JOHNS HOPKINS MEDICINE

The Johns Hopkins Heart Institute

Cardiovascular REPORT

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The Call to Closure

Cardiac surgeons take their skills to PDA patients beyond Hopkins

Luca Vricella makes house calls.

When pediatric cardiac surgeons **Duke Cameron** and **Luca Vricella** decided to put themselves on call to Baltimore-area hospitals to perform patent ductus arteriosus (PDA) closures at NICU bedsides, it was a surgical no-brainer.

"These babies already are traumatized," Vricella explains. "Transporting them to another location, whether it's to another hospital or to an OR within the hospital, just increases the chance for further instability."

Vricella and Cameron wanted that out of the equation.

In the past, patients often had to be transported to Hopkins. Where safety is paramount in these cases particularly, this simply ceased making sense, Vricella adds.

"PDA closure is one of the most delicate procedures to perform," he says. "There is zero margin for error."

At risk, Vricella explains, is perturbing the already-fragile physiology of these tiniest patients, many of whom are on the verge of death and some weighing in at a single pound. The duct itself is about the width of a small noodle, located behind a minuscule heart. The procedure is not open-heart, but rather is performed through a small incision on the left side of the chest. Specially designed long, thin instruments are used to isolate the PDA, and then a tiny clip is placed to block it.

It's about a 20-minute procedure, but the results are instantaneous.

"As soon as the clip is placed, we see immediate changes in physiology," says Vricella. "And, we've had no operative mortality."

In clinical practice, the condition occurs almost exclusively among premature babies. Because they're already endangered, PDA can exacerbate their tenuous condition swiftly and even fatally.

"It's rare to see this in full-term babies," says Vricella. "About 95 percent of PDAs happen in premature infants."

During fetal life, the ductus arteriosus acts as a natural bypass of the pulmonary circuit, directing blood flow from the right ventricle to the descending aorta. Shortly after birth, this small yet essential vessel remains as a short, thickened ligament for the rest of our lives. When this natural process doesn't occur, the vessel persists as a shortcut between the pulmonary artery and the aorta, and blood begins flowing from the more pressurized aorta into the lungs. The lungs are flooded, blood flow in the descending aorta is decreased, and this leads to dangerously low perfusion to the kidneys and bowel, and failure to thrive.

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When Image Is Everything

Nearly three decades ago, surgical ablation revolutionized the treatment of arrhythmias. As revolutions don't go backward, the procedure and its technology continued to evolve with the development of transvenous catheter ablation. But, despite its success, catheter ablation has been limited by a navigation system that doesn't account for true cardiac anatomy, an essential tool for guiding ablation procedures.

Today, says cardiologist **Hugh Calkins**, that's history.

"In the past, you had to move the catheter from place to place and try to recreate the anatomy of the heart," Calkins explains. "This was a tedious and time-consuming process that resulted in a cartoon-like depiction of cardiac anatomy."

And, where precision is the goal, image is everything.

Leading the way toward that goal, Hopkins was the first hospital in the world to introduce *image integration*, a novel technology that enables the assimilation of electroanatomic maps with preprocedural CT or MR images. That's been a significant benefit to patients with atrial fibrillation, the most common type of arrhythmia.

Hugh Calkins: "It's a superior technique."

Traditionally, catheter ablation has been guided by fluoroscopy and mathematically reconstructed 3-D maps that offer limited information and replication of cardiac anatomy. CT and MR imaging could reproduce true cardiac anatomy, but no electroanatomic mapping system could blend those images toward accurate catheter navigation.

Image integration not only is able to align preprocedural CT/MR images with real-time 3-D maps, but also can track and display the real-time catheter tip location and orientation at a given point in the cardiac cycle.

"Now you can take true anatomy based on the CT or MR," says Calkins, "and use that to guide manipulation of the catheter during the procedure." The system also reduces procedure time and radiation exposure and lowers complication rates.

Calkins now expects that the technology will evolve even beyond accurate reconstructions of cardiac anatomy.

"We want to be able to look at characteristics of tissues in real time during the ablation procedure," he says. "Detecting gaps in our ablation lesions, detecting scars that cause arrhythmias, identifying specifically where to ablate—this is where the research is taking us." ■

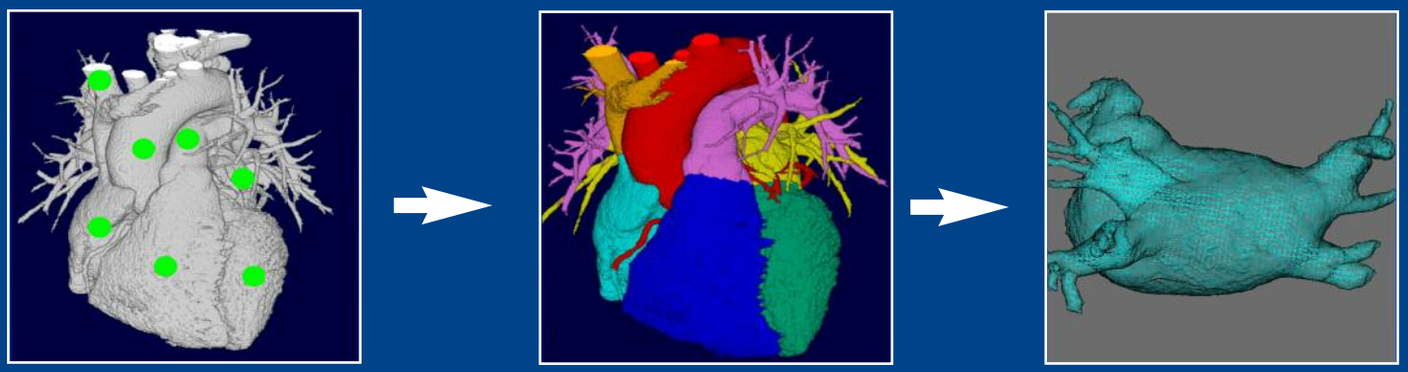

Image Segmentation and Extraction CartoXP with CartoMerge Image Integration Module

The Call to Closure

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With the number of premature births up by nearly 30 percent since the early 1980s, the incidence of PDA also has increased. Medications have their role in treating PDAs, but they can fail and have side effects that are overwhelming, increasing pulmonary perfusion at the expense of other, important organs.

When attempts at pharmacologic closure fail, surgical closure of PDA is its essential solution; Vricella is on a mission to make it happen quickly, safely and in as widespread a way as possible. Baltimore hospitals that include Franklin Hospital Center, Greater Baltimore Medical Center (GBMC), Sinai Hospital and St. Agnes Hospital have been quick to see the benefits of pediatric cardiac surgeons coming to their patients' besides.

At GBMC, which sees a handful of PDA cases annually, the advantages are unambiguous: Immediate treatment and access to highly specialized expertise.

"These babies are too critical to be moved and are often ill with other things," says GBMC neonatologist Maria Pane. "Having easy access to what is a very involved procedure with very vulnerable patients, and having it at our bedsides has made an extraordinary difference."

Though the combined number of PDA closures done at these other hospitals is low—about 15 or so annually compared to about 300 pediatric cardiac operations done at Hopkins—Vricella says the effort to accommodate them is important.

"If we can get other area hospitals with NICUs to recognize the benefits of having us come to them, we'll have taken one additional hurdle out of the way for these babies," he says. "They have so much ahead to grow into, and we want them to have that chance."

The beauty of 320-slice CT, says Joao Lima, is early detection.

Got a Second?

Hold your breath for one second, then let it out. You've just experienced the time it takes for the newest leap in imaging technology—the 320-slice computed tomography scanner—to do its job. In November, Hopkins became the first U.S. hospital to install the 320-CT, the most powerful imaging machine in its class.

For heart patients, and the physicians who treat them, it may be as close to the grail as you get, able to detect the signs of heart disease long before symptoms appear—even in the setting of arrhythmias and irregular heartbeats—in an almost literal blink of an eye.

Cardiovascular imaging director **Joao Lima** explains: "Blockages in arteries, veins or capillaries in any organ can simmer for years, with signs of chest pain, severe fatigue and headache emerging only after the disease has become seriously life-threatening."

The scanner's strength, he says, means it can find the earliest signs of restricted blood flow, long before symptoms appear or an organ becomes permanently damaged.

In the time it takes for one heartbeat, the 320-CT can acquire a full image of the heart, increasing the area covered from about 3 centimeters with the 64-CT predecessor to about 16 centimeters. For patients, it's the difference between holding one's breath for one second versus holding it for 10. "That means something to heart patients who have difficulty holding their breath, particularly the elderly and children," says cardiologist **Richard George**.

Radiation exposure—an ongoing concern with CT imaging—also is dramatically reduced to one-third or less. In part, that's due to the machine's ability to image the heart by exposing the patient to radiation for a very short period of time. The actual dosage delivery drops from 15 to 4 milliseiverts—the measurement of "absorbed" ionizing radiation—when comparing the 320-CT to the 64-CT.

Beyond the operational benefits, the clinical advantages are vast. The 320-CT may be able to replace more invasive cardiac catheterization for diagnostic testing. It takes less time, and research shows it's just as or more effective.

The 320-CT also offers the ability to rule out false positives from stress tests, a situation that would normally require follow-up cardiac catheterization, and it is about 95 percent effective in ruling out the presence of coronary artery disease.

"Negative predictive value is one of the measures of accuracy," says George. "It essentially tells us that, if a patient has a negative test, what the chance is that the test is truly negative."

The best candidates, he adds, are those with a low to intermediate risk for coronary artery disease. In those patients, the 320-CT can detect cholesterol plaques and blockages to the arteries of the heart, helping to more precisely determine whether an invasive procedure would be a benefit.■

The Quandary of Reperfusion

It's the Achilles' heel of angioplasty or induced thrombolysis. Opening and restoring blood flow to an artery following severe ischemia also opens the door for reperfusion injury, a phenomenon that's as tricky to predict as it is to reverse.

"This is a quandary," says cardiologist **Lewis Becker**. "Opening the artery is so important, but at the same time you may cause damage that takes away the maximum benefit."

Becker is on a hunt for the answers behind reperfusion injury in the hopes of finding a therapeutic target, one that might be offered universally to patients prior to reperfusion procedures.

Cardiac ischemia conditions the heart in ways that are not understood. It's that lack of understanding—physiologically and by individual patient—that also affects the predictability question. "It happens in most cases with patients who've had long-lasting ischemia, usually lasting an hour or longer," Becker explains. "But it doesn't happen to all patients, and we don't know why."

Becker heads a National Institutes of Health program project grant to study the mechanisms of injury following myocardial ischemia and reperfusion. So far, those investigations have revealed relationships among oxygen radicals and other proteins, and an inflammatory response that is initiated by the release of cytokines, messenger proteins produced by white blood cells.

It may be the perfect storm for reperfusion injury.

When blood flow is restored to an artery, it results in the return of oxygen and generates a burst of oxygen radicals, which themselves are injurious, Becker says. The oxidative stress produced by these radicals may also contribute to the activation of transcription factors within cells, causing the up-regulation of genes, which may exacerbate an inflammatory response.

"All of this may be setting the stage for problems when an artery is opened," Becker explains. "Understanding it better can help us to increase the maximum benefit of reperfusion for cardiac patients." ■

Knowledge Is Power in Myotonic Dystrophy

There may be ongoing debate over why and to what degree cardiac involvement occurs in patients with myotonic dystrophy. But for those who have the most frequently inherited neuromuscular disease of adult life, cardiologists agree on one thing: Close and ongoing surveillance is essential.

Patients with "classical," or type one myotonic dystrophy (DM1) account for 98 percent of DM patients, and cardiac disease is their most prevalent cause of death—accounting for up to 30 percent of fatalities, in many cases the result of sudden cardiac death.

Add to this some frustrating indecipherables, such as varying levels of cardiac manifestations within individual patients and an unpredictable disease progression, and you have a formula for would-be cardiac catastrophe.

But, knowledge is power, says electrophysiologist **Gordon Tomaselli**. "What we do know is that cardiac involvement is common in DM1 patients, and that conduction system abnormalities are the most common manifestation," he says. "And, while progression rates are unclear, we know that conduction abnormalities are progressive."

These predilections for heart involvement should always be on the radar of physicians who are treating patients with DM1, he adds, beginning with immediate and perpetual cardiac evaluation, regardless of the absence of cardiac symptoms.

Also important to recognize is the heritable aspect of DM1. The autosomal dominant disease exhibits a phenomenon known as "anticipation." As the disease is passed from one generation to the next, it begins earlier in life, and its signs and symptoms are more severe. That applies to its cardiac manifestations as well.

"Directed cardiovascular evaluation, including the array of diagnostics from ECG to electrophysiology studies to cardiac MRI, is used to detect cardiac involvement in DM1 patients," says Tomaselli. "And, when something is discovered, device therapy is key."

Implantable pacemakers and cardioverter debrillators, as well as cardiac resynchronization therapy when heart failure and dyssynchrony are advanced, remain the standards of care for treating conduction system abnormalities and heart muscle involvement.

Gordon Tomaselli, recently named head of Hopkins Clinical Cardiology, is known for his expertise in cardiac electrophysiology and arrhythmias, Tomaselli leads clinical research efforts within Hopkins' Donald W. Reynolds Cardiovascular Clinical Research Center as co-director. He's also principal investigator on the PRospective Observational Study of the ICD in Sudden Cardiac Death (PROSE-ICD).

"Most people with myotonic dystrophy readily compensate for their skeletal muscle disability," says Tomaselli. "The danger is when any of the manifestations, but particularly those in the heart, progress; then it's anyone's guess how quickly and to what degree cardiac involvement occurs. This is why evaluation is so critical." ■

Contact Information

Cardiology Access Line (CAL)
For physicians or their agents to refer an outpatient to cardiology
410-502-0550 or CAL@JHMI.EDU

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Johns Hopkins Medicine
Referring Physicians Services
901 S. Bond St., Suite 350
Baltimore, MD 21231-3339

Editors
William Baumgartner, M.D.
Lowell Maughan, M.D.

Managing Editor
Mary Ann Ayd
mayd@jhmi.edu, 410-955-2902

Writer
Daphne Swaneutt

Photographers
Chris Hartlove, Keith Weller

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