

Heart & Vascular INNOVATIONS



Advances in VAD Technology Benefit Patients and Researchers

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University Hospitals Case Medical Center and Case Western Reserve University School of Medicine are consistently recognized as two of the premier institutions in the nation, according to U.S. News & World Report's annual rankings.

From the Director

Changing the Standard of Care



As one of just 18 hospitals named to the U.S. News & World Report Honor Roll, University Hospitals Case Medical Center is committed to building upon a legacy of medical discovery that began nearly 150 years ago and continues today. In this issue of Heart & Vascular Innovations, we demonstrate how cardiovascular medicine and surgery within University Hospitals Harrington Heart & Vascular Institute is not merely building upon past accomplishments, it's improving them.

Just as technological breakthroughs in stents and local drug delivery revolutionized the treatment of coronary artery disease, so too do similar advances portend success in the treatment of blockages in the periphery. In our "Research Connection," **Sahil Parikh, MD**, and **Vikram Kashyap, MD**, describe how knowledge gleaned from percutaneous coronary intervention has informed cutting-edge approaches to peripheral artery disease.

Although heart replacement therapy with transplantation recently celebrated its 46th anniversary, the history of mechanical circulatory assistance with ventricular assist devices (VADs) has been relatively brief. Nonetheless, **Soon Park, MD**, explains in our cover story how, over just two decades, VAD placement for bridge and destination therapy has matured to the point that mechanical circulatory assistance is now capable of extending patients' survival and quality of life in meaningful ways. As the evolution continues — from wireless battery power to magnetic-based rotors — the VADs of tomorrow show great promise for continued improvement.

The advent of powerful chemotherapies and radiation treatments has bolstered the fight against cancer, but has introduced a new, unintended foe:

treatment-related cardiotoxicity. In our "Feature Story," **Guilherme Oliveira, MD**, discusses the new Onco-Cardiology Program at UH Harrington Heart & Vascular Institute and University Hospitals Seidman Cancer Center. This unique program is focused on better identifying, preventing and treating cardiac dysfunction in cancer patients.

Finally, in our "Case Study," **Trevor Jenkins, MD**, and **Robert Schilz, DO, PhD**, explain how, after years of evaluating dyspnea in patients at rest, UH Case Medical Center's newly opened Dyspnea Center is helping cardiovascular and pulmonary medicine shift its focus from static assessments to highly accurate, exercise-based diagnostic approaches.

The constant drive for leading-edge innovative therapies and disruptive technologies is the spirit that enables us to not only deliver outstanding care, but also to truly advance care for our patients.

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The commitment to exceptional patient care begins with revolutionary discovery. University Hospitals Case Medical Center is the primary affiliate of Case Western Reserve University School of Medicine, a national leader in medical research and education and consistently ranked among the top research medical schools in the country by U.S. News & World Report. Through their faculty appointments at Case Western Reserve University School of Medicine, physicians at UH Case Medical Center are advancing medical care through innovative research and discovery that bring the latest treatment options to patients.

To receive future cardiovascular-related communications from UH Case Medical Center, please email HVInnovations@UHhospitals.org.

Reinventing History

Revisiting the treatment of coronary blockages informs novel interventions for peripheral artery disease



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Vikram S. Kashyap, MD, FACS, Chief, Division of Vascular Surgery and Endovascular Therapy, University Hospitals Case Medical Center; Co-Director, UH Harrington Heart & Vascular Institute; and Professor of Surgery, Case Western Reserve University School of Medicine

Peripheral artery disease (PAD) is highly prevalent in patients with atherosclerotic risk factors. PAD occurring within the superficial femoral artery (SFA) is especially common. Revascularization of the SFA can be complex due to the mechanical stress and strain imposed by the legs during daily activities.

Increasing awareness of these complexities, as well as of the correlation between PAD and the risk of myocardial infarction and stroke, has underscored the need for collaborative care from multiple cardiovascular subspecialties, thereby facilitating and promoting optimal technical and procedural approaches for these patients.

New Knowledge

“Peripheral arterial disease can lead to devastating problems, including amputation. At University Hospitals Harrington Heart & Vascular Institute, we have a collaborative, multidisciplinary effort that emphasizes optimal medical and surgical care, endovascular strategies and wound care,” says **Vikram S. Kashyap, MD, FACS**, Chief, Division of Vascular Surgery and Endovascular Therapy, UH Case Medical Center; Co-Director, UH Harrington Heart & Vascular Institute; and Professor of Surgery, Case Western Reserve University School of Medicine. “We attempt to provide blood flow in the least invasive manner, but in some patients leg bypass surgery is needed to restore perfusion.”

Minimally invasive approaches, such as endovascular balloon angioplasty and stent placement, have advantages over bypass surgery, but they are not without their problems.

“Angioplasty or stents alone are not a durable strategy for revascularization compared with conventional bypass in some cases. Endovascular therapies cause injury, leading to restenosis and the need for repeat target vessel revascularization,” explains **Sahil A. Parikh, MD**, Director, Experimental Interventional Cardiology Laboratory, University Hospitals Case Medical Center; Director, Interventional Cardiology Fellowship Program; and Assistant Professor of Medicine, Case Western Reserve University School of Medicine. “As a result, we started using stents, which have better patency than balloon angioplasty, but still are not ideal.”

Stents can be suboptimal due to mechanical stress, making them prone to fracture. In response, Drs. Parikh and Kashyap are investigating three novel strategies for treating PAD.

Designing the Future

The first method utilizes redesigned stents that resist fracture. In clinical trials, these interwoven Nitinol™ stents demonstrated very high primary patency and will soon be approved by the FDA for use in patients with complex SFA disease.

Next, new angioplasty balloons now feature scoring elements to modify arterial plaque more effectively, resulting in greater expansion of narrowed vessels with less trauma and flow-limiting dissections. Drs. Parikh and Kashyap and their colleagues are leveraging University Hospitals Case Medical Center’s expertise in optical coherence tomography imaging in various clinical trials to determine whether these new balloons are more effective than standard angioplasty balloons, particularly in patients with calcified atherosclerotic plaques.

Lastly, drug-coated balloons draw heavily upon technology designed for drug-eluting stents that have markedly reduced restenosis and the need for repeat coronary artery revascularization procedures. These devices have been designed to have the advantages of stent-based drug delivery without the structural and mechanical disadvantages of the stents themselves. UH Case Medical Center is actively participating in pivotal clinical research trials using this technology. Early results demonstrate superior long-term outcomes rivaling those of stents.

Expanded Innovations

For patients with treatment-resistant hypertension, sympathetic renal denervation offers an innovative solution – especially in individuals with severe hypertension (i.e., blood pressure greater than 160 mmHg), who are taking three or more antihypertensives at maximum dosage. But the latest wave of research from UH Harrington Heart & Vascular Institute may help renal denervation reach a larger population of patients. Additional protocols are actively recruiting patients with persistent moderate hypertension (140-160 mmHg) who are taking three medications at peak dosage.

Learn More

To schedule an appointment in the Vascular Center, please call **216-844-3800**. For any questions regarding clinical research trials for PAD or renal denervation for moderate-severe hypertension, please email Stacey Mazzurco, RN (**Stacey.Mazzurco@UHhospitals.org**).

VADs Get an Upgrade

Advances in technology benefit patients as well as researchers



Soon J. Park, MD, Chief, Division of Cardiac Surgery, University Hospitals Case Medical Center; Co-Director, University Hospitals Harrington Heart & Vascular Institute; and the Jay C. Akeney Chair in Cardiothoracic Surgery and Professor of Surgery at Case Western Reserve University School of Medicine

Each year, roughly 2,000 hearts become available for donation to the more than 10,000 people in need of a transplant—many of whom are living with severe heart failure. This gap has been and continues to be the inspiration for clinicians and researchers determined to develop better therapies for patients in need of a new heart as a “bridge” to transplantation or as “destination” therapy.

Attempts to create a fully implantable total artificial heart back in the 1960s were unsuccessful, but those efforts led to the development of the ventricular assist device (VAD). While the original devices demonstrated promise in improving survival, the VADs of today – and tomorrow – offer even better outcomes thanks to advancements in design and function.

Going With the Flow

When the VAD was first developed, it was designed to be as similar as possible to the native heart, utilizing a pulsatile motion that mirrored the contraction and relaxation of the heart’s natural pumping mechanism.

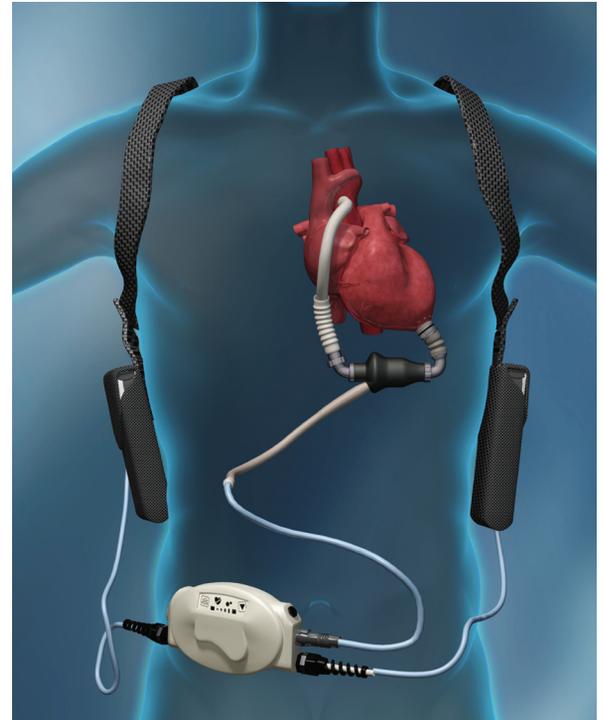
“The trouble with this design was that, although the pump was effective, the amount of mechanical stress that the device had to endure was unsupportable over time. The device simply didn’t last long and had to be replaced surgically within one or two years,” explains

Soon J. Park, MD, Chief, Division of Cardiac Surgery, University Hospitals Case Medical Center; Co-Director, University Hospitals Harrington Heart & Vascular Institute; and the Jay C. Akeney Chair in Cardiothoracic Surgery and Professor of Surgery at Case Western Reserve University School of Medicine. “We realized that we needed a mechanical pump with fewer moving parts and lower mechanical stress in order to improve the device’s durability.”

What researchers developed was a novel platform that utilized a rotor, either axial or centrifugal, similar to that of a propeller on a boat or airplane, enabling blood to circulate continuously rather than cyclically. These continuous flow pump VADs proved significantly more durable than their pulsatile ancestors.

“That type of technology really opened up VAD therapy in the clinical arena,” says Dr. Park. What’s more, he adds, these newer VADs are much smaller and quieter than pulsatile devices – making them more patient-friendly.

“Now that the continuous flow pump has been



HeartMate II assembly. Image reprinted with the permission of Thoratec Corporation.

shown to be effective and safe in clinical settings, many more new and improved devices will be available to patients through clinical trials in the near future,” he says. “It is truly an exciting period for patients with advanced heart failure.”

The Next Generation

The latest clinical trials for VADs include investigation of one that eliminates the use of the external drive line, which extends outside the patient’s body and connects to a controller and battery source. These wireless VADs use transcutaneous energy transfer to power them, giving patients more mobility and lowering the risk of infection.

Other areas of study include reducing problems at the blood-contact surface of future VADs. The current generation of technology attempts to minimize potential trauma to blood cells and clot formation, but Dr. Park says there is still room for improvement.

“The axial rotors in today’s devices are mechanically anchored at two points, and those points can become sites of mechanical wear and stagnation in flow, where blood could become static and form a clot,” he says.

Consequently, the next wave of technology could use rotors that are magnetically levitated, comparable to electromagnetic trains. This would allow for greater blood clearance between the housing and rotor, reducing the likelihood of sheer stress-related trauma to blood cells, flow stagnation and thromboembolic episodes.

Elevated Outcomes

What do these improvements mean for patients?

When the pulsatile VADs were first implanted in people awaiting cardiac transplantation, survival increased by two-fold compared with medical therapy. However, many patients still died within approximately two years due to infection and device failure. With the introduction of continuous flow VADs, survival again nearly doubled versus pulsatile device therapy, providing an overwhelming survival benefit over medical therapy.

Such survival statistics depend greatly upon the population in question. Patients who deteriorate and develop multisystem organ failure, for instance, face significantly increased operative morbidity and mortality. But for most patients who are undergoing an elective VAD implant, today's expected survival rate is approximately 85 to 95 percent at one year, with people generally living five years and beyond.

The subjective patient experience of living with a VAD also has changed, including quality of life and satisfaction with the device (see "Inside Information").

Inside Information

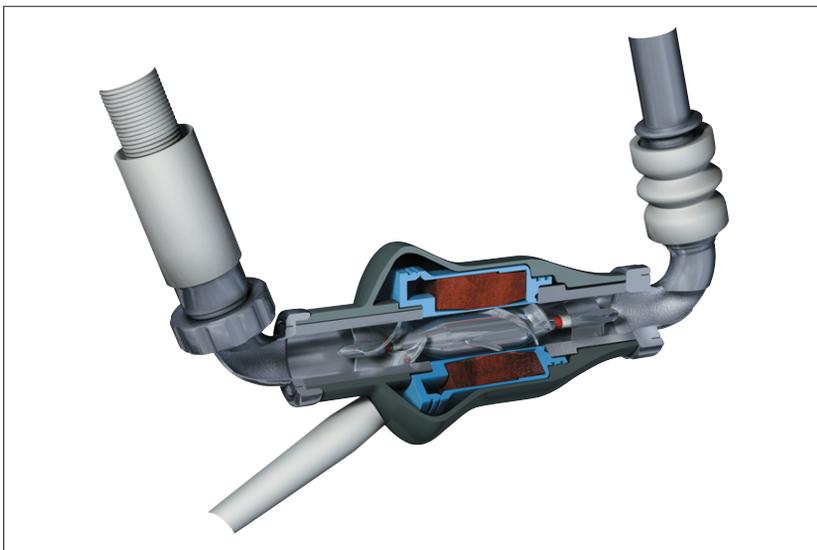
Individuals don't automatically have an accurate grasp of what living with a VAD will be like. But as innovations in technology have allowed more people to receive the device, awareness and acceptability have similarly improved. From videos available on YouTube® to the growing number of support groups, including our own at University Hospitals Case Medical Center, today's VAD patients can learn more from each other than ever before. For more information on our program, email Diane Gorbey, MSN (Diane.Gorbey@UHhospitals.org).

A vast majority of patients with severe heart failure, indicated by a New York Heart Association Class IV designation, will now improve to Class I or II post-implant. As a result, people can be significantly more active without experiencing dyspnea, fatigue and other debilitating symptoms. Although some limitations remain – recipients cannot swim and must remain on anticoagulants, for example – the technology clearly has proven to be very beneficial in improving a patient's longevity, functioning and quality of life.

A Team Approach

The heart failure program at University Hospitals Harrington Heart & Vascular Institute is based on a multidisciplinary team approach, drawing on expertise

from various cardiovascular medicine specialists (interventional, electrophysiology and heart failure/transplantation), nurse practitioners, technicians and perfusionists, cardiac anesthesiologists and cardiac surgeons. "We have a highly dedicated team of experts who are committed to providing the most appropriate and personalized care, whether it involves conventional or innovative therapies," says Dr. Park. "We are excited to offer our program to all those who suffer from advanced heart failure symptoms."



Cutaway of HeartMate II device. Image reprinted with the permission of Thoratec Corporation.

Dual Objective

Experts in oncology and cardiovascular medicine team up to optimize outcomes for cancer patients



University Hospitals

Seidman Cancer Center

Harrington Heart & Vascular Institute



Guilherme H. Oliveira, MD, Director, Heart Failure & Transplant Center and Director, Onco-Cardiology Program, UH Harrington Heart & Vascular Institute; and Associate Clinical Professor of Medicine, Case Western Reserve University School of Medicine

Advancements in chemotherapy and radiation treatments have given patients with cancer a greater chance of living longer, healthier lives. However, the potential cardiotoxic effects of these treatments have increasingly been recognized to negatively affect cancer treatment and survival.

Because of the unique aspects of cardiovascular care in cancer populations, UH Harrington Heart & Vascular Institute and UH Seidman Cancer Center have created the Onco-Cardiology Program. This initiative features state-of-the-art technology and expertise for risk-stratifying, monitoring and treating cancer patients who have or develop cardiovascular disease during cancer therapy. This innovative program has the potential to improve cancer outcomes and significantly alter the way cancer patients are cared for in the future.

The Sooner, the Better

Research has clearly established a link between certain oncological treatments – notably anthracyclines, Herceptin/trastuzumab, VEGF inhibitors and radiation therapy (particularly to the chest) – and the development of cardiovascular complications, such as coronary disease, ventricular (LV) dysfunction, valve disease, arrhythmias, hypertension and heart failure. Furthermore, because of the increased prevalence of heart disease and cancer with aging, many older patients diagnosed with cancer have established or clinically silent heart problems, placing them at even greater risk.

Close collaboration between oncologists and cardiologists, therefore, becomes important to individually tailor the best type of cancer treatment based on each patient's cardiovascular risk profile. In addition, co-management by both specialists helps determine whether and when cancer treatment needs to be adjusted or even temporarily halted.

Guilherme H. Oliveira, MD, Director, Heart Failure & Transplant Center and Director, Onco-Cardiology Program, UH Harrington Heart & Vascular Institute; and Associate Clinical Professor of Medicine, Case Western Reserve University School of Medicine, explains that early cardiovascular screening and intervening early give patients the best chance of maximally benefiting from uninterrupted cancer therapy.

“Every patient with breast cancer whose planned therapy includes trastuzumab, radiation or anthracyclines undergoes a comprehensive cardiovascular evaluation before initiating their treatment,” he says. “This way, we can minimize their cardiac risk by both discovering and

treating cardiac problems as well as preventing future problems caused by their cancer treatment.”

Powerful New Tools

The availability of state-of-the-art advanced diagnostic methods within the Onco-Cardiology Program allows doctors to more accurately and prematurely detect cardiovascular disease than had previously been possible with traditional tools.

Cardiac magnetic resonance imaging, for example, provides a more precise assessment of ejection fraction than traditional echocardiogram. Calcium-computed tomography scans offer reliable, noninvasive screening for coronary artery disease in patients with a history of chest radiation. This is especially important because every gray of radiation increases the chances of experiencing a coronary heart disease event by 7.4 percent.

Right ventricular endomyocardial biopsy is selectively used to determine the degree of cardiotoxicity associated with anthracycline by revealing specific patterns of myocardial histology indicative of myocardium damage. The use of echocardiography with speckle tracking helps to more precisely and prematurely detect LV dysfunction so that cardiologists can intervene early and increase the chances of cardiac recovery.

“We know that if someone has LV dysfunction, and we detect and treat it early as opposed to late, not only are the chances of cardiac recovery substantially higher, but those who recover live longer,” says Dr. Oliveira. “We believe that our approach to care is prolonging lives and improving patient outcomes.”

For more information on our Onco-Cardiology Program, email Jamie Wilson, CNP (Jamie.Wilson@UHhospitals.org).

Forecasting the Future

Three-dimensional strain echocardiography (also called echocardiography with speckle tracking) is a novel technology used in very select centers around the world. It enables clinicians to monitor changes in LV functioning much more precisely than with traditional two-dimensional echocardiography, which only measure LV ejection fraction. This enhanced monitoring allows physicians to predict future episodes of LV dysfunction and detect subclinical problems.

“If we intervene once a drop in the strain numbers is detected, it prevents future objective decreases in heart function,” explains Dr. Oliveira. “It is used not only as a monitoring method but also as a way to initiate treatment before it is too late.”

Taking Action on Dyspnea

Using exercise-based testing to improve diagnosis and treatment



Trevor Jenkins, MD, Co-Director, Dyspnea Center, University Hospitals Harrington Heart & Vascular Institute; and Assistant Professor of Medicine, Case Western Reserve University School of Medicine



Robert J. Schilz, DO, PhD, Co-Director, Dyspnea Center, University Hospitals Harrington Heart & Vascular Institute; Interim Chief, Division of Pulmonary, Critical Care and Sleep Medicine, University Hospitals Case Medical Center; and Associate Professor of Medicine, Case Western Reserve University School of Medicine



Colleen G. Lance, MD, Director, Clinical Sleep Operations, University Hospitals Case Medical Center; and Assistant Professor of Medicine, Case Western Reserve University School of Medicine

Shortness of breath, or dyspnea, is a frequent complaint as patients age. Numerous potential etiologies may be involved, so objective evaluations from cardiology, pulmonology, sleep medicine and neurology are needed.

To address the difficulties of accurately assessing dyspnea, University Hospitals Harrington Heart & Vascular Institute, in collaboration with the Division of Pulmonary, Critical Care and Sleep Medicine at UH Case Medical Center, recently joined the ranks of a small number of major academic medical centers offering specialized care for dyspnea.

Discussion

Causes of dyspnea can be multifactorial, involving dysfunctions in the heart, the lungs or even the muscles, where deconditioning can overwhelm the oxygen transport system. Complicating the picture is the fact that initial tests, such as chest X-rays, blood work or heart ultrasounds, are performed while patients are at rest, yet they usually experience symptoms while active.

Trevor Jenkins, MD, Co-Director, Dyspnea Center, UH Harrington Heart & Vascular Institute; and Assistant Professor of Medicine, Case Western Reserve University School of Medicine, explains that the key to accurately identifying and understanding dyspnea is capturing a person's symptoms during activity.

"In many cases, initial tests performed while the patient is at rest fail to make the diagnosis on their own," he says. "For this reason, we established a multidisciplinary Dyspnea Center to evaluate these challenging cases."

Robert J. Schilz, DO, PhD, Interim Chief, Division of Pulmonary, Critical Care and Sleep Medicine, UH Case Medical Center; and Associate Professor of Medicine, Case Western Reserve University School of Medicine, serves as Co-Director of the Dyspnea Center.

Evaluation

The clinic, which opened in July, uses exercise-based assessments of gas exchange and hemodynamic measurements to determine the presence and etiology of dyspnea. Exercise stress tests, for example, can identify stiffness in the heart or problems with lung circulation based on imaging of right and left ventricular dysfunction. Even more extensive examinations can be performed using cardiopulmonary exercise testing (CPET), which directly measures oxygen and carbon dioxide gas exchange and more accurately quantifies a person's exercise capacity and limitations. Many patients with breathlessness will have both heart and

lung disease. Patterns of oxygen utilization, therefore, can help determine contributions of each organ system resulting in exercise limitation.

A more leading-edge approach is invasive hemodynamic monitoring coupled with CPET. During this procedure, placement of a pulmonary and radial arterial catheter generates hemodynamic data as well as patterns of exercise gas exchange. This approach can reveal specific pathologies not easily defined with static testing, including exercise-induced pulmonary hypertension, exercise-induced diastolic heart failure and valvular incompetence.

Outcome

Invasive CPET can help clinicians identify new patterns in the causes of dyspnea. Any patient for whom it is not clear why breathlessness is present, based on conventional diagnostic methods such as chest X-ray, should be referred. Depending upon test results, a patient's treatment plan might include follow-up care with a pulmonary hypertension specialist, referral to a heart failure clinic or even specific exercise prescriptions.

"Members of our team work collaboratively using state-of-the-art evaluations based on exercise to better understand the reasons for a patient's exercise limitation and dyspnea," say Drs. Jenkins and Schilz. "We think this approach will eventually become the gold standard, especially among patients in whom conventional testing fails to adequately define their dyspnea."

To schedule an evaluation for your patients in the Dyspnea Center, please call **216-844-3800**.

For any questions, please email Dr. Jenkins (Trevor.Jenkins@UHhospitals.org) or Dr. Schilz (Robert.Schilz@UHhospitals.org).

The Sleep Connection

The importance of recognizing interrelationships between cardiovascular dysfunction and sleep-disordered breathing (SDB), including obstructive and central sleep apnea, is emerging as a multidisciplinary focus.

"Obstructive respirations and increased negative pressure within the chest cavity increase workload on the left ventricle," explains **Colleen G. Lance, MD**, Director, Clinical Sleep Operations, University Hospitals Case Medical Center; and Assistant Professor of Medicine, Case Western Reserve University School of Medicine. "Furthermore, patients with heart failure can have central sleep apnea, treatable with noninvasive ventilation."

To schedule an evaluation for sleep-disordered breathing, please call **216-844-6261**.



Save the Date

5th Annual Update on Vascular Disease

Saturday, April 5, 2014



Registration starts at 7:30 a.m.

Presentations 8 a.m. – 3 p.m.

Embassy Suites Cleveland-Independence

5800 Rockside Woods Blvd.

Independence, OH 44131

\$50 registration fee

Breakfast and lunch will be served

Clinical-based presentations will include:

- Case-based discussion of common vascular presentations
- Effective use of the vascular laboratory and imaging modalities
- Discussion of emerging therapies and techniques for managing vascular disease

Register online at <http://casemed.case.edu/cme>
or by phone at **216-983-1239** or **1-800-274-8263**.

Physician Accolade



Congratulations to **Jonathan Stamler, MD**, recipient of the 2013 American Heart Association Distinguished Scientist Award. Dr. Stamler, Director, Harrington Discovery Institute at University Hospitals Case Medical Center; Robert S. and Sylvia K. Reitman Family Foundation

Distinguished Chair in Cardiovascular Innovation; Director, Institute for Transformative Molecular Medicine; and Professor of Medicine and Professor of Biochemistry, Case Western Reserve University School of Medicine, is an internationally renowned physician-scientist, recognized for the discovery of protein S-nitrosylation, a ubiquitous mechanism for controlling protein function. His work has focused on the molecular and cellular mechanisms through which S-nitrosylation operates and the molecular basis of dysregulated S-nitrosylation in disease, including multiple cardiovascular disorders. His research is notable for new insights into physiology, including cardiac and skeletal muscle contractility and red blood cell-mediated vasodilation, which plays an important role in the respiratory cycle. These findings anchor the development of new therapeutic approaches to disease characterized by aberrant S-nitrosylation.

New Physician Leader



Soon J. Park, MD

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Dr. Park, known and respected worldwide as a gifted heart surgeon, researcher and passionate educator, has mentored over 100 clinical and research fellows worldwide. He has led many significant National Institutes of Health and industry-funded clinical trials, including the landmark REMATCH trial with the HeartMate XVE, the HeartMate II destination therapy (DT) trial and the HeartWare DT trial.

Dr. Park's clinical practice spans all aspects of adult cardiac surgery with world-renowned expertise in treating patients with advanced heart failure. His longstanding research interests include myocardial recovery, cardiac xenotransplantation, stem cell therapy, left ventricular assist device (LVAD), and other innovative surgical therapies. His recent pioneering work was in establishing LVAD therapy for patients with restrictive cardiomyopathy, providing hope for those suffering from advanced cardiac amyloidosis.

- Bachelor's/Master's degrees in Chemistry and Doctor of Medicine from University of Chicago
- Completed General Surgery Residency at University of Washington and Thoracic Surgery Residency at University of Minnesota
- Served as Surgical Director for Heart, Lung and Cardiac Assist Device Programs at the University of Minnesota; rose to Associate Professor of Surgery with tenure and was named St. Jude Medical Chair in Biomedical Engineering
- Served as Chairman of the Department of Thoracic and Cardiovascular Surgery at California Pacific Medical Center and Marin General Hospital in California
- Served as the Director of the Ventricular Assist Device Program at Mayo Clinic, Rochester, Minnesota; rose to Professor of Surgery
- Served on the Board of Directors for the International Society of Heart and Lung Transplantation
- Published over 150 peer-reviewed articles or book chapters
- Currently a member of the editorial boards of The Journal of Thoracic and Cardiovascular Surgery, Journal of Cardiac Surgery and Clinical Transplantation