



56th Annual Scientific Session  
March 24 – 27, 2007 New Orleans

EMBARGOED FOR RELEASE  
Saturday, March 24, 3:00 PM CDT

CONTACT:  
Leslie Humbel, 202-955-6222  
[lhumbel@spectrumsience.com](mailto:lhumbel@spectrumsience.com)  
Amy Murphy, (202) 375-6476  
[amurphy@acc.org](mailto:amurphy@acc.org)  
In New Orleans (March 24-27):  
Marriott Convention Center  
504-613-2418

## **STUDIES DEMONSTRATE PROGRESS IN UNDERSTANDING CARDIOVASCULAR DISEASE, SURGERY OPTIONS IN PEDIATRIC PATIENTS**

**NEW ORLEANS, La. (March 24, 2007)** — Heart problems in children are quite different from those in adults, and four studies presented today at the American College of Cardiology's 56th Annual Scientific Session look at how pediatric cardiologists take different approaches to better understand and manage cardiovascular disease in this population, including insights into fundamental cardiac mechanisms and testing of new procedures. ACC.07 is the premier cardiovascular medical meeting, bringing together cardiologists and cardiovascular specialists to further breakthroughs in cardiovascular medicine.

"Congenital heart disease is one of the most common birth defects seen in the United States today, and it is important we continue supporting research that will improve the diagnosis and treatment of infants, children and young adults with these problems," said Roberta Williams, M.D., of the Children's Hospital of Los Angeles. "These studies show how a better understanding of new technologies can save lives and establish a better quality of life for children living with cardiovascular disorders."

### Long-term Follow-up of Stents Placed in Infants with Congenital Heart Disease (Presentation Number 1017-27)

Stents have been credited with saving thousands of lives by treating blocked coronary arteries. While the implantation of balloon-expandable stents in infants has been shown to be

## *2 – 2 – 2 Issues in Pediatric Cardiology*

technically feasible, there is essentially no long-term data showing that this treatment remains effective as an infant grows. In order to determine the benefits of stent implantation in infants, researchers from Miami Children's Hospital in Florida conducted a retrospective analysis on the earliest consecutive series of infants who underwent stent placement between October 1995 and December 1999.

During this time period, 33 stent implantations were attempted in 27 infants. Implants were successful in 94 percent of these patients (n=31). Three non-procedure related deaths were reported within 30 days of implantation, one patient was lost to follow-up and one experienced acute thrombosis of the stent. The remaining 22 patients, which account for 26 of the stent implantations, were analyzed for this follow-up study.

Patients were followed for an average of 101 months following stent implantation. A total of 44 re-catheterizations were performed over this time period, during which 19 stents in 17 patients underwent 32 re-dilations. There were no procedural complications or deaths during these follow-up procedures. At the most recent catheterization (63 months post-implant on average) in patients who underwent re-dilation, researchers noted an increase in stent diameter of 24 percent since initial implantation, suggesting that these devices can be effectively enlarged to keep pace with a young child's normal growth.

Seven stents were electively removed at the time of a planned cardiac surgery without complications and all remaining stents (n=18) are currently free of significant obstruction. At the latest study follow-up, 21 of 22 patients are alive and well, with one unrelated death occurring 51 months after stent implantation.

"More than ten years ago, Miami Children's Hospital demonstrated that balloon expandable stent implantation in infants was safe and effective, and we now provide evidence that there is a sustained long-term benefit to these children," said Evan M. Zahn, M.D., of Miami Children's Hospital, and lead investigator of the study. "As a young child grows over time, these stents can be safely and effectively enlarged in the catheterization laboratory or removed in the operating room during another scheduled procedure. The next step will be to assess whether a stent implanted during infancy can ultimately be enlarged to a normal adult size, essentially providing a lifetime of effective treatment from a catheter procedure performed in infancy."

### *3 – 3 – 3 Issues in Pediatric Cardiology*

*Dr. Zahn will present this study on Monday, March 26, at 10 a.m. in Hall H.*

#### Six Years' Experience of Outcome After Percutaneous Pulmonary Valve Implantation (Presentation Number 823-4)

In 2000, percutaneous pulmonary valve implantation (PPVI) and repair has emerged as an additional therapy to avoid re-operation in young patients with congenital heart disease. Although long-term outcomes are not yet available, researchers from the Great Ormond Street Hospital for Children and UCL Institute of Child Health in London have collected sufficient information to offer the first mid-term evaluation of this technique.

Over the past six years, peri- and post-procedural complications in children with congenital heart disease have led to the removal of percutaneous pulmonary valves. In this study, researchers sought to analyze the influence of learning curve and technique modification on the need for device removal. To do this, patients were divided into two study groups: one which included the first 50 patients, and a second group of patients (n=87) who underwent PPVI after improvement of the engineering of the device, better patient selection and improvement in procedural technique, such as introducing post dilatation. Survival curves for freedom of device removal were calculated for both cohorts.

During follow-up, 19 out of the total 137 patients underwent device removal. In the first group, reasons included the following: "hammock effect" (vein wall hanging into stent, narrowing of a passageway, n=4), stent fractures (n=1), valve dislodgement (n=2), coronary compression (n=1), right pulmonary artery obstruction (n=1) and residual stenosis (n=6). These complications led to modification of the technique, including device alterations, second PPVI, enhanced imaging and improved patient selection. In group two, device removal was necessitated by complications including endocarditis (infection of the heart lining, n=2), outgrown conduit or stent (n=1) or thrombosis (n=1), for which no technique modification could be considered.

"Recently introduced as an alternative to surgery, percutaneous pulmonary valve implantation is one of the most exciting developments in the field of interventional cardiology," said Sachin Khambadkone, M.D., of Great Ormond Street Hospital and an investigator on this trial.

#### *4 – 4 – 4 Issues in Pediatric Cardiology*

“Overall experience proves that PPVI is not only feasible, but provides an important benefit to patients who would otherwise have to endure additional surgeries. In addition, our data clearly demonstrates that changes in technique resulted in a significant improvement in the need for device removal, and further progress is expected in the future,” said Dr. Khambadkone.

*Philipp Lurz will present this study on Monday, March 26, at 4:15 p.m. in room 228.*

#### Developmental Changes in the Modulation of Contractility in Human Ventricle (Presentation Number: 1011-33)

The ability of the heart’s ventricles to contract, known as contractility, has been shown to increase with age in animal models. Treatments to alter contractility, particularly after surgery, have been well established in adult patients. However, because few studies have measured contractility in the ventricles of infants, it is unknown whether treatments designed for adults following heart surgery are beneficial or harmful to this patient population.

A study conducted at Emory University and Children’s Healthcare of Atlanta in Georgia examined developmental changes in the effects of drugs and the response to stimulation rate in human right ventricle tissue during the first year of life. Specifically, researchers compared tissue from newborns (less than one week, n=5) undergoing shunt implantation for left side underdevelopment, to tissue from infants (three to 12 months, n=6) undergoing repair for Tetralogy of Fallot, a congenital heart disease involving four structural defects in the heart. Tissue removed from the right ventricle as part of the surgical repair was obtained directly from the operating room and immediately studied in the lab.

Researchers electrically stimulated the tissue to produce contractions and measure the tension produced by the tissue. They then applied 100 nM isoproterenol or 10  $\mu$ M forskolin (drugs used to stimulate the heart via cell signaling) in order to determine the effect of these drugs on the contractility of the tissue. They also measured the force frequency relationship, or FFR, which is the response of the tissue to faster stimulation rates. Additionally, the study determined the levels of three proteins involved in contractility and calcium balance in the heart, including Na/Ca Exchanger (NCX), SR Ca-ATPase (SERCA) and phospholamban (PLB). Results showed that:

### *5 – 5 – 5 Issues in Pediatric Cardiology*

- Response to isoproterenol and forskolin were significantly smaller in newborn ventricle tissue compared to infant (152 vs. 292 % of control for isoproterenol and 183 vs. 380 % of control for forskolin).
- Typically, when the adult heart beats faster it also beats with more force and is able to pump more blood to the body, and thus is said to have a positive FFR. In this study, researchers found that FFR for newborns was flat, with no increase in developed force at faster rates of stimulation, whereas infant tissues had a significantly positive FFR, increasing to 182 percent of control at the fastest rate of stimulation.
- NCX levels were two fold higher in newborns than in infants, whereas the levels of PLB were significantly smaller in the newborn group. The levels of SERCA were unchanged between newborns or infants. The differences in the levels of these proteins may underlie the poor regulation of contractility seen in the newborn tissue.

“This study shows, for the first time, that the newborn human ventricle, in addition to having reduced response to stimulation with isoproterenol or forskolin, also has a diminished ability to respond positively to increased heart rate, when compared to infants three to 12 months old,” said Carlo M. Zeidenweber, M.D., of Emory University, Children’s Healthcare of Atlanta Sibley Heart Center and lead investigator on this study. “This suggests that it may be difficult to improve contractility at birth, but that our ability to intervene increases over the first year of life. Further studies in this patient population will seek to determine the specific causes for differences in the newborn heart, including the possibility of altered levels of specific proteins, such as NCX and PLB.”

*Dr. Zeidenweber will present this study on Sunday, March 25, at 2:30 p.m. in Hall H.*

[Congenital Vascular Rings And Slings Are A Significantly Under-diagnosed Cause Of Childhood Diseases: Screening Of 186,213 School-aged Children By Echocardiography](#) (Presentation Number: 1005-32)

Vascular rings are congenital anomalies that occur early in the development of the aortic arch (the part of the aorta that leaves the heart and turns downward) and great vessels (five vessels above the aortic arch). This group of anomalies has been thought to be rare and doctors most often maintain a high index of suspicion of nonspecific signs of vascular rings via changes to

the structures encircled by the rings, primarily the trachea and esophagus. Such changes could include stridor (a harsh, high-pitched respiratory sound) or breathing noises, recurrent lung infections and asthma, as well as difficulty breathing and swallowing. Prompt diagnosis and treatment of these congenital abnormalities can be lifesaving.

In a collaborative study conducted by researchers at Chung Shan Medical University Hospital in Taiwan and Baylor College of Medicine and Texas Children's Hospital in Texas, 186,213 primary and junior high school children in Taichung County were screened for signs of cardiovascular abnormalities by medical history, physical examination, electrocardiogram (ECG) and portable 2D echocardiography (2DE) from 2001 through 2004. If any significant congenital cardiovascular diseases (CCVD) were suspected or not definitive, especially congenital vascular ring and sling abnormality (CVRSA), the patient was referred to a tertiary care center for a complete evaluation, which included a standard 2DE, computed tomography (CT) scan, magnetic resonance imaging (MRI) or angiography (X-ray of blood vessels).

Of the children screened, a total of 2,319 cases with CCVD were diagnosed. There were only four complex CVD cases, of asymptomatic congenitally-corrected transposition of the great arteries (L-TGA, a combination of two heart abnormalities that cancel each other out) in this age group. Newly diagnosed CHDs were frequent, including: patent foramen ovale (hole between right and left atria, n=618); patent ductus arteriosus (blood vessel in heart which fails to close, n=213); atrial septal defect (abnormal opening between left and right atria, n=180); pulmonary stenosis (narrowing between right ventricle and lung artery, n=54); ventricular septal defect (hole between left and right ventricles, n=37); aortic stenosis (abnormal narrowing of aortic valve, n=6); and others (n=17). CVRSA was the most prevalent of the abnormalities (6 in every 1,000 children), including:

- Left aortic arch with aberrant right subclavian artery, or LAA/ASCA, which pushes the trachea and esophagus forward (n=992);
- Right aortic arch with left ligamentum, which forms a complete vascular ring and leads to airway compression (n=83);
- Pulmonary artery sling, in which the left pulmonary artery arises unusually from the right pulmonary artery and lies between the trachea and esophagus (n=11); and
- Double aortic arch, where the main aorta tube splits into large left and right branches before becoming one tube (n=8).

## *7 – 7 – 7 Issues in Pediatric Cardiology*

Patients with LAA/ASCA and pulmonary artery sling had less common and less severe clinical signs and symptoms than complete vascular ring, including recurrent respiratory infections, asthma, difficulty in swallowing, failure to thrive, exercise intolerance, seizure or mental retardation. Of the patients with a complete vascular ring, 66 (69 %) underwent surgical correction with no mortality or significant complications.

“Congenital cardiovascular diseases, especially congenital vascular ring and sling abnormalities, have a higher prevalence in school-aged children than indicated in previous literature,” said Shuping Ge, M.D., of Texas Children's Hospital and lead author on this study. “Such abnormalities are primarily undiagnosed and can cause significant morbidities, making awareness and cost-effective screening strategies necessary for timely diagnosis and treatment. Our study found that echocardiography appears to be a sensitive tool for screening of CVRSAs, and future tests will further validate a recommendation to use this across broad pediatric populations.”

*Dr. Fong-Lin Chen will present this study on Sunday, March 25, at 10 a.m. in Hall H.*

###

The American College of Cardiology ([www.acc.org](http://www.acc.org)) represents the majority of board certified cardiovascular physicians in the United States. Its mission is to advocate for quality cardiovascular care through education, research, promotion, development and application of standards and guidelines- and to influence health care policy. ACC.07 and the i2 Summit is the largest cardiovascular meeting, bringing together cardiologists and cardiovascular specialists to share the newest discoveries in treatment and prevention, while helping the ACC achieve its mission to address and improve issues in cardiovascular medicine.