-risk candidates for VAD support.

Methods: Case report

Results: Case report
In vivo testing of the Penn State Infant VAD with Progressive Reductions in Anticoagulation

W. J. Weiss, J. B. Clark, J. M. Izer, B. Lukic, B. Bixler, T. Cooper. Surgery and Bioengineering, Penn State Hershey Medical Center, Hershey, PA.

Study: The Penn State Infant Ventricular Assist Device (VAD) is a 12–14 ml stroke volume pneumatic pulsatile VAD intended for infants. Previously published results have shown excellent biocompatibility in 20-30kg lambs using unfractionated heparin anticoagulation at low doses based on 2x normal aPTT and 2x normal TEG R-time protocols.

Methods: Based on these positive results, we have recently extended the testing to eliminate all heparin anticoagulation except for the immediate post-operative acute phase (typically 2–3 weeks) when the animal would be hypercoagulable without anticoagulants. Under this 1x R-time “normo-coag” protocol, heparin is only given during the acute phase to maintain TEG R-time in the normal (1x) range, after which heparin is discontinued. Platelet inhibitors are not used in any of the protocols.

Results: Results for 4 studies performed under the 2x R-time protocol, and 2 studies performed under the 1x R-time normo-coag protocol, are shown below (mean ± sd). Average heparin doses were lower in the 1x group. The TEG coagulation index was nearly normal in the 1x R-time group. There were no significant differences between pre-op and post-op coagulation measures, which together with the undetectable levels of heparin antifactor Xa, indicates extremely low levels of heparin activity. At necropsy, 3 of the 4 animals in the 2x R-time protocol had grossly normal kidneys, one with microscopic chronic lesions. Of the 2 animals in the 1x R-time protocol, one had grossly normal kidneys with 1 microscopic cortical infarct, and the other showed 2 chronic cortical infarcts in one kidney. In summary, progressive reductions in, and elimination of, heparin anticoagulation during testing of the Penn State Infant VAD in lambs presents a challenging test for VAD biocompatibility. Initial results in small numbers of animals are encouraging, with no clinical evidence of thromboembolism.

<table>
<thead>
<tr>
<th></th>
<th>2x R-time protocol (n=4)</th>
<th>1x R-time (normo-coag) protocol (n=2)</th>
<th>Pre-op normal (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heparin (U/kg/hr)</td>
<td>24.6 +/- 13.1</td>
<td>1.95 +/- 0.35</td>
<td>0</td>
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<tr>
<td>aPTT (secs)</td>
<td>30.5 +/- 9.2</td>
<td>33.5 +/- 4.31</td>
<td>30.1 +/- 5.4</td>
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<td>ACT (secs)</td>
<td>167 +/- 8.3</td>
<td>170 +/- 13.4</td>
<td>171 +/- 18.2</td>
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<td>Anti-Xa (IU/ml)</td>
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<td>&lt; .05</td>
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<tr>
<td>TEG R-time (mins)</td>
<td>17.4 +/- 4.5</td>
<td>13.2 +/- 6.4</td>
<td>13.9 +/- 9.8</td>
</tr>
<tr>
<td>TEG Coag Index</td>
<td>-6.3 +/- 5.6</td>
<td>-4.9 +/- 7.1</td>
<td>-4.2 +/- 8.7</td>
</tr>
</tbody>
</table>

Weaning of a Continuous Flow Left Ventricular Assist Device: Decision to Exclude the Device

M. B. Jones, G. Oldenburg, A. Lowry, J. Scheel. Critical Care Medicine, Children's National Health System, Washington, DC

Study: Introduction: Continuous flow left ventricular assist devices (LVAD) have been successfully implanted in pediatric patients with advanced heart failure as a bridge to transplant. Cardiac recovery and subsequent device explant or exclusion is rare in the pediatric population, and reports in the literature are scarce.

Methods: Case Description: EY is a 13 year old female with osteosarcoma and acute fulminant heart failure requiring ECMO support following her chemotherapy course. She had previously undergone a below-the-knee amputation of the affected limb. EY failed to wean from ECMO support and at 10 days a Heartmate II LVAD (Thoratec Corporation, Pleasanton, CA) was implanted. Six months after VAD implant, her echocardiogram demonstrated recovery of cardiac function. After a series of testing we decided to exclude her device in the cardiac catheterization lab using two vascular plugs in the outflow of the VAD, stopping the pump and excising the driveline.

Results: Discussion: The published reports for testing prior to VAD explantation rely heavily on exercise stress testing. With her prosthesis, EY was not physically able to do the standard treadmill stress testing. We developed a customized weaning protocol based on recommendations from other centers and reports in the literature. On echocardiogram, her left ventricular systolic function is normal on VAD flow of 8400 rpm. Temporary VAD weaning trials demonstrate no decrement in systolic function. Initial results in small numbers of animals are encouraging, with no clinical evidence of thromboembolism.
Development of a Pediatric Lung Assist Device for Cystic Fibrosis Patients

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Study: Cystic fibrosis (CF) is a genetic respiratory disease that is the leading cause for lung failure and the necessity for lung transplants in pediatric patients. Lung transplantation commonly involves the use of extracorporeal membrane oxygenation (ECMO) or mechanical ventilation (MV) as a bridge to transplant. However, many studies have shown that the use of these methods can cause poor post-transplant outcomes for the patient. The Medical Devices Laboratory is developing the Pediatric Paracorporeal Ambulatory Lung (P-PAL). This device will utilize the concepts of active mixing in a hollow fiber membrane (HFM) bundle design, building on the previous work with the use of impellers for active mixing in gas exchange devices. The P-PAL will be used to address problems associated with the use of ECMO and MV in pediatric patients with respiratory conditions, such as CF. Hypothesis: In this study, we hypothesize that the active mixing in the P-PAL device will produce at least 60% of the patients’ necessary gas exchange at 3 LPM with a reduced surface area of 0.3 m2 with a pressure head of at least 70 mmHg. The patient population for the P-PAL consists of cystic fibrosis patients weighing 10–40 kg.

Methods: The P-PAL device was adapted from previous work in the lab that used computational flow dynamics to optimize active mixing. The P-PAL was tested for pumping ability, gas exchange efficiency and hemolysis values in a mock circulation loop using porcine blood.

Results: Results and Discussion: The experimental oxygenation capacity of the P-PAL in porcine blood tests was 76 mL/min, satisfying the gas exchange requirements for patients up to 30 kg. At 1200 RPM and 3 LPM, the P-PAL also satisfies the pumping requirement necessary to use a 22 Fr cannula.

Evolution and Impact of Ventricular Assist Device Program on Pediatric Heart Transplant Waiting List

I. Adachi,1 M. S. Khan,1 F. Guzman-Pruneda,1 C. D. Fraser, 3rd,2 C. M. Mery,1 S. W. Denfield,3 W. J. Dreyer,3 D. L. S. Morales,4 E. McKenzie,1 J. S. Heinle,1 C. D. Fraser, Jr.1 1Congenital Heart Surgery, Texas Children’s Hospital, Houston, TX; 2University of Texas at Houston School of Medicine, Houston, TX; 3Pediastrics, Texas Children’s Hospital, Houston, TX; 4Congenital Heart Surgery, Cincinnati Children’s Hospital, Cincinnati, OH.

Study: We sought to evaluate the impact of the evolution of a pediatric mechanical circulatory support (MCS) program on outcomes of children listed for heart transplantation at our institution.

Methods: All patients listed for isolated heart transplantation from 1995 to 2013 were included. The use of MCS while on the wait-list was recorded. Wait-list and posttransplant outcomes were compared before and after 2005, which was when we became capable of providing long-term MCS without size limitation.

Results: In total, 259 patients were listed for transplant and 201 (78%) reached transplant. The use of MCS was significantly increased between the eras (13% and 37%, p = 0.0001). Wait-list mortality was significantly decreased (25% and 11%, p = 0.0006). Among transplant recipients, the proportion of patients who underwent MCS was significantly increased (13% and 37%, p = 0.0002). Of these MCS patients, the use of long-term devices was significantly increased (50% and 98%, p = 0.0004). Median duration of MCS was significantly increased (12 and 78 days, p = 0.004). Kaplan-Meier estimates showed a trend (p = 0.08) toward improved survival after bridge-to-transplant both at 1 year (70% in the early era and 88% in the late era) and at 5 years (60% and 78%, respectively). Outcomes of pediatric heart transplantation have significantly improved over the last 2 decades. We believe such improvement is, at least in part, attributable to maturation of MCS strategy, characterized by avoiding the use of temporary devices such as extracorporeal membrane oxygenation as a bridge-to-transplant and a more aggressive use of long-term devices.
Pediatric Heart Transplantation on Impella LVAD Support
S. Burki,1 S. W. Denfield,1 W. J. Dreyer,2 A. Liou,2 H. Justino,2 I. Adachi.1 1Congenital Heart Surgery, Texas Children’s Hospital, Houston, TX; 2Pediatric Cardiology, Texas Children’s Hospital, Houston, TX.

Study: We describe our experience with Impella as bridge to transplant in a pediatric patient.

Methods: A 15 yo male (BSA 2m2) was referred to our institution with abdominal pain, vomiting and cough. History was significant for heart transplant 10 years ago. Examination revealed gallop, decreased basal breath sounds and hepatomegaly 4cm below RCM. He was also oliguric. Lab investigations were significant for BNP 1293pg/mL and elevated creatinine. Chest xray showed cardiomegaly and bilateral pleural effusions. Severely depressed LV function, superimposed on global cardiac dysfunction, was found on echo. LVEDD was 4.3 cm (-1.8 z-score) with mitral regurgitation. He was diagnosed with heart failure secondary to presumed graft rejection, with associated kidney injury. During induction for diagnostic catheterization, he suffered cardiac arrest requiring CPR. Due to inadequate response, ECMO and Impella CP support was commenced. In the interim he also became dialysis dependent. Biopsy confirmed antibody-mediated rejection and an aggressive immunosuppressive regimen was started. This treatment strategy resulted in overall hemodynamic stabilization, enabling ECMO decannulation on POD12 and Impella weaning on POD18. Despite gradual improvement, he complained of new onset syncope 3 weeks later. Echo revealed LVEDD of 4.9 cm (-0.8 z-score), LVEF 26% and worsening RV function. Inotropes were resumed for hypotension. In the setting of deteriorating cardiac output despite maximal medical management, surgical options for BTT were explored. Consensus opinion favored Syncardia TAH, preceded by Impella 5.0 to mitigate end organ dysfunction. 10 days after Impella was reinitiated, the patient was successfully bridged to transplant.

Results: The use of Impella LVAD in children lags behind adult population. Reported applications in children include bridge to longterm device, which was the goal in this patient. However, the fortuitous availability of a suitable heart redirected our strategy to BTT after support totaling 28 days.

Thromboelastography/Platelet Mapping in Children Supported with the Berlin Heart EXCOR Pediatric: When Might It Not Work and What Are the Alternatives?

Study: Background: Pediatric centers rely primarily on Thromboelastography and Platelet Mapping™ (TEG/PM) to dose-adjust platelet inhibitors in children supported with the Berlin Heart EXCOR® Pediatric. It is unclear whether TEG/PM™ results are accurate because PM has not been validated in children. We sought to evaluate the agreement between 3 platelet function assays in a Berlin Heart recipient who had a poor PM™ response despite high-dose platelet inhibitor therapy.

Methods: Platelet function was measured serially using TEG/PM™, standard optical platelet aggregometry (OA) and Multiplate (MP) in a 3 year-old boy supported with a Berlin Heart. For TEG/PM™, ASA response was evaluated by % inhibition to Arachidonic Acid (AA) while DPA and clopidogrel response was evaluated by % inhibition to adenosine di-phosphate (ADP). Platelet aggregation for OA was evaluated by % aggregation and for MP by standardized units (out of 100).

Results: Following EXCOR® implant, ASA was uptitrated to a target dose of 30 mg/kg/day, DPA to 4 mg/kg/day and clopidogrel to 1 mg/kg/day as per institutional protocol. At target doses, the %AA inhibition from TEG/PM™ (N=34) ranged from 0% to 33% and the %ADP inhibition ranged from 0% to 35% consistent with a poor response. By contrast, OA revealed a %AA and %ADP aggregation of of 5–35% and MP revealed ASA and ADP aggregation of <30 U, both consistent with good platelet response.

Conclusion: In selected patients PM™ has poor agreement with OA raising questions about its validity. By contrast OA has good agreement with MP, which requires a smaller blood sample (<1 cc) suggesting it may have advantages over PM™. Further studies are need to determine the optimal method for measuring platelet function in children.
Outpatient Management of Ventricular Assist Device in a Child With Unrepaired Single Ventricle

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1 Congenital Heart Surgery, Texas Children’s Hospital, Houston, TX; 2Pediatric Cardiology, Texas Children’s Hospital, Houston, TX.

Study: Since contemporary pediatric VADs are extracorporeal, most children with VAD are managed as inpatient. Ongoing device miniaturization will result in greater impact on the community due to associated unique anatomic and physiologic complexities. We describe the outpatient management of a child with unrepaired congenitally malformed heart, where VAD support has generated a unique physiology that has rarely been experienced before.

Methods: A 10yo female with single ventricle physiology presented with cardiogenic shock. She had atroventricular septal defect in the setting of Heterotaxy syndrome. She had undergone multiple palliations culminating in bilateral Glenn physiology. Due to severe common atrial hypertension, the lungs were hypoperfused, exaggerating cardiac dysfunction. She was placed on ECMO. Severity of heart failure precluded ECMO weaning. Her innate pulmonary function was tested and found to be adequate. She was transitioned to a HeartWare HVAD despite this approach having never been described in such malformations. Multidisciplinary care was instituted to facilitate discharge. Foremost, familial support network was evaluated. The constant presence of a chaperone was emphasized. Caregivers received training in device management. The patient’s power company was contacted to ensure a secure connection. She had two field trips. 2 months later, she was discharged, and managed for 2.5 months as outpatient with regular clinic visits. Physical therapy and a cardiac dietitian were consulted to improve her physical status. At 5 months of support, she was successfully transplanted.

Results: Outpatient management of children on VAD will challenge the pediatric community, particularly if VADs are employed in children with complex congenital heart disease. Given the increasing number of children with unrepaired SV in the setting of ongoing revolution of miniaturized VADs, it would be reasonable to expect that community practitioners will encounter such patients.

Physical Recovery in Children Undergoing Long-term Ventricular Support With a Miniaturized Implantable Device

F. Guzman-Pruneda,1 A. Jeewa,2 B. A. Elias,3 C. M. Mery,1 E. McKenzie,1 J. S. Heinle,1 C. D. Fraser, Jr.1 I. Adachi1
1 Congenital Heart Surgery, Texas Children’s Hospital, Houston, TX; 2Pediatric Cardiology, Texas Children’s Hospital, Houston, TX.

Study: We report our HeartWare HVAD experience at a single pediatric center.

Methods: We conducted a retrospective review of consecutive patients who underwent HVAD placement. Data are presented as medians with ranges. Non-parametric, related sample tests were performed to compare end-points.

Results: HVAD was implanted in 10 children. Median age and body surface area were 10 (5–14) years and 0.9 (0.6–2.0) m2, respectively. Diagnoses included: cardiomyopathy in 7 and end-stage congenital heart disease in 3 (2 biventricular and 1 univentricular physiology). Median ventilatory support and intensive care duration was 1 (0–3) days and 14 (9–16), respectively. There was 1 hospital mortality due to ischemic bowel perforation. Outcomes of the 9 remaining late survivors: bridge to transplantation (n=4), ongoing support (n=1), explantation due to myocardial recovery (n=1), with a median support duration of 5 (4–42) months. There were no neurologic complications, except a minor stroke in a patient with antiphospholipid syndrome. Long-term support allowed for somatic growth and nutritional optimization: pre-implantation vs. last follow-up or explantation pre-albumin (13.1[3.7–17] vs 18.8[6.9–28.8] mg/dL; p=0.03); albumin (3.8[2.9–4.4] vs 4.0[3.8–5.1] g/dL; p=0.02); weight (24.8[13.7–85.2] vs 31.8[17.2–92.8] kgs; p=0.03); BSA (0.9[0.6–2.0] vs. 1[0.7–1.9] m2; p=0.03). The HVAD can effectively support children with a body surface area as low as 0.6 m2. Long-term, outpatient management allows for full physical recovery and offers opportunity to assess for potential myocardial recovery.
Inolivent: An Advanced Liquid Ventilator Prototype for Preclinical Research in Total Liquid Ventilation

R. Robert,1 M. Nadeau,1 O. Avoie,1 J. Vandamme,1 J. Mousseau,1 M. Sage,1 M. Kohlhauer,1 J. P. Praud,1 H. Walti,1 R. Tissier,1 P. Micheau.1 1Mechanical Engineering, Universite de Sherbrooke, Sherbrooke, QC, CANADA; 2Physiology, Universite de Sherbrooke, Sherbrooke, QC, CANADA; 3INSERM U-955 Team 3, Maison-Alfort cedex, FRANCE; 4Pediatrics and Physiology, Universite de Sherbrooke, Sherbrooke, QC, CANADA.

Study: Total liquid ventilation (TLV) consists in completely filling the lungs with a perfluorocarbon liquid (PFC) and using a liquid ventilator to move the PFC into and from the lungs. We have developed a liquid ventilator technology (Inolivent) which incorporates advanced pump, temperature and pressure controllers in order to ensure efficient and safe TLV.

Methods: The technology was experimentally tested for two therapeutic treatments in two different laboratories. The fast induction of hypothermia by TLV in a juvenile rabbit model was evaluated at Inserm U955 (Créteil, France) with Inolivent-5. The lung lavage on newborn lambs by TLV was evaluated at Université de Sherbrooke (Canada) with Inolivent-6 (a copy of Inolivent-5).

Results: The experimental protocol was approved by the institutional Ethics Committee for Animal Care and Experimentations. Animals were intubated, anaesthetised and paralysed. Lambs were placed in respiratory distress by meconium instillation (PaO2/FiO2< 100mmHg). Afterward, they were ventilated in TLV during 4 hours (n=6). At the end of the TLV, the blood gas were normal (PaO2=112.7 ± 23.6 mmHg and PaCO2=46.4 ± 6.2 mmHg). The minute ventilation achieved was 150 ± 10 ml/min/kg for a tidal volume of 21.7 ± 1.3 ml/kg at a PEEP of 3.8 ± 0.4 cmH2O. Rabbits were ventilated in TLV during 30 minutes (n=5), the PaO2 and PaCO2 were 346 ± 44 (FiO2 of 100%) and 46.7 ± 2.8 mmHg, for a tidal volume of 21.7 ± 1.3 ml/kg at the minute ventilation of 92 ± 13 ml/min/kg. The PEEP was 2.8 ± 0.6 cmH2O. The arterial and tympanic temperatures reached the targeted temperature of 33.5°C in 5.6 ± 1.8 and 14.4 ± 5.7 minutes respectively. The results show that the technology Inolivent can be used for therapeutic treatments, while supporting the patient’s ventilation. These cumulated results demonstrate that the technology Inolivent can be successfully used in different research centers by clinician on different protocols to evaluate the potential of TLV for clinical applications.

Veno-Venous Versus Veno-Arterial Extracorporeal Membrane Oxygenation for Patients with Acute Respiratory Distress Syndrome Requiring Pre-cannulation Hemodynamic Support: A Review of the ELSO Registry

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Study: In addition to severe hypoxia and hypercapnea, acute respiratory distress syndrome (ARDS) can present with significant hemodynamic compromise requiring inotropic/vasopressor support. Either veno-venous (VV-ECMO) or veno-arterial (VA-ECMO) extracorporeal membrane oxygenation can be offered in this situation. However, a comparison of these two cannulation strategies has yet to be well described.

Methods: The ELSO registry was reviewed for all adult ARDS cases between 2009 and 2013 in patients that required inotropes/vasopressors prior to ECMO initiation. Demographics, pre-ECMO/ECMO variables, and outcomes were compared based on initial cannulation strategy to either VV or VA-ECMO.

Results: Of 717 ECMO runs, there were 591 VV and 126 VA-ECMO cases. Over the study period, the proportion of VA-ECMO cases decreased from 20% (2009–2010), to 19% (2011–2012), to 14% (2013). VV-ECMO support was associated with fewer pre-ECMO inotropes/vasopressors (1.2 ± 0.9 vs. 1.7 ± 1.1, p<0.001). Mean duration of ECMO support was similar between VV and VA-ECMO cases (11 ± 15 vs. 11 ± 16 days, p=NS), and conversion from VV to VA-ECMO was 4%. VV was associated with less gastrointestinal bleeding (5% vs. 9%, p=0.073) and hemolysis (7% vs. 13%, p=0.038); but overall rates of bleeding, stroke, and renal failure were similar compared to VA-ECMO. Survival to discharge was 58% for VV in contrast to 43% for VA-ECMO (p=0.002). Multivariable regression analysis revealed VV to be an independent predictor of survival to discharge relative to VA-ECMO.

Conclusions: In this review of ARDS patients requiring pre-ECMO hemodynamic support, VV was associated with superior survival and lower complication rates compared to VA-ECMO. These data suggest that, in this population, it may be reasonable to initially institute VV support, reserving VA-ECMO for conversion in patients with refractory hypotension.
Correlation Between End Tidal CO2 and PaCO2 in Alcohol Withdrawal Patients

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Investigation: A common adverse reaction of benzodiazepines is respiratory depression that is defined as when ventilation is insufficient to achieve the necessary gas exchange for normal metabolic function. In order to monitor for this unwanted outcome, arterial blood gas (ABG) is the standard of care to track the partial pressure of carbon dioxide (PaCO2) levels. This retrospective study was carried out in order to assess the value of ETCO2 in comparison to PaCO2 from ABGs in monitoring respiratory depression secondary to benzodiazepine treatment in alcohol withdrawal patients. We wanted to look for a surrogate marker that is cost effective, rapid, and less labor intensive.

Methods: Patients admitted to the ICU experiencing alcohol withdrawal have been retrospectively evaluated for respiratory depression using ABG’s and ETCO2 simultaneously. The ICU protocol stated at the time of presentation, ABGs should be drawn 30 mins after reaching a total dose of 650 mg intravenous boluses of Phenobarbital and at the time of reaching 30 mg/hr of lorazepam infusion to monitor early signs of respiratory depression. ETCO2 will be recorded at the time of every arterial blood draw and every hour until they are out of delirium tremens. ETCO2 is currently measured by sampling the exhaled air through endotracheal tube for patients who require mechanical ventilation. We looked into the above-mentioned patient’s charts and gathered the data pertaining to their medical history, ICU course, vital signs, CIWA score at the time when ABG was drawn, PaCO2 and ETCO2 values.

Results: Total of 36 patients (83% males) included in the study, with a mean age of 46 (SD-10). Their mean CIWA was 12 (SD-8). A total of 92 paired PaCO2 and ETCO2 variables were gathered. A Pearson Correlation was performed to correlate PaCO2 (Mean 39.94 mmHg SD-7.16) and ETCO2 (Mean 30.15 mmHg SD-6.32). We found a positive correlation of r=0.564 (p<0.001). ETCO2 - PaCO2 gradient can be a more efficient, less invasive way to monitor non-intubated patients with acute hypoventilation.

Evaluation of Thrombus Distribution in an Oxygenator After Long Term ECMO

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Investigation: Some of oxygenators in ECMO systems have been demonstrated durability for over 1 week continuous use recently. Blood-gas data is measured over time during ECMO, and used as an index of management. On the other hand, thrombus distribution is extremely difficult to evaluate during ECMO. In this study, we conducted ECMO experiment using a membrane oxygenator (BIOCUBE2000), and systematically evaluated the change of thrombus formation due to conditions of anticoagulant therapy and ECMO period by quantifying the thrombus distribution in the oxygenator after ECMO using an image processing.

Methods: An ECMO system was consisting from the oxygenator, and its entire blood-contacting surface was coated with a heparin bonding material (T-NCVC). VA-ECMO was conducted on 8 goats (19–30 kg). Four groups (n = 2 each) were determined from the combination of 2 types of anticoagulant therapy (continuous heparin administration with keeping ACT of 150–200 sec or no continuous anticoagulation using heparin etc.), and 2 types of ECMO period (2 weeks or 5 weeks). After each experiment, we took section images of inlet side, middle and outlet side of blood passage in the oxygenator. Each image was normalized for brightness, and the red thrombus area was distinguished by converting the image to binary format, and ratio of red thrombus area to all area was calculated.

Results: The average area ratios of red thrombus at inlet side, middle and outlet side were 0.002, 0.000 and 0.000 in the group for 2 weeks with heparin administration, 0.049, 0.001 and 0.013 in the group for 2 weeks without continuous anticoagulation, 0.052, 0.001 and 0.000 in the group for 5 weeks with heparin administration, 0.147, 0.178 and 0.249 in the group for 5 weeks without continuous anticoagulation, respectively. The change of thrombus formation in the oxygenator due to the difference in the presence or absence of continuous anticoagulant therapy and ECMO period could be evaluated quantitatively by expressing thrombus distribution as the area ratio at each section.
The Requirements That We Should Be Careful for Effective Single-cannulation in Venovenous Extracorporeal Membrane Oxygenation
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Study: The Avalon Elite® double-lumen catheter (DLC) for venovenous extracorporeal membrane oxygenation (VV-ECMO) is available in several countries. DLC has few risks of bleeding and infection without requiring dual site puncture and it can lead to facilitation of early mobilization. However, bypass flow may be limited because the lumen diameter of DLC is smaller than that of catheter for dual cannulation. Therefore, blood oxygenation may be insufficient and return blood may become jet stream. The aim of this study is to investigate necessary bypass flow for blood oxygenation and measure return circuit pressure.

Methods: 23Fr (n = 2) and 27Fr (n = 4) DLCs were inserted to adult goats (BW 60.1 ± 0.6 kg) under general anesthesia. Cannula positions were confirmed radiographically. The ventilator was stopped and ECMO was started at the same time, and sufficiency of oxygenation was examined by measuring the arterial oxygen saturation (SaO2) and pressure (PaO2). In addition, the return circuit pressure (RP) between DLC and circuit was measured. The goats were sacrificed after experiment, and they were observed the superior vena cava, inferior vena cava and heart.

Results: In the ELSO guideline, adequate support is defined as a SaO2 of greater than 80% in VV-ECMO, that condition was satisfied when the bypass flow rates were higher than 2 L/min. Twenty minutes after starting VV-ECMO, PaO2 was 23.0 ± 1.5, 50.6 ± 5.2, 110.7 ± 29.8 mmHg at 1, 2 and 3 L/min respectively. When 23Fr DLCs were used, the RP was greater than 300 mmHg at 3 L/min in the right atrium at sacrifice. Stable bypass flow was able to maintain even 4 L/min when 27Fr DLCs were used, and the injury was not observed around the heart. DLC is useful for sufficient oxygenation. However, when we intend to increase bypass flow more than necessary, complications increases. The use of DLC in the appropriate range is important.

Novel Methods to Mitigate Serious Adverse Events Associated With Nitrogen Dioxide (NO2) During Inhaled Nitric Oxide (NO) Therapy
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Study: A serious risk associated with delivery of inhaled NO is the unavoidable co-delivery of NO2. NO2, an unwanted toxic contaminant, is generated by the interaction of O2 with the NO during delivery to the patient. NO2 triggers extracellular effects in the airways when it oxidizes normally protective components, such as the antioxidant, glutathione, within the epithelial fluid lining (EFL). These reactions of NO2 within the EFL trigger oxidative stress, swelling, edema, bronchoconstriction, and a reduced FEV1 (forced expiratory volume in 1 second). A new approach that converts NO2 to NO, reduces co-delivery of NO2 during NO therapy and may minimize the typical sequelae of NO therapy.

Methods: The delivery of NO2 to the patient can be minimized utilizing a cartridge that converts NO2 back to NO. As NO2 passes through the cartridge, an antioxidant strips off one atom of oxygen converting it to NO prior to delivery to the patient. A clinical trial was conducted using the GeNO LLC cartridge to evaluate NO2 levels for eight patients treated with 4 LPM inhaled-NO in air for 15–30 minutes. NO2 levels were measured with a cavity-attenuated phase-shift spectroscopy (CAPS) detector following the patient dosing and the final values were calculated.

Results: The NO levels remained within the intended dose of 80 ppm. The average NO2 level after 15 min of NO delivery was 0.07 +/- 0.01 ppm. The NO2 levels remained well below the OSHA, FDA, and NIOSH limits of 5.0, 3.0, and 1.0 ppm, respectively. Therefore, this technology may reduce NO2 levels compared to current treatment methods, and subsequently minimize potential adverse effects attributed to NO2.

Disclaimer: CAUTION Investigational device. Limited by Federal (or United States) law to investigational use.
Experimental Measurements of the Anisotropic Darcy Permeability for the Blood-Side Flow in Oxygenators


Study: Hollow fiber membranes in oxygenators are modeled as isotropic porous media for computational fluid dynamics (CFD). The purpose of this study was to experimentally investigate the anisotropic Darcy permeability, which represents the linear relation between velocity and pressure drop, for the blood-side flow in oxygenators in all three directions in space. The findings can be used to implement a model of an anisotropic porous media for CFD in oxygenators.

Methods: Representative volume elements of different fiber bundle configurations were investigated in a hydrodynamic test. The volume elements can be perfused in all three directions independently in order to evaluate the anisotropic permeability. The experimental setup runs with a Newtonian fluid mimicking blood with a dynamic viscosity of 3.6 cPs. It allows to investigate the anisotropic Darcy permeability for different Reynolds numbers. Two different fiber diameters (OD 300 µm and OD 380 µm, respectively) and two different fiber angles (24° and 90°, respectively) were used, thus four different fiber configurations were investigated.

Results: The results show anisotropic flow behavior for all fiber configurations and all investigated Reynolds numbers ranging from 0.01 to 1.58 (see figure). Overall, the anisotropic effect (ratio of the maximum and the minimum permeability for one configuration) is higher for 24° than for 90° angles with 4.5 and 1.6, respectively. In general, the linear Darcy relation is limited to a certain range of Reynolds numbers. The maximum Reynolds number for that range for porous media is given by literature with Re=10. The results for Reynolds numbers smaller Re=0.2 show a nonlinear effect of the Darcy permeability. That indicates a lower limit for the linear relation of velocity and pressure drop for oxygenators in this range, which is still relevant for the blood flow in oxygenators.

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Oxygenator Test Circuit with Double-Reservoir for Continuous Testing


Study: Normative in-vitro testing of oxygenators for gas transfer rates following the FDA Guidance 510(k) can be done with a simple circuit containing one test oxygenator, one deoxygenator, and one blood reservoir. However, the time for blood sampling from the circuit is short and often interrupted; a lot of time is needed for deoxygenation of blood to restore venous parameters. Therefore, continuous blood sampling for the calculation of the gas exchange rate would be beneficial. Based on literature describing deoxygenation circuits, the aim of this study was to investigate the dependency in blood flows between test oxygenator and deoxygenator in order to achieve a circuit that could provide venous blood parameters at the blood inlet of the test oxygenator constantly.

Methods: Fig. 1 shows a schematic drawing of the test setup containing a custom-made double-reservoir with two chambers, one circuit for testing and one circuit for deoxygenation. Three identical oxygenators (Medos Hilite 7000 LT) were used for both, test oxygenator and deoxygenators. The reservoir consists of two PMMA cylinders, two PVC lids on either side, and in the middle a PVC slice with a cut-out window to provide two different fluid compartments and an overflow between both. The maximum priming volume of each reservoir compartment till overflow is 2.5 L, other volumes are easily achieved with different length of the cylinders. Fig. 2 shows the reservoir during an oxygenator test.

Results: Oxygen removal by the deoxygenator is the limiting parameter, as it is only related to the gas exchange area. The reloading with CO2 is dependent on its sweep gas ratio. A gas exchange area in the deoxygenators of 2.8 m² is required to maintain 1 L/min venous blood flow for the test oxygenator. No differences between the parallel and the serial setup of the deoxygenators were found. The reservoir provides a constant pre-load for the pump in the test circuit and a constant afterload as well.
Current Oxygenator Research

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Study: Hollow fiber membranes (HFM) are used exclusively in current oxygenators, as they enable compactly designed devices and provide high gas transfer rates. As there are still limitations, research on lung support has two goals: 1) to reduce adverse effects of the devices during therapy and 2) an implantable device as substitute for lung transplants. Assuming new devices should be more effective than current devices to benefit the patient, a literature review was performed.

Methods: The lung and the oxygen demand of an adult are used as a baseline. Average characteristics of the “commercial device” were calculated using datasheets of three manufacturers. Using data from publications, oxygenators with integrated pump, paracorporeal devices, and micro-capillary devices were compared regarding the base line. Micro-capillary devices were included, as they aim to increase the surface-to-volume ratio and the efficiency compared to HFM.

Results: The results were calculated using the higher “# Devices….”. Oxygenators with integrated pump may reduce the required surface area and priming volume. Thus enhancing the hemocompatibility, but increasing hemolysis due to the interface between the blades of the pump and the HFM. Paracorporeal devices are an intermediate step towards an implantable artificial lung. Therefore, specifications differ from normal oxygenators, like imitating pulmonary compliance and low resistance to prevent right heart damage, resulting in a high priming volume. Some micro-channel devices have an increased surface-to-volume ratio. Due to the size of these micro devices, blood flow and gas exchange are very limited. As several thousand layers will have to be combined, flow distribution and stacking are major challenges. Pressure loss within the devices may become quite high due to high flow rates and small channel size. The overall efficiency can be improved by optimizing the flow path, showing the still hidden potential of the hollow fiber and the design. Micro-channel devices cannot provide clinically sufficient gas transfer yet.

A Novel OxyRVAD Circuit Using the SYNERGY Micropump as Right Heart Support in a Swine Model of Pulmonary Hypertension


Study: As clinical experience with extracorporeal life support (ECLS) continues to grow, pulmonary hypertension remains a potential target for intervention and investigation. Pulmonary hypertension (PH) is a rare but severe, progressive disease that, when untreated, can lead to right heart failure and death. ECLS has the potential to address both pulmonary and cardiac dysfunction, and thus provide a life saving intervention in this disease.

Methods: In this study, we assessed the blood biocompatibility of the SYNERGY pump in conjunction with a Quadrox D oxygenator in a novel OxyRVAD circuit in a swine model of pulmonary hypertension. Four pigs were placed on an ECMO circuit configured as an OxyRVAD with venous drainage of the right atrium and outflow to the pulmonary artery via a synthetic conduit anastomosed in an end-to-side fashion. The circuit consisted of a SYNERGY pump, Quadrox D oxygenator, and Cobe E Pack 3/8 inch tubing. PH was induced by banding the pulmonary artery proximal to the device’s arterial outflow. After banding, mean pulmonary artery pressure (mPAP) increased from 17 mmHg to 39 mmHg.

Results: All animals survived the 6-hour OxyRVAD run without catastrophic biocompatibility issues. There was no significant difference in hemoglobin concentration from baseline, with levels ranging from 6.6 to 7.8 g/dl (p = 0.117). Platelet count did not change significantly from baseline, with total platelets ranging from 320,000 to 414,000/μl (p = 0.126). Indirect measurements of hemolysis were assessed by total bilirubin and lactate dehydrogenase. Total bilirubin ranged from 0.23 to 0.29 mg/dl (p = 0.308) and lactate dehydrogenase ranged from 495 to 825 U/L (p = 0.043). This study demonstrates the short-term biocompatibility of the SYNERGY pump as a component for an OxyRVAD device in the simulated clinical context of pulmonary hypertension and subsequent right heart failure.
Organ Care System® Promotes a Tissue Protective and Anti-inflammatory Response Within Lung Transplantation

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Study: Within INSPIRE trial standard cold storage (SOC) is compared to normothermic, ventilated donor lung preservation (Organ-Care-System®, OCS). As lung preservation may influence immune mediators (IM), thereby clinical outcome, lymphocyte subsets and cytokines released from lungs into perfusion solutions (PS) and peripheral blood (PB) were analysed.

Methods: From 31 OCS and 23 SOC patients, IM and T cell subsets were analysed in PS and PB by multiplex and FACS-analyses. Clinical outcome, donor and recipient demographics were assessed.

Results: Clinical evaluation revealed (OCS vs SOC): mean donor age 44 vs 48 years, mean recipient age 50 vs 50 years, underlying diagnosis: IF (n=15 vs n=11), CF (n=7 vs n=6), IPAH (n=2 vs n=2) and emphysema (n=7 vs n=4). Mean CCT for right (434 vs 421 min) and left lung (563 vs 537) did not differ significantly. Higher %predicted FEV1 at discharge was seen in OCS (68% vs 60%), as well as higher paO2/FiO2 ratio at T0 (367 vs 321). Lymphocytes were mobilized into PS in both with significant differences of higher proportions of CD3+CD8+ T cells and CD3+CD4+CD56+ T helper cells in OCS. Presence of CD56+ T cells in OCS PS correlated with Th2 cytokines, which were dominated by IL-4, IL-10, IL-31 and sCD40L as activation markers and induced by IL-33. This anti-inflammatory Th2 response maintained also in OCS recipients suppressing IL-6-mediated inflammation post Tx. Since high IL-6 levels in PB of SOC post Tx negatively correlated with PaO2/FiO2 ratio, suppression of IL-6 by Th2 cells and their cytokines represent an important mechanism for improved immune status of OCS preserved lungs. In conclusion, OCS preservation generates an anti-inflammatory Th2 milieu, induced by IL-33 production. It also changes lymphocyte and cytokine release from lungs towards a tissue-protective milieu associated with lower immunogenicity seen by different T cell compositions. Several factors correlate with lung function and may represent biomarkers for clinical outcome.

Snaring the Guide Wire in Avalon Cannula Placement in VV ECMO

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Study: We describe a simple and effective technique to guide the J-wire placement in times of repeated coiling and misplacement during the insertion of the Avalon cannula for initiation of Venovenous Extracorporeal Membrane Oxygenation (VV ECMO).

Methods: We perform Avalon Elite dual lumen cannula placement in the setting of a fully equipped operating room with backup cardiothoracic surgery availability. 2 units of packed red cells are kept available and a dedicated 9 Fr line for volume administration is placed at a site other than the RU vein prior to initiating placement of the Avalon cannula. A 55 year female was emergently transferred to our hospital for VV ECMO due to severe ARDS from H1N1 Influenza. She was taken to the operating room for cannulation after placement of a 9 Fr right femoral vein catheter. A flexible 145cm 0.035” J-tip wire was passed through the R IJ under fluoroscopy and TEE guidance. Despite repeated attempts the wire was entering the hepatic veins instead of passing into the IVC. We then introduced a snare (ENSNARE STD 18-30MM 120 CM, Merit Medical Systems, South Jordan, USA) under fluoroscopy and TEE guidance. Despite repeated attempts the wire was then grasped and brought down to the level of the right iliac vein. The flexible guide wire was then exchanged over an angiographic catheter with a 180cm 0.035” extra-stiff guide wire and after sequential dilation to a 30-Fr diameter the Avalon elite cannula was advanced over the wire and the wire removed. In the past we used the same technique to guide wire placement in another patient when the wire was repeatedly coiling back in to the right atrium despite multiple attempts to advance into the IVC.

Results: Bi-caval dual lumen cannula like the Avalon Cannula is the preferred cannula for VV ECMO. Placement of these large cannulae may be associated with risk of vascular injury or heart perforation. We propose using a snare from the R femoral vein to grasp and guide the flexible J-wire in cases of repeated re-coiling or misplacement for safer cannulation.
ASAIO PULMONARY ABSTRACTS


Study: The University of Pittsburgh is developing the Paracorporeal Ambulatory Assist Lung (PAAL) device, intended to provide 70% to 100% lung support through two approaches, a Passive exchange PAAL (P-PAAL) and an Active mixing PAAL (A-PAAL). The P-PAAL approach focuses on improving efficiency through hollow fiber membrane (HFM) bundle design, whereas the A-PAAL focuses on improving efficiency through impeller design. We previously presented a method for improving oxygenation efficiency by altering fiber bundle diameter, and developed a high efficiency P-PAAL bundle. We have continued this work to develop an integrated and portable P-PAAL device, around the previously developed fiber bundle geometry. This would allow meeting the oxygenation requirements with a 0.65 m2 surface area.

This study investigates the in vitro performance of the P-PAAL device.

Methods: The P-PAAL features a 1.75 inch diameter cylindrical HFM bundle of stacked sheets, with a surface area of 0.65 m2. In vitro gas exchange was conducted on the P-PAAL fiber bundle in bovine blood, in accordance with AAMI 7199 standards. Hemolysis was also measured on the fiber bundle in accordance with ASTM F1841 standards. A previously developed impeller was integrated into the device to provide pumping support for overcoming cannula and vascular resistance. An ambulatory drive system was also built to run the device.

Results: Oxygenation of 168 ml/min at 3.75 L/min of blood flow was obtained for the P-PAAL fiber bundle, resulting an efficiency of 259 ml/min/m2. The NIH for the bundle was 0.010 g/dL at 3.75 L/min. The impeller was able to pump 3.75 L/min at 216 L/min at 1900 RPM. Further work involves verifying the performance of the full device through acute in vivo studies.

223 Prolonged Veno-Venous ECMO in Acute Respiratory Distress Syndrome B. Akkanti, R. Hussain, S. Nathan, I. Rajapreyar, J. Patel, M. Patel, I. Bajnac, I. javoniak, K. Patel, P. Loyalka, I. Gregoric, B. Kar. Memorial Hermann -Texas Medical Center / University of Texas Health Science Center at Houston, Houston, TX.

Study: Introduction: Veno-venous Extra Corporeal Membrane Oxygenation (VV-ECMO) is being used for refractory Acute Respiratory Distress Syndrome. We report a case of a patient where VV-ECMO was utilized for one hundred and ninety three days.

Methods: Case Report: A thirty-year-old Hispanic gentleman with no previous medical history presented to an outside hospital with refractory hypoxemia after flu-like symptoms. Given progressive hypoxemia despite aggressive measures, patient was considered for VV-ECMO. Patient was cannulated at the outside hospital by our interventional cardiology service and patient was life-flighted to our facility. Subsequently, patient was considered for VV-ECMO. Patient was weaned off after one hundred and ninety three days. Therapy during this time included right ventricular support with inhaled nitric oxide, milrinone, mobilization of the patient with rotebed for alveolar recruitment, and initiation of continuous venovenous hemodialysis for volume management.

Results: Discussion and conclusion: VV-ECMO should be offered in cases of refractory ARDS and recovery is possible despite the delay in recovery. Our patient survived and is now ambulatory and discharged home. This is the first known case of a patient who survived despite being on prolonged VV-ECMO for one hundred and ninety three days.

265 A Pulsatile Pump Integrated Gas Exchange Device D. Wang,1 J. Zhao,1 G. Zhao,1 J. Wang,1 C. Ballard-Croft,1 J. B. Zwischenberger.1 1Surgery, University of Kentucky, Lexington, KY; 1W-Z Biotech, LLC, Lexington, KY.

Study: Our goal is to develop a Pulsatile Pump Integrated Gas Exchange Device (PIGED) for an ambulatory paracorporeal artificial lung.

Methods: The PIGED consisted of a gas exchange device (GED) and an integrated pump. The pump was a small diaphragm displacement cylinder pump centrally located in the GED. Hollow fibers were packed around the cylinder pump. A cone-shaped flow redirector in the GED inflow end and a flow baffler in the GED outlet end were used to achieve an even blood flow pattern. Three PIGED prototypes were made with 40 ml pumping stroke volume and 1.5 M2 gas exchange surface area. The GED body was 9 x 9 x 11 cm and the longest pump dimension was 18 cm. An electronically controlled, pneumatic pump console (12X12x12 cm) was also developed to drive the integrated diaphragm displacement pump. The PIGEDs and pneumatic

Results: The PIGED can pump up to 4.4 l/min blood flow against 150 mm Hg delta P. At the conditions of 3.5 l/min pumping blood flow, 38% inlet venous SO2 and 77 mm Hg PvCO2, the O2 transfer was 327 ± 12 ml/min and CO2 removal was 274 ± 10 ml/min.

Conclusion: Our compact PIGED prototype achieves excellent pumping and gas exchange performance.
Control of Left Atrial Pressure During Ex Vivo Lung Perfusion: A Novel Approach
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Study: Ex vivo lung perfusion (EVLP) is emerging as a technique for reconditioning and evaluating marginal donor lungs for clinical transplantation utility. Current techniques employ either an open left atrium, where left atrial pressure (LAP) is not controlled, or closed left atrium where LAP is controlled. Currently, closed systems rely on gravity to regulate LAP. We have developed a novel closed EVLP circuit where LAP is regulated by a computer controlled centrifugal pump, permitting a more compact design where reservoir height does not have to be varied to adjust desired LAP.

Methods: Our EVLP platform employs two centrifugal pumps that have been modified to allow computer control of pump RPM. The computer takes input from pulmonary artery pressure and flow sensors, and a left atrial pressure sensor, and then varies RPM to maintain a desired constant pulmonary artery flow (or pressure, user selectable) and constant left atrial pressure. The system was tested utilizing 10 domestic pig lung blocks, perfused with acellular STEEN solution at normothermia.

Results: The figure demonstrates the ability of the system to react to changes in vascular resistance over time. To demonstrate this more effectively, pulmonary vasoconstriction was induced by ventilating the lungs with 100% nitrogen at points A, B and C. As pulmonary vascular resistance increased with the system running in constant pressure mode, the pulmonary artery pump RPM decreased, thereby maintaining constant pressure. Likewise, as flow decreased, the left atrial pump rpm increased to maintain a constant left atrial pressure. This novel EVLP platform provides precise regulation of pressure and flow based on user preference, and allows tight regulation of these parameters with minimal input from the user once the settings have been entered.
Outside-In Hemofiltration For Prolonged Operation Without Clogging - Hydrodynamics, Filter Designs and Challenges

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Study: Hemofiltration (HF) is used extensively for continuous renal replacement therapy (CRRT), but long-term treatment is limited by thrombosis leading to fiber clogging. Maximum filter life is typically less than 20 hours. For the first time in the field, we have achieved continuous and consistent hemofiltration for more than 100 hours using outside-in hemofiltration with the blood flow into the inter-fiber space (IFS) with minimal increase in filter pressure.

Methods: To evaluate the principles and regularities of the outside-in HF, we have performed experimental and theoretical studies.

Results: Although thrombi do deposit in the IFS, they have minimal effect on the blood flow and filtrate flux due to the three-dimensional system of interconnected hydrodynamic flow channels in the IFS. Microscopic examination of sections of the fiber bundle showed that deposited thrombi have dimensions about the size of the gaps between the hollow fibers, and remain isolated from each other. Mathematical models have been developed to describe the effect of thrombi deposition on the fluid flow which accounts for the enhanced filter performance arising from the interconnected flow. The hydrodynamic advantage of the outside-in HF technology is expected to minimize the need for complex anticoagulation systems like regional citrate anticoagulation (RCA). For successful uninterrupted blood processing with the new outside-in HF technology, new filter configurations and designs are required. These results clearly demonstrate the significant potential advantages of using outside-in hemofiltration for long-term CRRT and for other extracorporeal therapies including hemodialysis and hemodiafiltration. The advantages, disadvantages, and challenges of this new technology will be elaborated.

Convective Leakage Renders Heparin Lock of Central Venous Catheters Ineffective within Seconds

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Study: This study investigates the mechanisms behind locking solution leakage from central venous catheters (CVCs).

Methods: The dynamics of heparin leakage are investigated in vitro. CVCs are placed in a model of the Superior Vena Cava as part of a flow loop replicating the flow in the SVC (Re=1000, Wo=9). Particle Image Velocimetry is used to quantify the local flow velocity in the test section, and Planar Laser-Induced Fluorescence concentration measurements are collected downstream of the catheter tip. Combining these two measurement techniques, time-resolved locking fluxes from a CVC are computed along the cardiac cycle. Pure diffusion (no flow inside or outside the catheter) and catheter instillation (flow inside the catheter but no flow outside) leakage are measured with fluorescent flux and mass balance before and after experiments.

Results: Pulsatile experiments show a loss of 43% of the initial locking solution inside the CVC. When instillation without blood flow is studied, locking solution losses drop to 28% (p<0.01). Convective transport of locking solution out of the CVC tip and into the SVC flow is very effective due to the high inertia and pulsatility of the SVC flow. Diffusion experiments show that a mere 2% of initial heparin mass is lost from the CVC in a 24-hour period. Concentration and convective mass flux are high for ~10 s after instillation and then decay quickly, Fig 1. In multi-port CVCs, blood flows in the lumen through side ports proximal to the tip, displacing locking solution out through the distal ports. Due to the low Reynolds number inside the catheter lumens, recirculation flow upstream of the side ports is negligible, so replenishment of locking solution near the tip is only due to diffusion. The negligible flux of locking solution measured after 5–10 cardiac cycles confirms that diffusion is inefficient and that the concentration of heparin at the catheter tip is ~0 M for the majority of the interdialytic phase, rendering the heparin-lock procedure ineffective.
A Micro-optofluidic Approach Towards Individualization of Dialysis by Continuous Electrolyte Monitoring

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Study: Most outpatient centers use dialysate with fixed electrolyte concentrations. But pre-dialytic serum concentrations of the major electrolytes (Na⁺, K⁺ and Ca²⁺) differ widely between individual patients. This “one-size fits all approach” leads to the occurrence of acute and chronic cardiovascular complications. As the age and additional disorders of the dialysis patient increase in number, a patient specific dialysate is preferable. Electrochemical methods need frequent calibration and are prone to fouling. Optical sensors offer intrinsic electrical safety, miniaturization perspectives, biocompatibility, less fouling and simultaneous real-time measurement of multiple ions. The aim of this work is to develop a fluorescent micro-optofluidic sensor based on photo-induced electron transfer (PET).

Methods: The PET principle exploits the selective quenching of molecular fluorescence. Sensors contain a fluorophore, spacer and an ion-specific receptor. The intensity ratio between fluorescence and absorption gives specific ion concentration. As a first step, we have built the proof-of-concept setup for the validity of the optical excitation and collection system (without a PET sensor). A micro-optofluidic device in poly(dimethylsiloxane) is fabricated with integrated optical fibers. The device is used to observe the fluorescence of Rhodamine B solution.

Results: The typical results show that the fluorescence signal is dependent both on flow rate and temperature, but with an optimized design and an integrated temperature sensor this effect can be compensated. An embodiment with PET molecules integrated into the device for in-line monitoring of electrolytes is foreseen in the coming months.
Relative Blood Volume Monitoring for Intradialytic Glucose Tolerance Test

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Study: An acute increase in plasma glucose concentration stimulates osmotic fluid shifts from the intracellular to the vascular compartment. The resulting hemodilution and the increase in blood volume should be detectable by on-line monitors used in hemodialysis (HD). It was the aim of this study to examine whether relative blood volume (RBV) measured by on-line techniques during HD could be used for intradialytic glucose tolerance testing.

Methods: Studies were done in non-diabetic patients during routine HD. Excess fluid volume was removed by constant ultrafiltration rate. RBV was measured by the ultrasonic blood volume monitor (BVM, Fresenius Medical Care, Germany) and/or by the optical CritLine Instrument (CLI, Hemametrics, Kaysville, UT), both using different measuring principles. A bolus of glucose (0.5 g glucose per kg body mass at dry weight) was administered into the venous blood line of the extracorporeal circulation approximately 30 min into dialysis (t=0). Plasma glucose concentration (g) in the arterial blood line was measured at times t=0, 3, 6, 10, 14, 20, 30, 40, and 60 min using standard laboratory techniques and compared to RBV data.

Results: Seven non-diabetic HD patients (3 female) completed the study. Infusion of glucose produced a distinct increase in RBV and a gradual decline back to baseline values within 60 min which was comparable for both BVM and CLI techniques (Fig. 1).

Linear regression analysis of corresponding g and RBV variables was highly significant: \( g = 2.7066 \times \text{RBV} - 264.06, r^2 = 0.92. \) RBV dilution curves measured during an intradialytic glucose tolerance test could serve as surrogate information for glucose disposal during HD and related extracorporeal applications. This could be of interest for simplified glucose tolerance testing during extracorporeal applications without blood sampling.
Single-shot In Vitro Phenotypic Characterization of Kidney Cells for Cell Therapy

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Study: Cell therapy in tissue engineering is predicated on the idea that cells will retain or adopt a particular phenotype with quantitative fidelity to the cells in the original organ. In vitro cell culture protocols are concessions to practicality that differ from in vivo conditions in almost every way. As part of our efforts to implement a bioreactor of human renal epithelial cells, we developed a rapid technique to measure key aspects of renal tubule cell function. We assessed active transport of sodium, secretion of organic anions, and barrier function in a single experiment.

Methods: Primary renal tubule cells and cell lines (e.g. LLCPK1) were grown to confluence on permeable supports. Apical culture medium was supplemented with 10mM/L lithium chloride and 0.1 mM/L sodium diatrizoate, and basolateral media was supplemented with 0.1mM/L para- aminohippuric acid and culture continued for 24 hours. Cells were allowed to recover and the experiment was repeated with addition of ouabain to the media. Aliquots were sampled at 6 and 24 hours. Lithium concentration in the basolateral media was measured by atomic absorption spectroscopy, and diatrizoate and PAH in basolateral and apical media were measured by C-18 HPLC with UV absorption.

Results: Diatrizoate concentrations in basolateral media were low unless cells were injured or subconfluent. PAH concentrations in apical media remained low, reflecting low OAT-1 expression in LLCPK1 cells. Lithium concentrations rose over time in basolateral media, and rose sharply when cells were injured. We have streamlined our functional assessment of cultured renal tubule cells and now have a straightforward go/no-go assay with which to define release criteria for tubule cell bioreactors.

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Heparin-albumin Priming in a Clinical Setting for HD Patients at Risk for Bleeding.

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Study: Patients on haemodialysis (HD) may have an increased risk for bleeding when performing HD i.e., before or after surgery, after brain haemorrhage or intestinal bleeding.

Methods: We use a priming solution containing heparin (H), 10,000 units, and 10 mL of albumin (A), 20%, added to 2 L of priming solution. This mixed solution is used to prime the dialysis circuit before connection of the patient. The residual fluid is removed when the blood fills up the circuit. A pilot study showed that it was possible to lower extent of added anticoagulation by this measure. This aim of this study was to evaluate a larger cohort of patients treated either by standard dose of anticoagulation only (Group-S, n=526) or a group that had initial HA priming performed before HD (Group-HA, n=882) with the aim to reduce the dose of systemic heparin or low molecular weight heparin.

Results: Comparing base line data between Group-S and Group-HA the mean age was higher (61.5 ± 16 vrs 59.5 ± 17, p=0.021), dialysis time was longer (3.3 hours ±0.7 vrs 3.2 ± 0.6, p=0.002) while there was no difference in extent of ultrafiltration (1.76 vrs 1.74 L), systolic blood pressure (141 vs 139), speed of blood pump (244 vs 243). The total dose of anticoagulation/dialysis was 4846 ± 1950 U vs 1844 ± 1974 U (p<0.001). In group-HA the total dose of anticoagulation (Units) was 0 Units/HD in 24%, and ≤1000 units/HD in 50% of procedures. Total clotting occurred to the same extent in both groups (4 versus 9 dialyses) and genders.

Conclusion: Heparin-albumin priming significantly reduces the extent of anticoagulation during HD in patients at risk for bleeding.

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A Lifelong Forearm Worn Artificial Pancreas

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Study: Last year we recognized a lifelong blood access for forearm worn artificial organs, the “In Situ Debranched Vein Fistula Graft” (VFG), with point compression to access A/V differential pressure. An efficient closed loop artificial pancreas (AP) might benefit ~20M insulin dependent patients in the developed world and reduce their expense for insulin down from the current ~$20B annually. A practical AP could significantly impact $1/2T current annual spending on all of diabetes and its complications in the developed world and should begin to address the plight of 200M potential patients worldwide. That our Blood-Based AP (BBAP) approach could offer a practical solution is predicted by: 1) Widespread clinical data from the bedside blood-based “Bistator”, which since the 1970’s has reliably “placed a clamp” on blood glucose levels, 2) “Obliteration of accessory veins” that is routinely, practiced to improve a failing to mature arteriovenous fistula (AVF). 3) Patient acceptance of the less cosmetic, multi-runoff vessels, AVF.

Methods: This year, we are specifically detailing the design of a VFG blood access powered artificial pancreas. Brief, compression-triggered minimal blood flows wash out prior extracorporeal content, for frequently monitoring true entral blood glucose. Pumping of appropriate insulin is according to a simple, thermostat-like algorithm. The device also proportionally self-injects anticoagulant, for full regional extracorporeal anticoagulation, while rendering the patient no more than marginally, prophylactically anticoagulated.

Results: Monitoring and pumping via relatively remote subcutaneous tissue, as pursued by other AP developers, will not guarantee the timely monitoring and therapy required to prevent thousands of deaths from hypoglycemia and millions of complications from hyperglycemia. ASAID Members: Nephrologists, Vascular surgeons, Interventionists and their Biomedical Engineers, long involved with blood-based extracorporeal devices, can do this.
Protective Effect of Coupled Plasma-Filtration Adsorption (CPFA) on Bile-associated Cast Nephropathy and Acute Kidney Injury through Direct Adsorption of Bilirubin and Liver-type Fatty Acid Binding Protein

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Study: Bile-associated tubular damage is the main cause of acute kidney injury (AKI) during liver dysfunction. Liver-type Fatty Acid Binding Protein (L-FABP) binds hydrophobic molecules including bilirubin. L-FABP enhances bilirubin uptake and damage of tubular cells. The aim of this study was to investigate the protective role of Coupled Plasma Filtration Adsorption (CPFA) on bile-associated AKI.

Methods: A kidney transplant patient developed sepsis, AKI and liver dysfunction and was treated by CPFA. We evaluated plasma levels of bilirubin and L-FABP. Kidney and liver biopsies, urine sediment, immunoelectrophoresis and NGAL were performed. In vitro, we tested: 1) static and dynamic adsorption of L-FABP to polystyrene resin; 2) pro-apoptotic effect (TUNEL and mitochondrial function) of patient’s plasma on tubular cells.

Results: A 50-year-old man was subjected to kidney transplantation with slow recovery of graft function. Kidney biopsy revealed acute rejection treated with Thymoglobulin. He developed septic shock (Legionella infection with multiple organ failures: creatinine 5.2 mg/dl; bilirubin 42 mg/dl, L-FABP 42 ng/ml, liver biopsy showing marked cholestasis, second kidney biopsy showing bile cast nephropathy, urine NGAL 356 ng/ml). After CPFA, we observed an increase of urine output, a decrease of bilirubin (10 mg/dl), L-FABP (7 ng/ml), urine NGAL (72 ng/ml) and low molecular weight proteins. In vitro, the polystyrene resin adsorbed bilirubin and L-FABP (100% adsorption after 15 min). After CPFA, the pro-apoptotic activity of patient’s plasma on cultured tubular cells was reduced. Plasma-induced tubular apoptosis and mitochondrial dysfunction were dependent on the presence of megalin, the L-FABP receptor. In conclusion, CPFA may have a protective role on bile-associated AKI through bilirubin and L-FABP adsorption.

Renal Artery Embolization for Minimally Invasive Induction of Renal Failure

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Study: New treatments for renal replacement therapy are being developed such as the BioArtificial Kidney; however, a large animal model of renal failure is needed to investigate their effectiveness. Embolization agents have been used to treat a variety of medical issues, e.g., tumors and aneurysms. We propose a minimally invasive technique to initiate complete renal failure in a swine model using a combination of nanoparticles and coils to embolize both renal arteries.

Methods: A 5Fr catheter was placed in the right femoral artery of a 55-kg female Yorkshire pig. After the renal arteries were identified with radiopaque contrast (Conray®), particle embolization was performed with polynvinyl alcohol flakes (Contour™, 250 - 700nm), followed by coil embolization (Tornado®). After complete occlusion was confirmed, the sheath was removed and the pig was allowed to recover. Meloxicam (15mg IM) and buprenorphine (0.12mg/kg IM) were administered once for post-procedural pain. Daily blood draws and clinical assessments were performed until euthanasia, which occurred based on the veterinarian’s assessment of severe metabolic derangement and/or signs of decomposition.

Results: The procedure was well tolerated with no significant rise in inflammatory markers (white cell count and C-reactive protein). Immediate renal failure resulted from the embolization as evidenced by complete cessation of urine output. There was a progressive rise in urea and creatinine from a baseline of 8 mg/dl and 1.35 mg/dl to 95 mg/dl and 21.62 mg/dl, respectively. This coincided with worsening uremic symptoms including lethargy and decreased oral intake. On day 5, the animal was euthanized due to severe lethargy and metabolic derangements (Potassium: 8.6 mEq/L). Nanoparticle and coil embolization of the renal arteries can induce immediate renal failure in a pig. This minimally invasive technique can serve as a viable large animal model for investigating the next generation of renal replacement devices such as the BioArtificial Kidney.
Acoustic and Ultrasonographic Measurements in Newly Performed Hemodialysis Arteriovenous Fistulas

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Study: Purpose: Early failure of maturation of arteriovenous fistulas (AVF) is a major problem occurring in 20 - 60 % of AVFs. In order to find a method to optimize surveillance of AVFs, we performed several acoustic and ultrasonic measurements in AVFs up to six weeks after surgery.

Methods: 25 patients suffering from chronic kidney disease (CKD G5) with a recent radiocephalic or brachiocephalic AVF were included. The fistulas were examined by using stethoscope sound recording, and estimates of fistula-diameter and blood flow were done by ultrasound (B-mode and Doppler). All measurements were performed in the region of the anastomosis, and also 5 cm and 10 cm downstream from the anastomosis. The patients underwent the examinations on the day of surgery and 1 week, 2 weeks, 4 weeks and 6 weeks later. Sound recordings were obtained for the duration of 15 seconds each, by the use of an electronic stethoscope (3M Littman 3200). Ultrasonic examinations were performed using a mobile device LOGIQ (General Electric Healthcare).

Results: Sound recordings in the three positions revealed that on average, changes in acoustic ratio (peak amplitude of 1200 Hz divided by peak amplitude of 100 Hz) obtained 5 times during the 6 weeks showed a u-shaped curve. (p< 0.05). Figure 1 depicts the acoustic ratio. Due to the u-shape of the acoustic ratio, no significant linear correlation was observed between the ultrasonic and the acoustic measurements. Figure 2 shows the fistula-diameter during the 6 weeks in the 5 cm position downstream, whereas Figure 3 shows Pulse-Wave Doppler velocity (cm/s) in the same position during the 6 weeks.

Conclusion: The finding of a u-shaped curve for the acoustic ratio over time might indicate a relationship between the acoustic phenomenon and the maturation of AVF after surgery. Further investigations including more patients are awaited in order to clarify whether the maturation of AVF follows a typical pattern of acoustic ratios in different positions.
Immunobarrier Characterization of Slit-Shaped Nanotopography for an Implantable Bioartificial Kidney

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Study: Renal tubule cells are known to suffer necrosis and apoptosis after exposure to inflammatory cytokines. We are using silicon nanopore membranes (SNM) to develop an implantable bioartificial kidney that consists of a high-permselectivity hemofilter coupled with a bioreactor housing renal tubule cells. In this study, we investigated the immunoisolation function of SNM with 7 nm-wide pores by examining the effect of cytokines on epithelial tight junction of renal cells.

Methods: Four different types of renal epithelial cells (MDCK, HK2, LLC-PK1, and HPTCs) were grown to confluence on 10 mm x 10 mm SNM substrates consisting of a central 6 mm x 6 mm slit-array patterned porous region surrounded by a 2 mm-wide smooth solid border. Transwell chambers were used as the control membranes. Human tumor necrosis factor-α (TNFα) was added to the apical side of the cells and the monolayer integrity after 6 hours of exposure was assessed via transepithelial electrical resistance (TEER), cell viability assay, and immunohistochemistry techniques.

Results: Without TNFα, cells on both Transwell and SNM maintained the monolayer integrity by expressing zona occludens (ZO1) protein at the intercellular junctions. Regardless of cell type, TNFα broke the monolayer integrity and caused apoptosis on the apical side of cells on both Transwell and SNM. In contrast, renal cells on the basal side of the SNM maintained monolayer integrity unlike their Transwell counterparts. These results suggest that SNM provide an immunoisolation function that could be used to encapsulate renal cells in the bioreactor of the implantable bioartificial kidney.
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