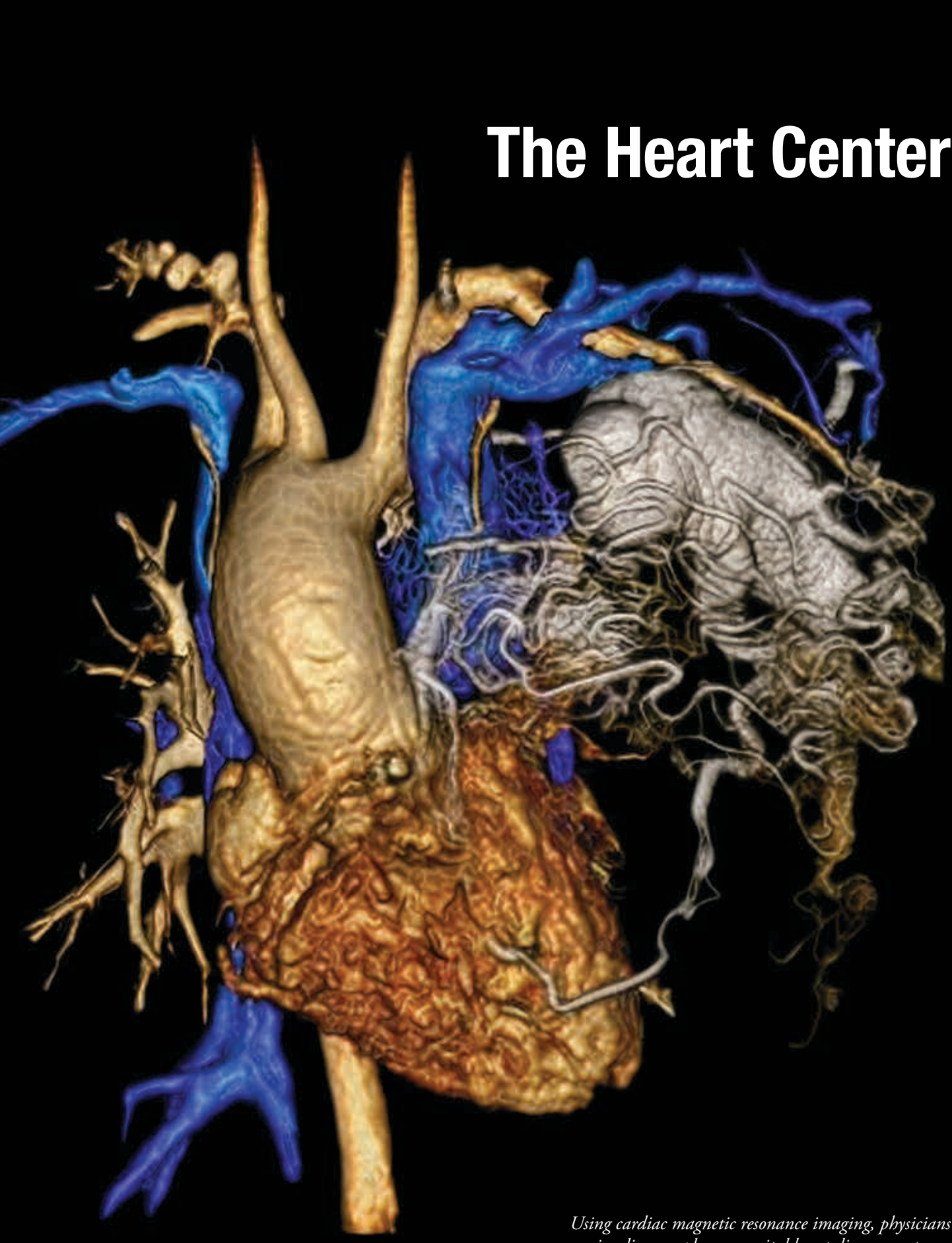
Our team treats every child as though they were their own. We apply the best care from the best team to achieve the best outcome. And we are working to develop the treatments of the future. There's no need to go anywhere else.

– Timothy F. Feltes, MD
Co-Director, The Heart Center

The Heart Center



Using cardiac magnetic resonance imaging, physicians can visualize complex congenital heart disease anatomy.

Inhibiting Notch1 Signaling Could Prevent Abdominal Aortic Aneurysms, Study Suggests

Inhibiting a key signaling pathway found in all mammals could help prevent abdominal aortic aneurysms (AAA), according to a study led by Vidu Garg, MD, director of Translational Research in The Heart Center at Nationwide Children's Hospital. The findings, the first to show a link between the Notch signaling pathway and this deadly condition, were published in the journal *Arteriosclerosis, Thrombosis and Vascular Biology*.

The Notch signaling pathway, which plays a key role in multiple cellular processes during development, has been implicated in numerous medical conditions, including cancer and cardiovascular disease. However, its exact function in aortic aneurysms was unknown.

For this work, the researchers built on earlier studies that suggested Notch1, one of four receptors in the pathway, was involved in inflammatory responses to tissue injury. To examine its function more closely, they reduced the amount of active Notch1 receptor in mice with AAA, which prevented macrophage recruitment and attenuated the inflammatory response in the aorta.

The rupture of these aneurysms is among the leading causes of death in the U.S. Currently, the only treatment for AAA is surgery, but findings from this study suggest that a therapy blocking Notch1 signaling could potentially prevent these aneurysms.

"The dramatic effect that was seen with genetic deletion and pharmacologic inhibition of Notch signaling demonstrates the importance of macrophage recruitment for AAA progression," says Dr. Garg, a principal investigator in the Center for Cardiovascular and Pulmonary Research in The Research Institute at Nationwide Children's. "Additional investigation of the Notch1 pathway in macrophage recruitment and function may lead to novel therapeutics for AAA."

Dr. Garg is widely recognized for his work on Notch1 signaling and cardiovascular disease. In February, Dr. Garg authored an invited commentary for Nature Medicine on Notch signaling research, an area that has garnered the attention of leading experts in the field.

"There is increasing genetic evidence that the Notch signaling pathway has profound implications for human disease," Dr. Garg says. "This is leading to a growing interest in understanding mechanisms of the Notch signaling pathway in a variety of diseases."

Hans CP, Koenig SN, Huang N, Cheng J, Beceiro S, Guggilam A, Kuivaniemi H, Partida-Sánchez S, Garg V. Inhibition of Notch1 Signaling Reduces Abdominal Aortic Aneurysm in Mice by Attenuating Macrophage-Mediated Inflammation. *Arteriosclerosis, Thrombosis and Vascular Biology*. 2012 Dec;32(12):3012-23. Epub 2012 Oct 18. PMID: 23087364.

Misra C, Garg V. Compacting the Heart with Notch. *Nature Medicine*. 2013 Feb;19(2):133-4. PMID: 23389606.

NATIONWIDE
CHILDREN'S

THE HEART CENTER

The Heart Center at Nationwide Children's Hospital combines all clinical and research disciplines under one umbrella in order to meet our mission. We are out in front by discovering the causes of heart disease and developing the therapies of the future for our patients by taking on our patients one at a time and providing them with the state-of-the-art care they deserve, regardless of age. We support Nationwide Children's mission to provide our services in a safe environment.

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Chief, Cardiology
Professor of Clinical Pediatrics

Mark E. Galantowicz, MD
Co-Director
Chief, Cardiothoracic Surgery
Professor of Clinical Surgery

John P. Cheatham, MD
Co-Director
Director, Cardiac Catherization & Interventional Therapy
Professor of Pediatrics & Internal Medicine,Cardiology Division

FULL-TIME NCH FACULTY

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Aaron J. Trask, PhD
Assistant Professor of Pediatrics

In 2012, much advancement was made in all aspects of our mission to focus on providing the highest quality, most cost-effective, and comprehensive care to all congenital heart patients and, in doing so, becoming one of the nation's leading congenital heart disease centers. Our metrics indicate our success in distinguishing The Heart Center as an international leader in the field of congenital heart disease.

NATIONAL AND INTERNATIONAL REPUTATION

The Heart Center is a nationally and internationally recognized comprehensive center for patient care, education, and research. Recognition is demonstrated by the following:

- Ranking #10 for Heart and Heart Surgery Program in *U.S.News & World Report*, 2013-14
- OptumHealth Center of Excellence designation for CHD and Access Network for Pediatric Heart Transplant
- CIGNA LifeSOURCE Transplant Network for Pediatric Heart Transplant
- Aetna Institute of Excellence in Pediatric Congenital Heart Surgery
- Creating the world's first Hybrid Cardiac Catheterization Suites and first Hybrid Congenital Cardiac Operating Room in the nation
- One of the first children's hospitals in the nation to utilize 3D Video Assisted Thorascopy

OUR SERVICES

Comprehensive clinical care of our patients throughout life is our goal. Our highly qualified team provides state-of-the-art care in areas of diagnostic imaging, noninvasive diagnostics, interventional cardiology, electrophysiology interventions, anesthesiology, nursing, and thoracic surgery including heart, lung, and heart/lung transplantation. Our Adult Congenital Heart Disease Program is one of the largest in North America and leads the U.S. in centers with an annual growth of 30 percent. Our outpatient cardiology provides our cardiology services at centers convenient for our patients and their families at 11 regional sites. A substantial portion of our patients come from regions well beyond the traditional primary service area for Nationwide Children's. In 2012, we had 93 national and international surgical and interventional referrals to The Heart Center.

Quality, Safety, Service

The Heart Center leadership team is involved in top-down review for programmatic improvement. Patient quality care and safety issues are defined, measured, and monitored within each of the surgical, medical, and nursing aspects of The Heart Center. We are also involved in external quality review such as state and national quality initiatives related to surgical and catheterization/intervention outcomes. Other involvement includes

- Society of Thoracic Surgeons (STS) Congenital Heart Surgery Database
- Congenital Heart Surgeons' Society data center
- Joint Council on Congenital Heart Disease (JCCHD) that is a sponsored collaborative for quality improvement through The Center for Health Care Quality
- Adult Congenital Heart Association – Alliance for Adult Research in Congenital Cardiology (AARCC) collaborative sponsored by the NIH (RO3HL096135) to assess education and access-to-care issues for adults with congenital heart disease
- The state Ohio Doctor's Interested in Congenital Hearts (ODICH) reporting of all Ohio pediatric cardiology centers of data related to surgical and catheterization/intervention outcomes
- Pediatric Heart Transplant Study Group, Ohio Solid Organ Transplant Consortium
- Interventional cardiology participation in the IMPACT registry (Improving Pediatric and Adult Congenital Treatment), C3PO (Congenital Cardiac Catheterization Outcomes Project, one of eight participating centers and MAGIC registries, Congenital Cardiovascular Interventional Study Consortium [CCISC])
- American College of Cardiology, Adult Congenital and Pediatric Cardiology Section – noninvasive imaging, adult congenital heart disease, ambulatory cardiology quality metrics work groups
- American College of Cardiology – Adult Congenital and Pediatric Cardiology Committee Council members
- National Pediatric Cardiology-Quality Improvement Collaborative (NPC-QIC)
- Virtual pediatric ICU system
- National Cardiovascular Disease Registry - Internal Cardioverter Defibrillator (NCDR-ICD)

EDUCATION

The Heart Center's ACGME fellowship program offers a well-rounded experience in pediatric/congenital cardiology. We offer both a traditional Pediatric Cardiology Fellowship and a five-year Pediatric/Adult Cardiology Fellowship that is recognized by both the American Board of Internal Medicine and the American Board of Pediatrics. We have nine fellows and 100% of fellows with more than 1.5 years of training are presenting at national/regional peer-reviewed meetings.

RESEARCH

Investigators in the Center for Cardiovascular and Pulmonary Research, located in The Research Institute at Nationwide Children's, collaborate closely with clinicians from The Heart Center.

The center awards peer-reviewed intramural pilot projects to enhance clinician-initiated research. The success of this investment has resulted in extramural funding increasing eightfold from 2007 to 2012, totaling $2.3 million.

The centers recently received a National Institutes of Health Institutional T32 training grant renewal for MD and PhD fellows that is the first in the U.S. to focus on acquired and congenital heart disease that spans fetal life through senescence. This program provides 15 training slots through 2014. In addition, basic and physician-scientists continue to conduct innovative, mechanism-based research leading to improved therapies and outcomes for pediatric cardiovascular diseases. One aim is to foster preventive strategies and promote cardiovascular health in adults by altering risk factors during childhood.

Clinical/translational research initiatives include examining the effect of maternal caregiving on stress neurobiology in full-term infants with congenital heart defects, and examining whether timing of umbilical cord clamping among infants with prenatal diagnosis of congenital heart disease can positively affect clinical outcomes.

Current basic research includes investigating signaling cascades that regulate cardiovascular remodeling and function during disease progression, the genetic basis of congenital heart defects, molecular pathways regulating normal and abnormal cardiac development, and regulatory pathways that control vascular development and smooth muscle differentiation.

RESEARCH FUNDING (OVER $50,000) AWARDED

July 2012 – June 2013

Cheatham, John
Implantation of the Native Outflow Tract Transcatheter Pulmonary Valve (TPV) in Patients Indicated for Treatment of Pulmonary Regurgitation: Assessing the In Vivo Loading Condition for Product Development Specifications
Medtronic
$56,634

Hans, Chetan
Role of Notch1 Signaling in Abdominal Aortic Aneurysm - SDG
American Heart Association - National
$77,000

Lilly, Brenda
Role of Notch Signaling in Vascular Development and Function
American Heart Association - National
$77,000

Lincoln, Joy
Molecular Regulation of Heart Valve Development and Function
National Institutes of Health (NIH)
National Heart, Lung, and Blood Institute (NHLBI)
$416,151

Lucchesi, Pam
Training in Congenital and Acquired Heart Disease
National Institutes of Health (NIH)
National Heart, Lung, and Blood Institute (NHLBI)
$288,608

McBride, Kim
Exome Sequencing and Functional Studies in Familial CHD
National Institutes of Health (NIH)
National Heart, Lung, and Blood Institute (NHLBI)
$698,413

McConnell, Patrick
Double Valve Replacement
Industry Sponsor
$80,568

Trask, Aaron
Differential Macro- and Micro-Vascular Remodeling in Type 2 Diabetes
American Heart Association - National
$77,000

Yates, Andrew
Echocardiographic Assessment of Function During ECMO Support
American Heart Association - National
$55,000

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FAST FACTS

July 2012 – June 2013

Total Discharges: 1,057
- Heart Center Inpatient/Obs
- Inpatient Discharges: 630
- Observation and Outpatient-in-a-Bed Discharges: 427

Total Patient Days*: 7,257
- Average Length of Stay*: 11.5
- Average Daily Census*: 19.9

Cardiac ICU

Total Patient Days*: 3,729
- Inpatient Discharges: 576
- Average Length of Stay*: 6.5
- Average Daily Census*: 10.2

Total Cardiothoracic Surgeries: 418

Total Interventional Cardiology Procedures: 686

Total Non-Invasive Cardiology Visits: 27, 726

Total Clinic Visits: 13,169

**Excludes Observation and Outpatient-in-a-Bed Cases.*