

# Cardiovascular Report

NEWS FROM JOHNS HOPKINS MEDICINE

Summer 2016

## Aortic Replacement Brings Near-Zero Risk of Rupture

**W**hile Woody DelCorso was driving his car to work one day at age 20, his right lung suddenly collapsed for no apparent reason. It was the first clue that eventually led him to a diagnosis of Marfan syndrome. Now 39, DelCorso has had numerous surgeries at The Johns Hopkins Hospital to treat various symptoms of this condition, including valve-sparing aortic root replacement, installation of a pectus bar to correct his concave chest, emergency surgery to repair a dissected ascending aorta and another to repair his mitral valve.

“I know that I’m blessed to have had so many operations to save my life,” DelCorso says.

But his most extensive surgery to date, in April 2015, may have ended the need for future procedures to shore up his circulatory system. The operation was necessary to repair rapidly expanding thoracic abdominal aortic aneurysms. DelCorso had his descending aorta swapped with surgical graft, completing the replacement of his entire aorta.

“Now his risk for rupture is essentially zero,” says **James Black**, Johns Hopkins Medicine’s chief of the Division of Vascular Surgery and Endovascular Therapy, who performed DelCorso’s latest procedure alongside cardiac surgeon **Duke Cameron** and other colleagues. “There’s no more natural aorta left to develop aneurysms in the future.”

Such “root to boot” replacement takes place only at a handful of medical centers across the country with the expertise to care for patients with complex aortic disease like DelCorso’s, Black says. One of the riskiest aspects of such an extensive procedure, he explains, is the potential for paraplegia. Because the aorta supplies key circulation to vast swaths of



**James Black, shown holding the branched surgical graft for thoracoabdominal aortic replacement. He says Johns Hopkins is among a handful of the nation’s medical centers that perform “root to boot” aortic replacement surgery for patients with complex aortic disease.**

the spinal cord in some patients, surgery to replace it could cut off the blood supply long enough to severely and permanently damage key nerves.

As a precaution before surgery, DelCorso, like others who undergo this procedure at Johns Hopkins, required an arteriogram performed by the hospital’s neuroradiology team. Imaging revealed that DelCorso was in the one-third of patients whose aorta predominantly supplies circulation to the spinal cord. Armed with this information, Black and other members of the surgical team planned the operation using techniques that would avoid interruption to the spinal cord’s blood flow. For additional protection, the surgeons implanted a spinal drain to reduce pressure in the spinal column in the days following the procedure. They also used deep hypothermia during the operation itself, a technique that has proven useful in a variety of other medical circumstances to protect tissue from damage by slowing its metabolism.

DelCorso’s procedure was ultimately successful, his entire aorta replaced with no subsequent damage to the spinal cord. “I would anticipate that he’ll have a completely normal life span, with no future risk of aortic rupture,” says Black.

**“This is one of the most major operations that our hospital can provide, and we do it on a routine basis with a routine recovery for most patients.”**

—JAMES BLACK

For DelCorso and hundreds of other patients with complex aortic disease who seek help at The Johns Hopkins Hospital, adds Black, positive outcomes like these are a testament to the team approach and detailed protocols the hospital has developed to care for these patients, gathered through many years of experience.

“This is one of the most major operations that our hospital can provide, and we do it on a routine basis with a routine recovery for most patients,” Black says. “To be able to deliver this type of care to so many patients while building on a legacy of treating complex aortic disease is one of my favorite parts about practicing medicine here.” ■



Watch James Black discuss his role as Johns Hopkins Medicine’s director of vascular surgery:  
[bit.ly/JamesBlackVascularsurgery](http://bit.ly/JamesBlackVascularsurgery)

# The Next Chapters for Marfan Syndrome

When Harry “Hal” Dietz was training in pediatric cardiology at Johns Hopkins in the mid-1980s, he found himself increasingly frustrated about how little medicine had to offer for children with Marfan syndrome. The enigmatic condition caused his young patients to grow significantly taller than their peers, have defects in organs, ranging from the lungs to the eyes, and—most disconcerting—problems in the heart valves and aorta.

“Many of these children were going on to need multiple cardiac surgeries and experiencing early death,” recalls Dietz. “We didn’t seem to be making that much of a difference.”

That’s why Dietz decided to switch his focus, training in genetics to better understand Marfan syndrome. He worked alongside Clair Francomano and Victor McKusick, who launched the nation’s first medical genetics division and was among the first to describe the connective tissue disorder.

Dietz’s career change has proven fruitful: Over the next 30 years, he and his colleagues discovered the genetic mutation that caused this condition, the regulatory role that the protein produced by this gene provided, and that an existing blood pressure medication acts on this pathway, with the potential to slow the rate of aortic enlargement in these patients.

But Dietz isn’t one to rest on his laurels. “There’s a sense of progress, but there’s also a sense that there’s so much more to do,” he says.

Between seeing patients with genetic cardiovascular conditions once a week and researching other disorders that fall under this umbrella in his lab—including Loays-Dietz syndrome, a condition Dietz co-discovered, which shares many of the same features as Marfan syndrome—he has continued adding to the Marfan story.

One question he and his colleagues are currently focusing on was inspired by a study published in the *New England Journal of Medicine* in 2014, that showed an equivalently slow change in aortic root growth over time in patients given a standard dose of the blood pressure medicine losartan and a high dose of a beta-blocker known as atenolol. Dietz’s lab is now working to identify the optimal drugs, combination of drugs and doses for the care of Marfan patients.

He and his colleagues are also determined to better understand what happens at every step in the pathway between the gene defect that causes Marfan syndrome and the devastating aortic enlargement that eventually leads to aortic dissection. Part of their research relies heavily on investigating the biochemical events that occur in mouse models for this condition, developed in their lab. However, the team is also exploring this question in human families that carry the Marfan mutation.

“You see striking differences in the severity of disease among family members, despite the fact that they all have the same underlying gene defect,” says Dietz—putatively, he explains, because other genes are modifying the effect of the original mutation.

The team’s analysis identifies several points along the pathway that appear to be vulnerable to these genetic modifiers. In time, Dietz says, his and other labs hope to develop new treatments that could sway the course of this disease by targeting these vulnerable events.

Eventually, he says, Marfan patients may be able to live free of the fear that their bodies could fail them, while still avoiding multiple life-changing surgeries. “The Marfan story is far from over,” adds Dietz. “Our lab continues to add to this aggressive research domain.” ■



A world authority on Marfan syndrome, Hal Dietz continues to investigate treatments to slow aortic root growth in patients with the disease.

Marfan syndrome is thought to affect about **1 in 5,000** people.

The incidence of Loays-Dietz syndrome has not yet been determined, but many hundreds of families have been identified worldwide. Both conditions are equally prevalent in both genders and all ethnic groups.



## CARDIAC SURGERY

# Getting to the Root of Aortic Disease While Sparing the Valve

Of all the symptoms that present with connective tissue diseases and affect the cardiovascular system, such as Marfan syndrome or Loays-Dietz syndrome, it’s abundantly clear that the most serious is the effect on the aortic root. Without prophylactic surgery, this arterial section extending just a couple of inches out of the heart will expand over time and develop discrete weaknesses, eventually rupturing. For most

patients with this condition, there are no obvious external signs of the danger lurking within—just a quiet knowledge, derived from periodic imaging studies, that this ticking time bomb will eventually need to be addressed.

Ever since the late 1960s, surgeons have resolved this issue with an operation called the Bentall procedure, which typically replaces the ascending aorta, root and valve with a composite graft. While lifesaving for Marfan patients, it comes with a host of drawbacks, explains **Duke Cameron**, director of the Division of Cardiac Surgery at The Johns Hopkins Hospital. In particular, the artificial valves that replace the aortic valve may wear out over time, leading to additional risky surgery. Or, the procedure may require patients to be on anti-coagulation therapy for the rest of their lives, which comes with its own inherent problems.

That’s why Cameron has made valve-sparing procedures—operations that allow patients to

retain their own aortic valves while also mitigating their risk of an aortic aneurysm—a mainstay of his practice. Over the past two decades, he and his Johns Hopkins colleagues, including **Luca Vricella**, director of pediatric cardiac surgery, have performed more than 300 of these surgeries, with excellent long-term results.

Retaining the natural valve is a particularly attractive option for young patients, who typically have many years to live with the consequences of aortic repair, Cameron explains. “Keeping a patient’s own valves, with the hope that they’ll last a lifetime, can avoid the problems of artificial valves,” he says.

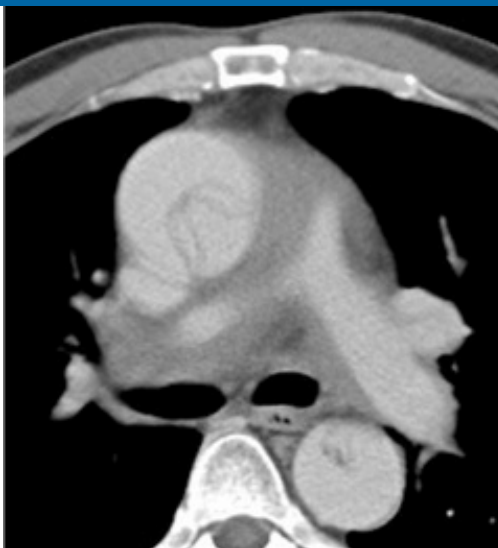
But youth adds an extra layer of challenge to this procedure, he notes. Because valve-sparing surgery was originally developed for adults, Cameron and his colleagues have worked to adapt the procedure for young patients, developing a set of guidelines to simplify the procedure and make it reliably reproducible in this population.

## The Aorta in 3-D: More Clarity and Accuracy

Computed tomography has undergone a revolution over the past few decades, morphing from scans that produce several hundred slices to those capable of producing several thousand. However, says Johns Hopkins radiologist **Elliot Fishman**, what this modality can't do is put this information together for surgeons in a way that shows them exactly what it looks like inside a patient—information that's pivotal for tracking disease progression, planning for a procedure or following a patient's progress after treatment.

"In radiology, we like to think we're in the business of providing information. But is it useful information?" Fishman, who directs diagnostic imaging and body CT at The Johns Hopkins Hospital, asks. "Whether it's a coarctation or an aneurysm, problems with the aorta are three-dimensional. This vessel is not a single slice or a series of slices."

To address this need, Fishman and his colleagues began developing 3-D CT nearly three decades ago. The team launched its work with Pixar, using hardware that the animation company developed to turn flat medical images into three dimensions. Over the years, these physicians and researchers have helped to fine-tune the software, making it not only faster—bringing the time it takes to reconstruct images from slices into three dimensions from more than a day to slightly more than a second—but also



**A sampling of 3-D imaging. Left, type A with mediastinal hemorrhage; right, type B with aneurysm of thoracic aorta; slow flow in the false lumen.**

portable. Now physicians have the ability to pull up 3-D images anywhere on their phones or tablets.

While 3-D imaging is valuable in many areas of medicine, it's particularly advantageous for the spectrum of aortic diseases. For example, Fishman says, 3-D CT has become pivotal for evaluating coarctations: the type, extent of narrowing and which procedure might work best to repair this defect. Similarly, for diseases that affect the aorta, such as Marfan syndrome or Loeys-Dietz syndrome, being able to view the problem in 3-D can help answer a bevy of questions, ranging from the extent of root involvement to how ectatic a patient's blood vessels have become.

Providing this material in three dimensions isn't just easier for surgeons to work with, Fishman explains. It's also more accurate. Studies comparing 3-D CT with flat CT slices have shown that 3-D images provide measurements that are between 20 to

30 percent more accurate—a difference that could be pivotal for medical decision-making.

Having a 3-D imaging modality also makes it easier to communicate with patients, Fishman adds, providing doctors the ability to bring videos of a patient's own images to the bedside to explain what's happening and to plan for the future.

Unlike many centers that use this technology, Johns Hopkins is able to provide 3-D CT scans 24/7. Scans can be done either on an urgent basis for patients coming in from the Emergency Department or for outpatients, Fishman says, with information customizable for referring physicians' specific needs. He and his team are currently working to make this information even more accessible by providing it in a virtual meeting environment, where he and other Johns Hopkins radiologists can discuss images and findings with referring physicians.

"We always want to make sure that we're doing the absolute best thing we can for every patient," Fishman says. "And each time technology advances, we're able to give our patients more and more." ■



**"Whether it's a coarctation or an aneurysm, problems with the aorta are three-dimensional. This vessel is not a single slice or a series of slices."**

—ELLIOT FISHMAN



View more of Fishman's images at [ctisus.com](http://ctisus.com).

After ensuring that a patient's valve is salvageable, the refined procedure involves assessing the size of the necessary graft that brings the natural valve's leaflets into an optimal closed position. The procedure is further simplified from the original one, developed by Tirone David at the University of Toronto, by securing the graft with two or three sutures at the bottom of the root.

Cameron and his colleagues have further modified the procedure for patients with Loeys-Dietz syndrome, a condition first described at Johns Hopkins only a decade ago. As they gather more information about this condition, it has become apparent that blood vessels in these patients are significantly weaker than those of patients with Marfan syndrome and other connective tissue disorders. As a result, these patients tend to develop pseudoaneurysms at the suture points. Consequently, the surgeons have crafted a technique to reinforce the weakest points to help prevent this complication.

Cameron and his Johns Hopkins colleagues have trained surgeons in these valve-sparing techniques at meetings around the world and in Johns Hopkins' own surgical suites, furthering their mission to help as many patients as possible through educating physicians.

"If you do 100 operations with great results, then you help 100 patients," says Cameron. "But if you train 100 residents to do operations with great results, it's a much broader and lasting impact. Being able to ease the burdens of the greatest number of patients, both here and elsewhere, is our ultimate goal." ■

**Valve-sparing procedures have become a mainstay of Duke Cameron's practice—reducing the risk of aortic aneurysms.**



## Letting Kids with Aortic Disease 'Be Kids'

"Our **Connective Tissue Disorder Clinic** allows ample time for each patient, which enables us to provide medical guidance as well as patient education. Patients often comment that their condition has never been explained to them in such detail before, and they walk away with a much better understanding of what to expect. We focus more on what we can do for the patients and what they are able to do, rather than on restrictions. One of the greatest challenges we face is to have to constrain our patients from certain activities because of the risk of aneurysm growth or even dissection—particularly because aneurysms are asymptomatic and are usually found incidentally, or due to related systemic features or a positive

family history. I spend 80 percent of my time in the lab trying to better understand these conditions and to develop new treatments. My greatest hope for these patients is that whatever the condition they have, it won't define their lives negatively. Rather, they will learn that with some modifications, they can live happy, productive lives with a normal life expectancy."



—Jennifer Pardo Habashi  
Pediatric Cardiologist  
Johns Hopkins Children's Center

# CardiovascularReport

The Johns Hopkins Heart and Vascular Institute *Cardiovascular Report* is one of the many ways we seek to enhance our partnership with our thousands of referring physicians. Comments, questions and thoughts on topics you would like to see covered in upcoming issues are always welcome. Contact [jminkov2@jhmi.edu](mailto:jminkov2@jhmi.edu).

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Johns Hopkins Medicine  
Marketing and Communications  
901 S. Bond St., Suite 550  
Baltimore, MD 21231

#### Heart and Vascular Institute

James Black III, M.D.; Duke Cameron, M.D.; Edward Kasper, M.D.;  
*Medical Editors*

#### Marketing and Communications

Dalal Haldeman, Ph.D., M.B.A., *Senior Vice President*  
Judy F. Minkove, *Managing Editor*  
Christen Brownlee, *Writer*  
Lori Kirkpatrick, *Designer*  
Keith Weller, *Photographer*

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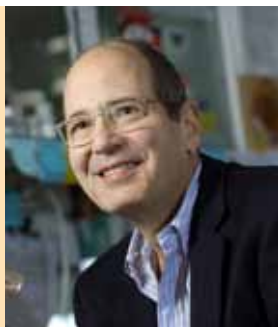
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