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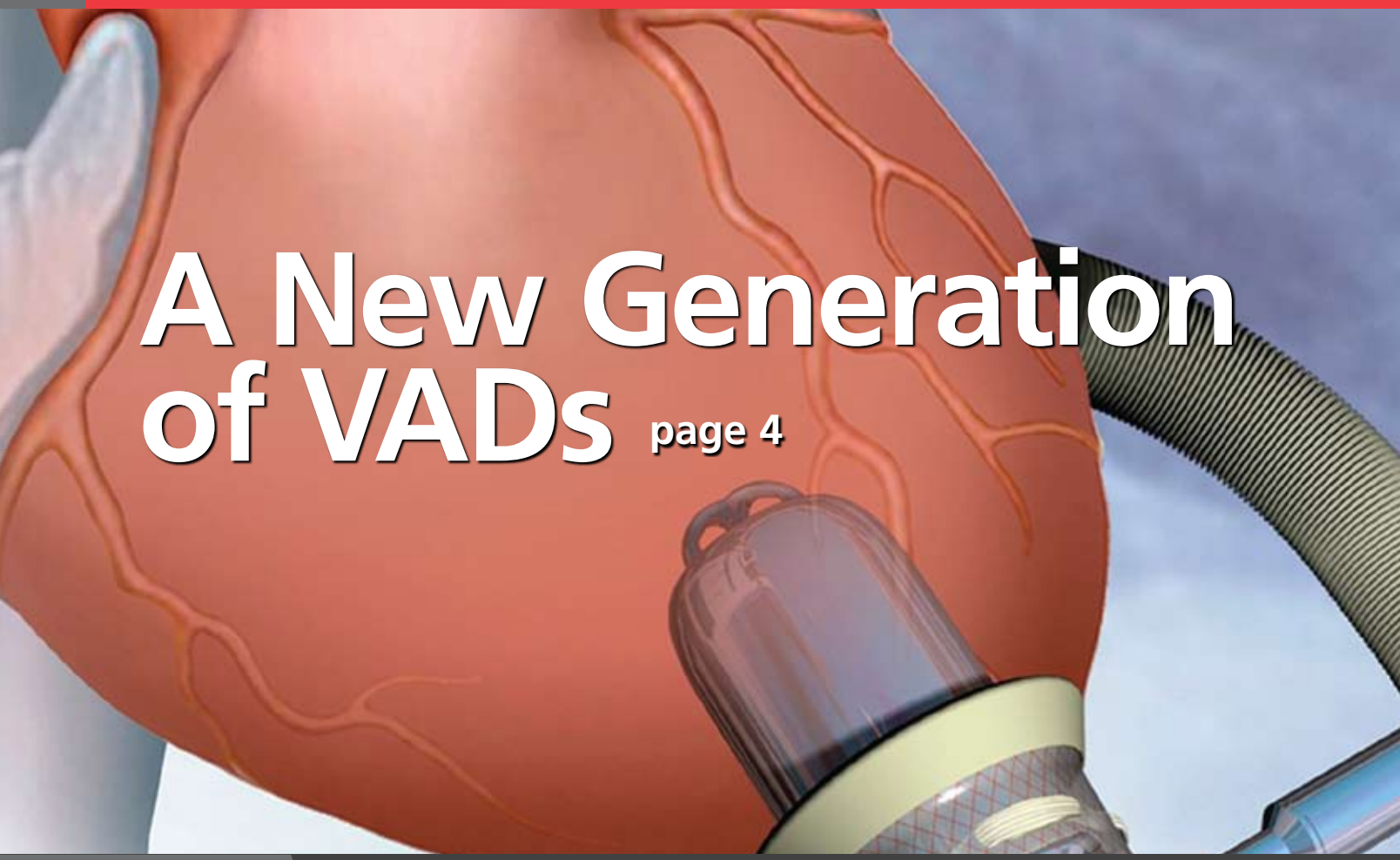
UH Heart & Vascular Innovations

University Hospitals Harrington-McLaughlin Heart & Vascular Institute



A New Generation of VADs page 4

Leading the Way

In this issue of *UH Heart & Vascular Innovations*, we reveal the cutting-edge translational and clinical research activities that are directly benefiting patients. One of the primary goals of the University Hospitals Harrington-McLaughlin Heart & Vascular Institute is to create a premier center of excellence for heart and vascular clinical care distinguished by the groundbreaking discovery and innovation of our talented physicians, surgeons and staff. We continue to bring together a first-class team of clinician-investigators who are leaders in scientific discovery as well as patient care and, in this issue, we describe several of our most innovative programs.

In our "No Need for High Blood Pressure Meds?" article, **John Blebea, MD**, describes his intriguing research on an alternative, nonpharmacologic approach to reducing high blood pressure. He envisions the possibility of managing high blood pressure by utilizing electrical stimulation of stretch receptors that surround the carotid arteries in the neck to activate the body's natural mechanisms to regulate blood pressure.

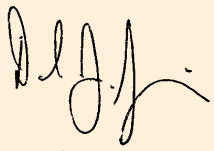
James Fang, MD, and **Arie Blitz, MD**, discuss their remarkable work with second-generation ventricular assist devices in "Heart Failure and Ventricular Assist Devices." These instruments are currently available to severe heart-failure patients as a "bridge" to heart transplantation or as "destination" therapy, providing hope to our sickest patients who may otherwise have "no options."

The exciting work of **Marco Costa, MD, PhD**, is presented in "Innovative Cardiovascular Imaging Technology." He is a worldwide leader in the development of a new cardiovascular imaging modality called optical coherence tomography, or OCT, which uses light rather than ultrasound to produce the highest resolution images of the coronary arteries. This transforming technology improves the ability of interventional cardiologists to evaluate the results of drug-eluting stent procedures.

In the Consultation Department, **Ross Ungerleider, MD**, describes an "Adaptation of the Ross Procedure in a Marfan Patient." While the Ross procedure is not typically indicated for treatment of patients with Marfan syndrome, Dr. Ungerleider details his innovative and successful use of the Ross procedure combined with the valve-sparing aortic replacement operation in a patient with the condition.

I am confident that after reading this issue of *UH Heart & Vascular Innovations* you will continue to be impressed by UH's ability to deliver excellence at all levels – physician education, translational clinical research and personalized patient care with cutting-edge treatment options for our patients. Thank you for being a supporter of University Hospitals Case Medical Center and the UH Harrington-McLaughlin Heart & Vascular Institute and for helping us advance our mission.

To Heal. To Teach. To Discover.



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UH Heart & Vascular Innovations, Winter 2010, Volume 1, Issue 2
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SCHOOL OF MEDICINE
CASE WESTERN RESERVE UNIVERSITY

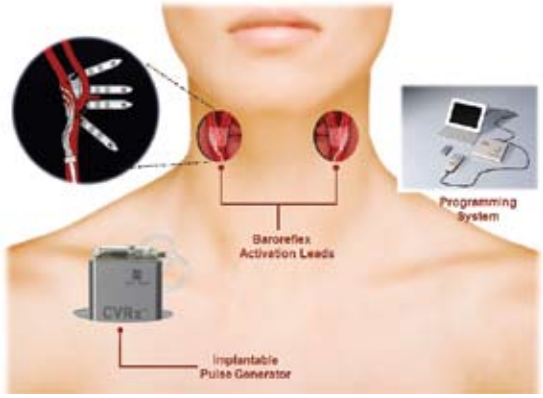
The commitment to exceptional patient care begins with revolutionary discovery. Faculty at the Case Western Reserve University School of Medicine, who also are physicians at UH Case Medical Center, are at the forefront of medical research and innovation. The School of Medicine is the largest medical research institution in Ohio and among the nation's top medical schools for research funding from the National Institutes of Health.

No Need for High Blood Pressure Meds?

A novel treatment for drug-resistant hypertension

John Blebea, MD, Chief, Division of Vascular Surgery and Endovascular Therapy, University Hospitals Case Medical Center; Director, Vascular Center, UH Harrington-McLaughlin Heart & Vascular Institute

Electrical stimulation of "stretch receptors" surrounding the carotid arteries in the neck may prove to be the next treatment for drug-resistant hypertension. Clinical researchers from the University Hospitals Harrington-McLaughlin Heart & Vascular Institute are part of an international research group examining the efficacy of this novel treatment. **John Blebea, MD**, Chief, Division of Vascular Surgery and Endovascular Therapy, University Hospitals Case Medical Center; Director, Vascular Center, UH Harrington-McLaughlin Heart & Vascular Institute; and Professor of Surgery, Case Western Reserve University School of Medicine, reports that this technique could enable patients to reduce or entirely discontinue use of their blood pressure medications.



Diagrammatic representation of the baroreceptor stimulator system illustrating the implantable battery/pulse generator placed subcutaneously in the infraclavicular location, the electrode activation leads wrapped around the carotid bifurcation, and the computer-based programming system.

SHOCKING TREATMENT

Performed under general anesthesia, the procedure involves surgical placement of electrodes around both carotid arteries in the neck. The electrode wires are tunneled beneath the skin to an area under the collarbone where a battery and control unit are placed. "The device is very similar to a [heart] pacemaker and, indeed, has been termed a pacemaker for high blood pressure," says Dr. Blebea. Electrical stimulation of the stretch receptors that surround the carotid arteries, known as baroreceptors, sends an electrical signal to the brain, causing it to use its natural pathways and mechanisms to relax blood vessels and lower blood pressure – the baroreflex. "The result is seen immediately after the device is turned on," says Dr. Blebea.

About 72 million adults in the United States suffer from hypertension, defined as having a systolic blood pressure of 140 mm Hg or higher or a diastolic blood pressure of 90 mm Hg or higher. Of these, about 4 million adults (approximately 6 percent) suffer from drug-resistant hypertension. This is a form of the disease that does not respond to normal treatments such as reducing salt intake or using various combinations of medications.

"We are not certain why some individuals are resistant to present therapies," says Dr. Blebea.

Two preliminary trials of the baroreflex stimulators, however, yielded encouraging results. "For patients who were on an average of five medications, the procedure reduced their systolic blood pressure by 37 mm Hg. This result was observed even after the device had been in place for three years," Dr. Blebea says. The Rheos® Baroreflex Hypertension Systems trial, sponsored by the developer of the device, CVRx Inc., is being conducted at 30 clinical sites and is planned to include 300 patients. Individuals enrolled in the study need to be over 21 years of age and have blood pressure that is at least 160/85 mm Hg. The study is currently in the Pivotal Clinical Trial stage of testing, which must be completed before final approval can be issued by the Food and Drug Administration. The device has already been approved to treat drug-resistant hypertension in Europe, but it will not be marketed there until the present study is completed.

POTENTIAL FOR ADDITIONAL APPLICATIONS

"If the device is demonstrated to be efficacious in patients with resistant high blood pressure and approved by the FDA, I see the possibility that it will be used in patients with other conditions," says Dr. Blebea. Another trial has begun to test the baroreflex stimulator device in patients with congestive heart failure. "Preliminary results in some patients show that their heart function has improved," Dr. Blebea notes, "so there are additional exciting possibilities for application of this technology."

Visit Us Online

To learn more about University Hospitals Harrington-McLaughlin Heart & Vascular Institute, including the cardiovascular medicine grand rounds schedule, go to **UHhospitals.org/heart**.

Heart Failure and Ventricular Assist Devices

An alternative one-on-one, patient-oriented approach is offered at University Hospitals

James C. Fang, MD, Medical Director, Advanced Heart Failure & Transplant Center; Associate Chief for Clinical Affairs, UH Harrington-McLaughlin Heart & Vascular Institute

Arie Blitz, MD, Director, Heart Transplantation and Mechanical Circulatory Assistance, University Hospitals Case Medical Center

The Advanced Heart Failure & Transplant Center at University Hospitals Harrington-McLaughlin Heart & Vascular Institute offers the community treatments for advanced heart disease and advanced heart failure. The Center specializes in pharmacologic and device therapy, mechanical ventricular assist devices (VADs), heart transplantation, investigational therapies and palliative care.

The Impella Percutaneous Devices

According to **James C. Fang, MD**, Medical Director, Advanced Heart Failure & Transplant Center; Associate Chief for Clinical Affairs, UH Harrington-McLaughlin Heart & Vascular Institute; and Professor, Case Western Reserve University School of Medicine, "The mission of the Advanced Heart Failure & Transplant Center is to provide the latest and most effective therapies to patients in Northeast Ohio and surrounding regions in a personalized one-on-one, patient-centered approach."

With a high level of expertise in treating heart failure, performing heart transplants, and implanting VADs (also known as heart pumps), the Center offers another sophisticated site in Ohio for patients to consider for their heart and vascular health. One of the most important services provided by the physicians at the Center is their ability to review a patient's current medical and device therapies and then to provide other treatment options to improve their prognosis and quality of life. "At University Hospitals Case Medical Center, we offer many options and a very personalized approach. We are proud of the fact that we offer very individualized care," says Dr. Fang. "Many patients don't recognize that they are suffering needlessly."

THE VAD OPTION

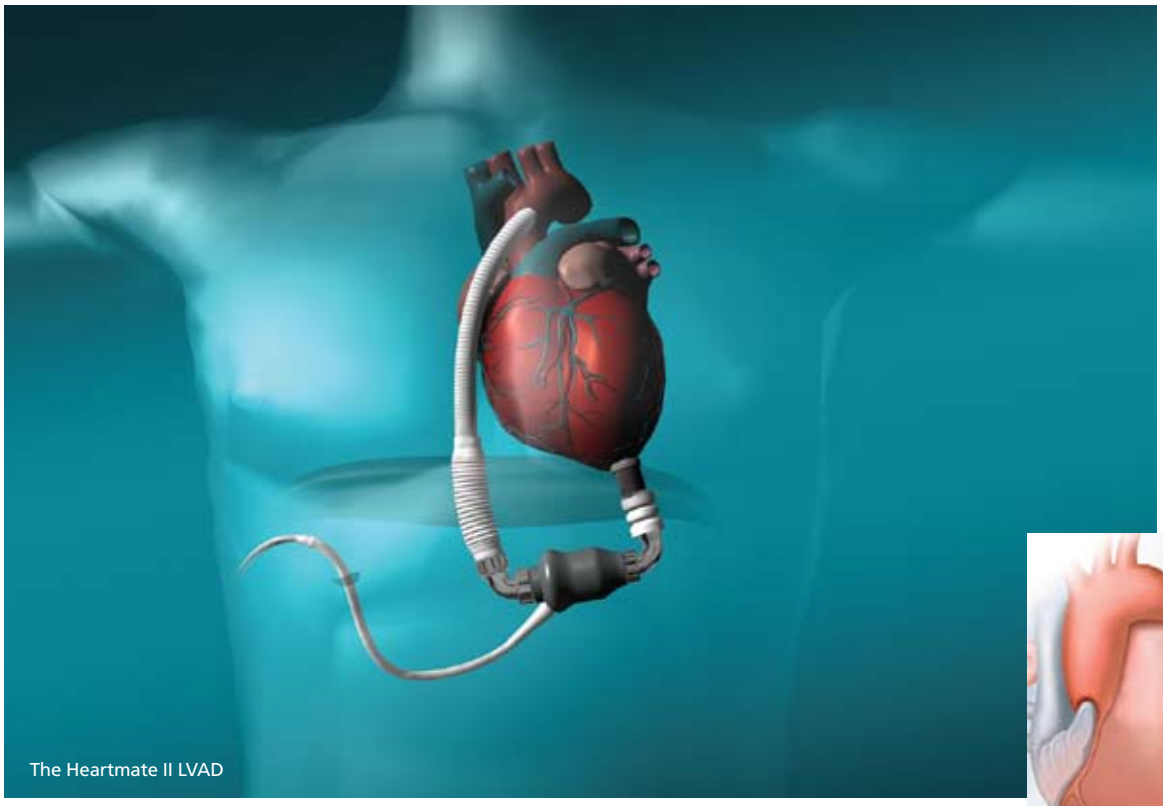
Patients seen at the Center have refractory congestive heart failure and continue to be short of breath despite medications, device therapy (such as biventricular pacemakers) and heart surgery. These patients find that even doing simple activities like taking a shower or sitting in a chair are difficult. In addition, they cannot stay out of the hospital for very long – they are often regularly admitted for shortness of breath and fluid buildup in the legs. Such patients may be candidates for heart transplantation or a VAD.

VADs are sophisticated, miniaturized pumps that help the heart to provide sufficient blood flow throughout the patient's body. "VADs are the newest form of a mechanical heart," says Dr. Fang. A healthy heart can normally pump about 5 L of blood per minute around the body at rest. If, for example, a patient's heart can pump only 1 L of blood per minute, the VAD will pump an additional 4 L, for a total of 5 L of blood per minute. "The heart pump helps," notes Dr. Fang, "without entirely taking over the function of the heart."

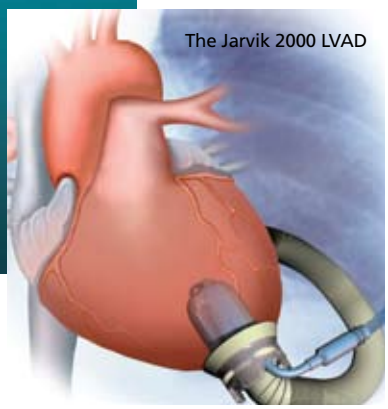
Typically, heart pumps are used temporarily while a patient awaits a heart transplant. Current first-generation VADs, such as the Thoratec Heartmate XVE, are also used as a "destination" therapy – a permanent solution for heart failure. These devices can function for 12 to 18 months before they must be replaced. It is anticipated that a new, second generation of heart pumps, now undergoing investigational study, will increase the duration of ventricular assistance to two to four years. Nationwide about 2,500 heart transplant operations are performed annually and the Advanced Heart Failure & Transplant Center's heart surgeons have collectively performed hundreds of heart transplants.

CUTTING-EDGE TECHNOLOGY

A second-generation device, the Heartmate II, made by Thoratec Corp., is about the size of a D flashlight battery. Once surgically implanted in the heart, the device pumps blood throughout the circulatory system, just as water flows through a garden hose, via an



The Heartmate II LVAD



The Jarvik 2000 LVAD

impeller (a corkscrew-type device) that spins at close to 10,000 RPM. The team has implanted this device in two patients this year as a bridge to heart transplant. Dr. Fang's colleague, **Arie Blitz, MD**, Director, Heart Transplantation and Mechanical Circulatory Assistance, University Hospitals Case Medical Center; and Assistant Professor, Case Western Reserve University School of Medicine, reports that "both patients have done exceedingly well and continue to have the device in place." According to Dr. Fang, the Heartmate II may be approved for "destination" therapy in patients with heart failure in the first quarter of 2010.

Dr. Fang and his team at the Advanced Heart Failure & Transplant Center have also been involved in investigational clinical trials using some of these new VADs. Dr. Fang's team is participating in a clinical trial evaluation of the Jarvik heart, which also uses an impeller to produce blood flow. This investigational device was implanted in a patient as a bridge to heart transplant, and the transplant was performed after the device had been in place for one year. The patient is doing well, notes Dr. Blitz. Worldwide, the Jarvik heart trial has been ongoing for several years, with dozens of patients now enrolled.

Yet another VAD used at the Center is the Impella, made by Abiomed Inc. It is presently used for individuals with catastrophic heart attack or for those who require a very high-risk angioplasty. The Impella is inserted into the heart via the groin using a catheter and is only for short-term use. "The first time we used it, this device saved the life of our patient who would otherwise not have survived," reports Dr. Blitz.

Dr. Fang's team was the first in Northeast Ohio to place the Jarvik heart and the Impella in heart patients. The team is involved in two of the clinical trials examining the Impella. While patients with the Heartmate II or the Jarvik heart are ambulatory after recovering from surgery, those who receive the Impella must lie in bed while the device is in place.

It is envisioned that at some point more durable and smaller VADs that can be implanted without surgery could be used as a "destination" therapy – and a heart transplant may never be needed. Although clinical studies of the long-term use of the newer VADs are part of research programs, Dr. Fang reports that the results from such studies are encouraging.

Contact Us

For more information regarding the advanced heart failure treatment and VAD programs at UH Harrington-McLaughlin Heart & Vascular Institute, contact James C. Fang, MD, at 216-844-8242 or Arie Blitz, MD, at 216-844-4988.

Innovative Cardiovascular Imaging Technology

University Hospitals Case Medical Center is at the cutting edge of optical coherence tomography

Marco Costa, MD, PhD, Director, Interventional Cardiovascular Center and Research & Innovation Center, University Hospitals Harrington-McLaughlin Heart & Vascular Institute

Interventional cardiology is a broad specialty area combining different procedures targeting the heart, cardiac blood vessels and peripheral blood vessels. Housed within the University Hospitals Harrington-McLaughlin Heart & Vascular Institute, the interventional cardiology division is a group of experts focusing on minimally invasive treatment for complex coronary artery disease, structural heart disease, and mitral and aortic valvuloplasty, as well as peripheral interventions for patients with lower-extremity, renal and carotid-artery disease.

NOVEL DIAGNOSTIC MODALITY

"Our program is unique in that we have a multidisciplinary team that specializes in complex cardiac care and therapies," says **Marco Costa, MD, PhD**, Director, Interventional Cardiovascular Center and Research & Innovation Center, University Hospitals Harrington-McLaughlin Heart & Vascular Institute; and Professor of Medicine, Case Western Reserve University School of Medicine. The mission of the interventional cardiology division is to provide cutting-edge therapies that combine the academic mission for scientific development and the clinical mission to improve patient care and outcomes.

"A key element of our research program is the use of a novel high-resolution imaging modality known as optical coherence tomography," explains Dr. Costa. A miniaturized technology that can be introduced directly into a patient's blood vessels via a 2 mm catheter, optical coherence tomography allows visualization of living tissues. The computerized device emits infrared light, and the backscattering of light yields super-high-resolution, real-time images of blood vessels, and has been used for the long-term assessment of stents and to detect risk of heart attack.

HIGH-RESOLUTION IMAGING IN LIVING TISSUES

Optical coherence tomography can achieve a resolution of 4-20 µm, which otherwise can only be achieved by microscope. The technique provides a six- to 30-fold increase in resolution over high-frequency intravascular ultrasound (110 µm) or a 20- to 100-fold increase in resolution over conventional coronary angiography (400 µm). Dr. Costa reports that his group has led more than 10 clinical trials of optical coherence technology pioneered by Light Lab Imaging Inc. and that the technology is now being used regularly in Europe and Japan. "We are the world leader in testing and optimizing optical coherence tomography, which is expected to be approved by the FDA for patient care in the U.S. in the next six months," Dr. Costa says. Physicians from across the U.S. visit the UH Harrington-McLaughlin Heart & Vascular Institute at UH Case Medical Center for training in the use of optical coherence tomography for coronary disease and the interpretation of the images produced. According to Dr. Costa, "This technology is revolutionizing imaging, diagnosis and cardiovascular therapies around the world."

Safe and Unique

Optical Coherence Tomography allows near-microscopic examination of living tissues. The technology is unique because it allows direct photographic examination of soft tissues, which cannot be easily accomplished using other modalities.

Other new developments in interventional cardiology include:

STEREOTAXIS-GUIDED INTERVENTION

The Institute's Interventional Cardiology Division is implementing stereotaxis-guided intervention, a technique that allows remote control of catheter-based diagnostic and therapeutic devices. The physician can visualize the images generated by this computer-aided technology on a video monitor. Magnets in the catheter and the control apparatus allow remote guidance of the catheter through the complex networks of blood vessels in the heart.

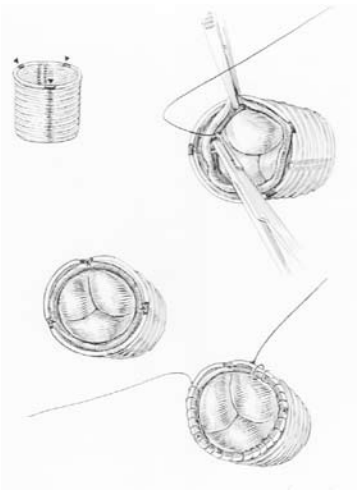
RAPID RESPONSE TO HEART EMERGENCIES

Over the past two years, a multidisciplinary team of cardiologists, paramedical and emergency medical services (EMS) personnel, and community members has been involved in a program to develop a rapid response Heart Attack Team (also called the "Time Is Muscle Network"). Emergency response teams now have the capability to transfer electrocardiograms from the field, allowing the catheterization lab to prepare to receive the patient and immediately proceed to catheterization as soon as the patient arrives at the hospital. "Our record time, from the time the patient arrived at our facility to the time when we opened the blood vessel, was 16 minutes, which matches the best possible data anywhere in the world," Dr. Costa says. "This is really an effort that helps create public awareness and improve outcomes in our city. We are very committed to this program."

Adaptation of the Ross Procedure in a Marfan Patient

Successful treatment of aortic valve insufficiency

The Ross operation combined with a valve-sparing aortic replacement operation has been used to successfully treat aortic valve insufficiency in a patient with Marfan syndrome, a connective tissue disorder that affects 1 in 5,000 people in the United States. This autosomal dominant, inherited disorder impacts the heart and blood vessels, bones and joints, and eyes.



The pulmonary valve autograft is inserted into a Dacron tube.

FRAGILE ARTERIES CAN RUPTURE

Because of the connective tissue abnormality, the arteries of patients with Marfan syndrome are fragile and can tear, resulting in aortic dissection or aortic aneurysm. In many patients a valve-sparing aortic replacement operation is appropriate in which the aorta is replaced but the aortic valve is preserved. Some Marfan patients may also have additional abnormalities of the aortic valve, in which case it must be replaced. Typically, the standard Ross operation is used for individuals who do not have Marfan syndrome. This procedure involves replacing the abnormal aortic valve with the patient's own pulmonary valve, yielding a living valve at the aortic position. The patient's pulmonary valve is then replaced with a cadaver valve. Patients are usually hospitalized for four to five days and fully recover in three to six months.

However, the pulmonary valve of a patient with Marfan syndrome is not normal, as it exhibits the genetic defect characteristic of the disease. "Patients with Marfan syndrome develop problems with aortic valve dilation and leakage of the valve. Surgeons hope to replace the aorta before it ruptures, but the Ross procedure is not generally indicated for patients with Marfan's, and in fact, it is contraindicated," says **Ross Ungerleider, MD**, Chief, Pediatric Cardiothoracic Surgery, University Hospitals Rainbow Babies & Children's Hospital; Director, Congenital Heart Disease Center, UH Harrington-McLaughlin Heart & Vascular Institute; and Professor, Case Western Reserve University School of Medicine.

UNIQUE APPLICATION PROTECTS VALVE INTEGRITY

Dr. Ungerleider's team has adapted the standard Ross procedure to overcome this limitation for Marfan patients. "We developed a unique operation, first done in October of 2004, where we combined the Ross operation and the valve-sparing aortic replacement operation. We do the Ross operation in a way where we totally contain the autograft, that is the pulmonary valve, within nondistensible Dacron," says Dr. Ungerleider, a specialist in congenital heart disease who has spoken internationally on the techniques involved. This particular patient with Marfan syndrome was 40 years old at the time. "He is now doing well five years since the surgery. The aortic valve has not dilated, and the autograft is working perfectly. He doesn't need to take blood thinners; he has his own living valve, and his aorta is not going to dilate because the valve is encased in a piece of Dacron," Dr. Ungerleider reports.

Ross Ungerleider, MD, Chief, Pediatric Cardiothoracic Surgery, UH Rainbow Babies & Children's Hospital; Director, Congenital Heart Disease Center, UH Harrington-McLaughlin Heart & Vascular Institute

A NEW OPTION FOR PATIENTS

The published literature shows that adults with congenital heart disease are best managed by congenital heart surgeons whose primary practice is devoted to congenital heart surgery, notes Dr. Ungerleider. "It is important for patients to know what's out there," he adds. "I think that the Ross operation is an outstanding operation if it's done by somebody who has experience doing it. …For patients with Marfan syndrome, although it has been contraindicated in the past, the Ross operation is now an option."

Delineating the Diagnosis

Diagnosis of Marfan syndrome is difficult, as the condition must be distinguished from several other connective tissue disorders. Marfan syndrome is due to a defect in the gene encoding the extracellular matrix protein fibrillin-1. Most patients develop cardiovascular problems, which can include aortic dilation, aortic aneurysm, aortic dissection, mitral valve prolapse and aortic regurgitation.

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Research & Innovation Center

University Hospitals Harrington-McLaughlin Heart & Vascular Institute at UH Case Medical Center offers cutting-edge therapies through clinical trials coordinated by its Research & Innovation Center.

If you are interested in referring a patient or would like more information, please contact Stacey Mazzurco, RN, Clinical Trials Manager, at **216-844-3130** or by e-mail: **Stacey.Mazzurco@UHhospitals.org**.

New Faculty

University Hospitals Case Medical Center is pleased to welcome:

EDWIN G. AVERY, MD
Chief, Division of Cardiothoracic Anesthesia, UH Case Medical Center; Chief Anesthesia Officer, UH Harrington-McLaughlin Heart & Vascular Institute; Associate Professor of Anesthesiology and Perioperative Medicine, Case Western Reserve University School of Medicine

Dr. Avery comes to University Hospitals from Massachusetts General Hospital, Boston, and Harvard Medical School

JOHN KLICK, MD
Cardiothoracic Anesthesia, UH Case Medical Center; Assistant Professor of Anesthesiology and Perioperative Medicine, Case Western Reserve University School of Medicine

Dr. Klick comes to University Hospitals from Massachusetts General Hospital, Boston, and Harvard Medical School

SAHIL A. PARIKH, MD
Director, Experimental Interventional Cardiology Laboratory, UH Harrington-McLaughlin Heart & Vascular Institute; Assistant Professor of Medicine, Case Western Reserve University School of Medicine

Dr. Parikh comes to University Hospitals from Massachusetts General Hospital, Boston, and Harvard Medical School

JOHN C. WANG, MD
Division of Vascular Surgery and Endovascular Therapy, UH Case Medical Center; Assistant Professor of Surgery, Case Western Reserve University School of Medicine

Dr. Wang comes to University Hospitals from Temple University School of Medicine, Philadelphia

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Update on Vascular Disease: Peripheral Arterial Disease

Saturday,
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8:00 a.m. to 1:00 p.m.

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