Development of a Bioresorbable Endovascular Stent for Neonatal and Infant Coarctation

($7,500 awarded for 2016)

Neonatal and infant coarctation (narrowing) of the aorta has traditionally been treated by open surgical repair. Transcatheter therapy with balloon dilation is reserved now only for newborns infants, who are deemed too sick for the surgical approach. Balloon dilatation alone is typically only a palliative procedure, due to high recurrence rates, and performed until they become well enough to undergo eventual surgical repair. Unfortunately, open surgical repair continues to have significant rates of mortality (2%), morbidity (up to 12–20%), and recurrent narrowing (up to 18%). Transcatheter stenting with a currently available bare metal stents (BMS) avoids the risks of open surgery and minimizes vessel recoil associated with balloon angioplasty alone. However the BMS that can be used in neonates and infants (due to size of the femoral artery where the stents are introduced) have a fixed diameter to which they can be maximally dilated. Unfortunately, as a child grows, the aorta needs to grow far beyond this maximal diameter, making stenting early on in life a less than desirable approach to this condition; the reason being that the patient is essentially predestined to eventually need a surgical patch repair with removal of the stent at some point in time.

Investigators at the University of Michigan are developing a pediatric bioresorbable stent (BRS) that would avoid many of the limitations ascribed to early stenting as outlined above. Specifically, a BRS would allow a vessel to be treated by a stent at a small diameter without preventing future growth to a larger diameter as the patient grows. Eventual complete absorption of these stents will avoid the need for redilation, unsafe "unzipping" procedures, or the requirement for eventual surgical removal of the stent and patch repair in the future. Bioresorbable stents also have the advantage of preserving side branches, preserving imaging options, facilitating reintervention, and being an option for even the sickest patients who could not tolerate surgery.

The current pediatric BRS prototype was manufactured in collaboration with a stent laser cutting company in Germany. To maximize potential federal funding for this project, we are seeking out stent manufacturers in the United States, who also have experience in laser cutting bioresorbable materials. One such company is Norman Noble (Highland Heights, OH), which provides stents for the vast majority of commercial stent providers in the US. We are asking Norman Noble to perform a feasibility study in making a first batch of stents from the novel material we are studying for this unique purpose. As we do not currently have outside funding for this small niche market device, philanthropic support of this feasibility study would go a long way to advance our team's progress.

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Novel Stem Cell Therapy for HLHS
($7,500 awarded for 2016)

Over the last funding period, we have been able to better understand and characterize the potent blood vessel forming ability of novel stem cells we have isolated from discarded tissue from neonates undergoing open heart surgery. We have begun to leverage this remarkable ability of these cells for both cardiac tissue engineering, in which this field is essentially at a standstill because of the lack of blood vessel networks in engineered tissues, as well as for stem cell therapy for the failing heart.

In HLHS, the single right ventricle is very susceptible to failure. The RV is intrinsically disadvantaged when placed as the systemic ventricle, which is responsible for functioning at higher pressures and is thus susceptible to injury secondary to oxidative stress and a lack of new blood vessel formation. With the support of Faith's Angels, we have obtained convincing evidence that our novel stem cells possess superior abilities to promote new blood vessel formation as well as protect heart cells against the damage from oxidative stress. We have small animal data that indicate the efficacy of these cells in other types of heart failure models and we are currently evaluating its potential in a RV failure model.

One of our long term goals is to apply these novel stem cells as a therapy for patients with HLHS to preserve and protect their right ventricles. Before we can translate these cells into patients as a seminal clinical trial, we will need large animal pilot data before we can apply for a FDA application and receive regulatory approval. Funding from Faith's Angels will tremendously help us in our quest to achieve this milestone, and significantly advance the clinical translation of these novel stem cells.

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Histotripsy (Therapeutic Ultrasound)
for the non-invasive treatment of congenital heart disease
($7,500 2016 continued research project, totaling $22,500 to date.)

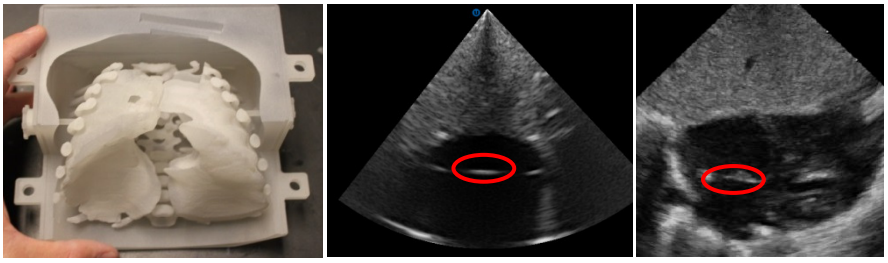

Image to the left represents a 3D printed replica of an infant torso generated from anatomic data. The middle image is the ultrasound image through this manikin once filled with tissue mimicking media. The image to the right is an ultrasound image of a human neonatal atrial septum which shows how similar the artificial replica mimics the human condition.

Over the past year, with support from Faith's Angels and other generous contributors, our research team has continued to further the development of the first ever therapeutic ultrasound device for the treatment of infants with congenital heart disease. Based feedback from the FDA in January 2015, the team has initiated and completed a clinical imaging study to optimize the design of the therapeutic transducer for life saving therapy of infants with HLHS. The transducers have been redesigned and optimized and have recently been delivered to our team from the manufacturer. The FDA has supported and pre-approved our plans for further pre-clinical animal testing prior to our official submission for approval for a clinical trial which we anticipate occurring in the next 6 months. In addition, we have designed and manufactured true-to-life replicas of infant torsos that we have been able to utilize for safety and efficacy testing, minimizing the necessity of animal experimentation.

Over the past year we have also applied for a Humanitarian Usage Device designation which we received in the fall of 2015. This designation will allow us to perform our clinical trial in infants with an emphasis on safety and once the trial concludes the device could then be used via a Humanitarian Device Exemption (HDE) mechanism, allowing easier access of the technology for patients throughout the country.

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In addition to moving full forward with the neonatal HLHS application we have also began investigating other congenital heart lesions as well as other cardiovascular issues that infant with congenital heart disease suffer from. Specifically, many of our congenital heart disease patients suffer from blood clot or occluded vessels because of the therapy they require. We have been developing histotripsy to treat clotted vessels and restore blood flow. We have tested this in acute animal models and plan to move forward with long-term studies in the near future. In addition, venous catheter malfunction because of clot formation is also an issue for many of our patients. We have plans to utilize histotripsy technology to treat clogged catheters and potentially spare children in the future from repeated venous catheters and catheter associated infections. With the financial support of Faith's Angels we plan to initiate bench top studies and then move into animal studies to test our hypotheses. Between that endeavor and developing other application of histotripsy technology, such as fetal heart therapy, our team will be busy and is truly appreciative of the support from Faith's Angels. As the budgets increase (we anticipate utilizing most of the Faith's Angel budget within the next 8-12 months) we anticipate the data generated by these early studies will enable the obtainment of further funding through the NIH or American Heart Association. Gabe Owens, MD