

Inside This Issue

Left Atrial Appendage
Occlusion – p3

MitraClip – p4

Gut Flora and
Heart Health – p6

Mona LSA Pilot
Trial – p12



Cardiac Consult

Heart, Vascular and Thoracic News from Cleveland Clinic | Fall 2013 | Vol. XXIII No. 3



Second-Generation
Bioabsorbable Scaffolds
Begin U.S. Clinical Trials – p8

Dear Colleagues:

How do we choose subjects for *Cardiac Consult*? Our first criterion is whether the subject will be informative or useful to our readers. The second is how well the subject differentiates Cleveland Clinic from other cardiac care programs. There's only one reason you'd be interested in Cleveland Clinic and why you'd refer a patient to us for care, and that is because you believe we offer something different and – we hope – better.

This issue of *Cardiac Consult* highlights several of our key differentiators. Among them is our broad range of interventional activities, both approved and experimental. We're especially proud of our role in the development of endovascular stent grafts to address aortic disease in tortuous, branched and otherwise awkward formations.

Reports on Cleveland Clinic trials of bioabsorbable scaffolds for the treatment of coronary artery occlusion and a new catheter-based treatment for mitral valve regurgitation are made possible by the tremendous volume of interventions we do in both areas every year – with excellent outcomes.

Another key differentiator is Cleveland Clinic's extensive research into the causes and treatment of cardiovascular disease in all its manifestations. We are thrilled to report on research from the lab of Stanley Hazen, MD, PhD, whose discoveries continue to make national news.

Seeking out the causes of cardiovascular disease, searching for new treatments, and giving every patient the best possible outcome and experience set Cleveland Clinic apart. We never stop trying to improve. That's one of the reasons Cleveland Clinic has been ranked No. 1 in America for cardiac care for the 19th year in a row (*U.S. News & World Report*).

Your interest, support and referrals make it all possible. We thank you.

Sincerely,

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Left Atrial Appendage Occlusion offers Atrial Fibrillation Management Options

Occlusion of the left atrial appendage is a treatment strategy offered for prevention of stroke in patients with atrial fibrillation who cannot take warfarin or other oral anti-coagulants safely. The procedure has potential benefits in reducing the risk of stroke without the risk of bleeding.

Electrophysiologists and interventional cardiologists in the Sydel and Arnold Miller Family Heart & Vascular Institute at Cleveland Clinic have collaborated in the investigation of left atrial appendage occlusion devices. These efforts are led by Walid Saliba, MD, and Oussama Wazni, MD, in the Cardiac Electrophysiology and Pacing Section, and Murat Tuzcu, MD, Samir Kapadia, MD, and Amar Krishnaswamy, MD, in the Invasive and Interventional Cardiology Section.

Making the Choice

The decision to deploy a left atrial appendage occlusion device should be made in the context of the overall management of atrial fibrillation. Although anti-arrhythmic medications may suppress episodes of symptomatic atrial fibrillation, their efficacy is low and clinical trials have shown persistent stroke risk if oral anticoagulants are discontinued.

Moreover, the risk of stroke or systemic embolization is just as high with paroxysmal as it is with persistent atrial fibrillation. Ablation of atrial fibrillation is more effective than antiarrhythmic medications for maintaining sinus rhythm, but there is a significant risk of recurrence of atrial fibrillation with its use. As a result, the consensus is that cardiologists should maintain patients on oral anticoagulants if their risk factors for stroke are high.

Studying the Difference

Multicenter randomized controlled trials comparing warfarin with the newer thrombin inhibitors or factor Xa inhibitors show an annual risk of major hemorrhage to be in the range of 2.1 to 3.4 percent and the risk of hemorrhagic stroke to be 0.1 to 0.5 percent. While the newer anticoagulants tend to compare favorably with warfarin, the risk of bleeding complications persists. These risks are particularly high in patients who require treatment with clopidogrel and aspirin because of coexisting coronary artery disease.

In the Framingham Heart Study, the risk of major bleeding associated with the combination of aspirin and warfarin over five years was 23 percent.

Physicians who manage atrial fibrillation face the dilemma that patients who are at highest risk of stroke are also at the highest risk of bleeding complications. Occlusion of the left atrial appendage may be a good option for such patients.

The risks of oral anticoagulation provided the incentive for development of left atrial appendage closure devices. One of these devices is the WATCHMAN™ LAA Closure studied through the PROTECT-AF trial. Long-term results of the trial were presented at the 2013 Annual Scientific Sessions of the Heart Rhythm Society. They showed that at a mean follow-up of 45 months, the left atrial appendage device was not inferior to warfarin in the prevention of stroke or systemic embolization. The study demonstrates that all-cause mortality, cardiovascular mortality and risk of hemorrhagic stroke were lower with the left atrial appendage occlusion device compared with warfarin. The U.S. Food and Drug Administration is considering this data while it deliberates whether to approve the left atrial appendage occlusion device and how to define indications for appropriate clinical use.

Cleveland Clinic currently offers access to left atrial appendage occlusion through two means. It is operating under Boston Scientific's Watchman Continued Access Protocol as well as enrolling for the Amplatzer™ Cardiac Plug trial (St. Jude Medical, Inc. St. Paul, Minn.), for which Drs. Saliba and Kapadia serve as co-investigators. ■

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MitraClip

FOR TREATMENT OF MITRAL VALVE REGURGITATION



Minimally invasive option alleviates heart failure symptoms and improves quality of life in patients considered too high-risk for surgery

MitraClip® (Abbott Vascular, Abbott Park, Ill.) is an emerging treatment option for patients with mitral regurgitation who are considered high-risk for surgery, as well as for patients with functional mitral regurgitation who exhibit heart failure symptoms. Interventional cardiologists Samir Kapadia, MD, Amar Krishnaswamy, MD, E. Murat Tuzcu, MD, and Patrick Whitlow, MD, who are intimately involved in clip implantation at Cleveland Clinic, say the minimally invasive, catheter-based treatment fills an unmet need.

“There is no question MitraClip is an incredibly effective option — more so than expected. Most patients experience a significant decrease in regurgitation, their ventricle shrinks, heart-failure symptoms resolve, medical management gets easier and hospital readmissions stop. Needless to say, patients are most grateful,” says Dr. Kapadia, who directs the catheterization laboratory.

Much of the experience with MitraClip has been obtained in Europe, where the device has been used since 2008. A post-marketing study known as ACCESS-EU, published in June 2013, found low rates of adverse events at 30 days and 12 months. The mean age of enrolled patients was 74, with 45 percent being 75 or older. One year after implantation, 78.9 percent of patients had a mitral regurgitation (MR) severity score $\leq 2+$, and 71.4 percent were New York Heart Association functional Class I (normal) or Class II (mild), as compared with 15 percent at baseline.

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Success in Reversing Heart Failure

Mitral regurgitation is a common cause of heart failure. Data from Cleveland Clinic's patient registry have shown that patients with mitral regurgitation and heart failure have higher rates of hospitalization and mortality when treated medically compared with patients whose mitral regurgitation is treated surgically. Treatment of mitral regurgitation is directed at improving lives as well as saving them.

Two different mechanisms can cause mitral regurgitation. In some patients, the mitral valve itself can be damaged (degenerative mitral regurgitation). In other patients, annular dilatation or abnormal tension on the chordae supporting the valve leaflets due to left ventricular dysfunction adversely impacts mitral valve function (functional mitral regurgitation). "For patients with degenerative mitral regurgitation, surgical repair is an excellent option, with more than 99 percent operative success rate and more than 90 percent 10-year survival rates when performed in a Center of Excellence such as Cleveland Clinic, where more than 1,000 mitral valve repairs are done every year," says Dr. Krishnaswamy.

Despite the success of surgery, however, an estimated 10 percent of patients with degenerative mitral regurgitation are not healthy enough to undergo the operation safely. On the other hand, patients with functional mitral regurgitation have a less durable response to surgery, and its benefits remain questionable, particularly in patients who do not need coronary revascularization and have impaired left ventricular function.

"Retrospective, propensity-matched studies have shown no difference in mortality between medical management and valve repair in these patients. Therefore, surgery is not strongly recommended for this population," says Dr. Tuzcu, Vice Chairman of Cardiovascular Medicine.

About 50 percent of patients with heart failure and severe functional mitral regurgitation are managed medically. These patients have high rates of recurrent congestive heart failure, requiring hospital admissions, and mortality. MitraClip is most likely to benefit these patients, for whom no other effective treatment exists. Although a similar catheter-based device, the CARILLION® mitral contour system® (Cardiac Dimensions® Inc., Kirkland, Wash.), is being tried in Europe and as many as 15 other devices are in the pipeline, none are likely to be approved in the near future. "This is a reason for the FDA to be proactive with MitraClip," says Dr. Kapadia.

Ameliorating FDA Concerns

In March 2013, an advisory panel of the FDA composed of cardiologists and cardiac surgeons recommended approval

of MitraClip for patients with symptomatic regurgitation ($MR \geq 3+$), who were deemed too high-risk for open surgery. There was no question about the safety of the device, but opinions about its efficacy were not unanimous: Five of the eight members felt the benefits of MitraClip exceeded the risks.

Their cautious optimism was largely based on concerns that the clinical trials and registry data used to support the FDA application did not clearly define the patient population most likely to benefit from the device, or establish that patients at high surgical risk benefited above and beyond contemporary optimal medical management.

To clarify these issues, the FDA has requested a new study in which eligibility for valve repair surgery will be determined by a heart team that includes cardiac surgeons and cardiologists specializing in heart failure management and interventional cardiologists specializing in the MitraClip procedure. Dr. Kapadia serves on the steering committee for this 420-patient, open-label randomized trial known as COAPT (Clinical Outcomes Assessment of the MitraClip Percutaneous Therapy for High-Risk Surgical Patients). Enrollment began recently, but results are not expected for at least three years.

While refinement of the target patient population continues, Cleveland Clinic cardiologists are confident that they have a good understanding of how MitraClip fits into the spectrum of treatment options for patients with mitral valve disease. "We understand it is not the answer for all patients with mitral regurgitation. But there's no question that it's the right treatment for some," says Dr. Krishnaswamy.

Referrals of potential candidates for MitraClip are welcomed. The screening process involves an evaluation of cardiac anatomy, including the coronary arteries and valves, and a heart failure consultation. By the time the screening process has been completed, FDA approval of the MitraClip is likely for some patients; others may potentially qualify for the COAPT study.

Importantly, the heart team approach identifies other treatment options. "When a patient is better suited for surgery or other conventional therapy such as biventricular pacing, it can be performed immediately," says Dr. Kapadia. "Awareness of evolving therapies for patients with heart failure and mitral regurgitation is critical and timely, because treatment options are rapidly evolving." ■

For more information, contact Dr. Kapadia at 216.444.6735 or kapadis@ccf.org.

Gut Flora and Heart Health

– A New Novel Pathway?



“In our future, we may think about gut flora as the largest endocrine organ in the body,” says Stanley Hazen, MD, PhD. “Gut flora, depending on the nutrients we eat, make distinct biologically active substances that act somewhere else in the body. That fulfills the definition of a hormone.”

Adding to previously published work about gut flora, and a potential pathway for detecting enhanced cardiovascular risk, Dr. Hazen, Vice Chair of Translational Research for the Lerner Research Institute and Section Head of Preventive Cardiology and Rehabilitation, published two studies in the spring about the relationship between the work of gut microbes in the intestines and atherosclerosis.

One of the studies was related to choline, a byproduct of lecithin, an abundant component of egg yolk, and animal products. The other was related to consumption of L-carnitine, which is abundant in red meat and a frequent additive in many energy drinks. Choline is a semi-essential nutrient, meaning humans do not synthesize all of the nutrient that their bodies need — so they require some choline in their diet. In contrast, healthy subjects make all the carnitine needed, making carnitine supplementation largely unnecessary.

These studies suggest a biochemical mechanism is at work in heart disease above and beyond dietary cholesterol consumption. But interestingly, the gut flora pathway is still linked to cholesterol. The gut flora generates a metabolite that alters cholesterol metabolism in the artery wall and other locations within the body.

Discovery of this pathway could crack the code as to why increased meat consumption increases risk for heart disease more than does cholesterol alone.

Tracking the TMAO Pathway

Building on years of previous work in animal models, Dr. Hazen and a team of researchers sought to prove that the digestive action of microbes within the intestinal

tract was producing chemicals that amplified the deleterious effects of dietary cholesterol.

What they found was that gut microbes turn dietary phosphatidylcholine and L-carnitine into trimethylamine (TMA), which is then absorbed into the bloodstream and metabolized by the liver.

It's the substance that is then produced by the liver, trimethylamine-N-oxide (TMAO), that is linked to increased cardiovascular risk in humans.

The research team also wanted to show that manipulation of the gut flora would impact the rate at which TMAO would ultimately increase through dietary exposure. To suppress the gut flora, study subjects were given a course of antibiotics prior to taking part in a “phosphatidylcholine challenge” in which each subject consumed two hard-boiled eggs and deuterium-labeled phosphatidylcholine.

The study, published in April in the *New England Journal of Medicine*, also presented findings from three years of follow-up on more than 4,000 patients who underwent elective coronary angiography. In that population, the relationship between fasting levels of TMAO and major adverse cardiovascular events was examined. A positive relationship was discovered.

These studies build on data that were reported in *Nature* in April 2011. In both studies, a relationship between the action of the intestinal microbes and the production of TMAO from dietary sources was shown. The increase in TMAO was found to have an impact on negative cardiac outcomes, more than what would be expected from an omnivorous diet.





Just Meat, or Energy Drinks?

L-carnitine is abundant in red meat and has a trimethylamine structure similar to that of choline. It is also added to energy drinks.

Dr. Hazen and colleagues, suspecting that results would be similar to those found when looking at TMAO related to choline, initiated another challenge. Volunteers consumed 8 ounces of steak and a deuterium-labeled L-carnitine capsule to see if the TMAO levels would similarly increase.

When subjects who professed to be vegans or vegetarians accepted this variation of the dietary challenge (without the steak, except in the case of one adventurous vegan), the TMAO levels after consumption of the meat and the supplement did not catch up with those who were habitual red meat eaters.

This additional study was published in *Nature Medicine* in May 2013.

Food for Thought

Diet is one of the largest environmental exposures that humans have to chemicals, says Dr. Hazen. Recognizing that gut flora participate in additional biochemical pathways that contribute to heart disease opens the door to someday finding treatment options to address those pathways. “In viewing the gut flora as a player in the disease process, we’ve recognized them as a ‘druggable target,’ meaning that we can identify therapies to impact them in the future.”

TMAO is easy to measure through mass spectrometry in a research laboratory, but that equipment is not typically available in hospital laboratories. Instead, the diagnostics company LipoScience (Raleigh, N.C.) is perfecting an instrument on which a TMAO clinical test will be available. LipoScience specializes in personalized nuclear magnetic resonance (NMR) diagnostics; currently that technology is used to measure lipoprotein particle subfractions in LDL and HDL particles.

LipoScience’s measurement device has recently been cleared by the U.S. FDA for hospital labs, and it is expected that the assay for TMAO detection will be available for research purposes very soon.

One day, tests for TMAO could be as commonly ordered as lipid panels currently are. Similar to the test for C-reactive protein, it is hoped that TMAO testing will gain ground as an early predictor of atherosclerosis.

Dr. Hazen makes clear that the studies are not meant to be nutritional recommendations. At present, he says, dietary guidelines that suggest moderation across a variety of food groups should be considered for a variety of reasons. And, further study is warranted.

“We’ve focused research efforts on the discovery of pathways involved in the genesis of cardiovascular disease and its adverse consequences like heart attacks,” says Dr. Hazen. “We’re looking at gut flora as one of those pathways. Now, we need additional human clinical studies to figure out mechanistically exactly how this works and how we can block it from happening, to our advantage.” ■

For more information, contact Dr. Hazen at 216.445.9763 or hazens@ccf.org.

HDL Protein May Fight Cancer

A recent study led by Stanley Hazen, MD, PhD, has found an additional benefit to high density lipoprotein — fighting cancer. The study, published in *The Journal of Biological Chemistry*, found that the major protein component in HDL, apolipoprotein A1 (apoA1), reduces the growth and spread of malignant melanoma and lung cancer.

Using a mouse tumor model, the researchers showed that mice lacking apoA1 developed tumors much more quickly and were more likely to die than mice that had intact apoA1. Furthermore, the researchers found that apoA1 does not inhibit tumor growth directly but acts by altering the immune system to create an inhospitable environment for tumors. Specifically, it converts tumor-associated macrophages from pro-tumor to anti-tumor.

These results suggest that apoA1 could be used as an effective treatment for cancer. ApoA1-elevating drugs are currently used to treat cardiovascular disease, and Dr. Hazen’s work suggests that they should also be evaluated for treating various types of cancer.

Second Generation Bioabsorbable Scaffolds Begin U.S. Clinical Trials

**ABSORB Scaffolds Designed to Improve
on Current Drug-Eluting Stents**

In January of this year, Abbott's ABSORB III™ clinical trial launched in the United States. This randomized, controlled trial, which will enroll approximately 2,250 patients in the U.S., and is designed to compare the performance of Abbott's drug-eluting Absorb™ Bioabsorbable Vascular Scaffold (BVS) device with the company's XIENCE™ family of drug-eluting stents.

Absorb is a second-generation drug-eluting, fully BVS. The scaffold is constructed from polylactide, a naturally dissolvable material that is commonly used in sutures. Similar to a metallic drug-eluting stent, BVS works by opening a clogged vessel and restoring blood flow to the heart. While still the standard of care for coronary lesions, metallic drug-eluting stents leave behind metal architecture and residual polymer, which cause complications in some patients.

With an Absorb BVS, all that remains after the scaffold dissolves are four tiny metallic markers. The markers' sole purpose is to help physicians position the scaffold.

The Absorb BVS delivers everolimus, the same anti-proliferative that Abbott uses in its XIENCE stents.

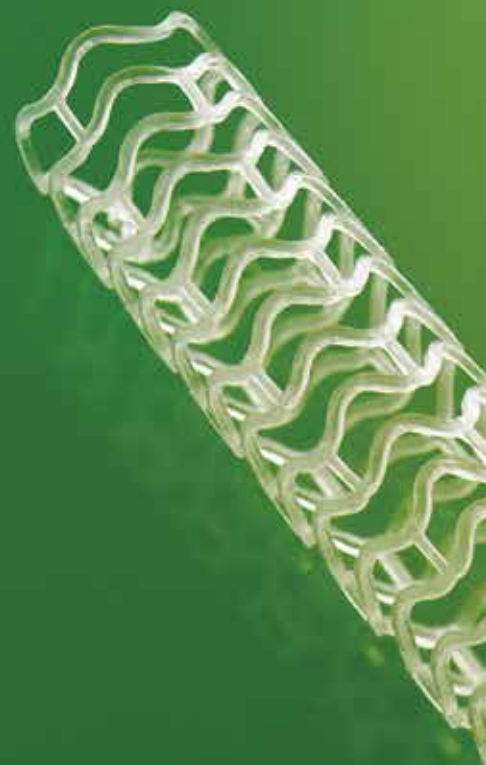
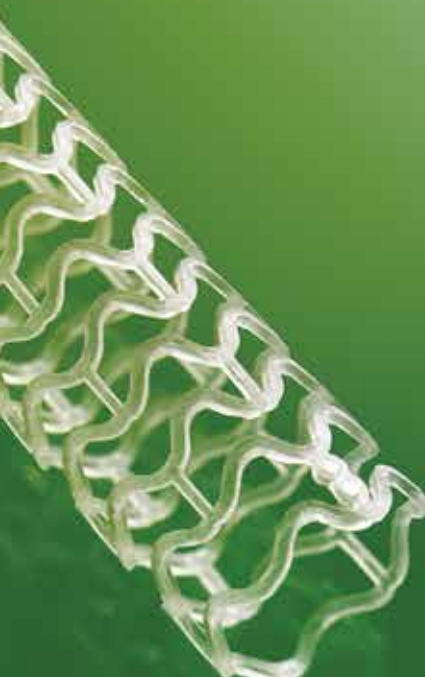


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“By providing a device that **initially matches the performance of DES** and then totally resorbs, we hope that the occasional long-term complications with standard stents **will be eliminated.**” – Stephen Ellis, MD

The Evolution of the Bioabsorbable Scaffold

Stephen Ellis, MD, Section Head of Interventional Cardiology and Co-primary Investigator on the ABSORB III trial, says that the trial will address issues that are experienced in patients who receive current state-of-the-art drug eluting stents (DES).

“The long-term presence of a polymer in an artery is pro-thrombotic,” Dr. Ellis says. “Current DES contain a very durable polymer.” The next iteration of these scaffolds, he says, will hopefully address this and other concerns.

Dr. Ellis says that patients with DES experience a stent thrombosis rate of 0.3 to 0.8 percent per year over five years often leading to heart attack or death. The totally bioabsorbable product seeks to improve on that rate.

The ultimate goal, Dr. Ellis says, is to open a blocked vessel yet leave very little behind so that the opened vessel regains more natural motion after the scaffold has fully dissolved, a stumbling block of current metal scaffolds.

In human studies performed overseas, the Absorb BVS loses its structural integrity over the course of the first year, and dissolves completely in two to three years.

A dissolving polymer causes less inflammation in the vessel, which allows for more natural vasomotion when the patient participates in normal activities such as exercise. But the perfect balance must be struck: The scaffold needs to remain largely intact long enough to allow the everolimus to do its work and then allow as much of the natural vessel function to return as possible.

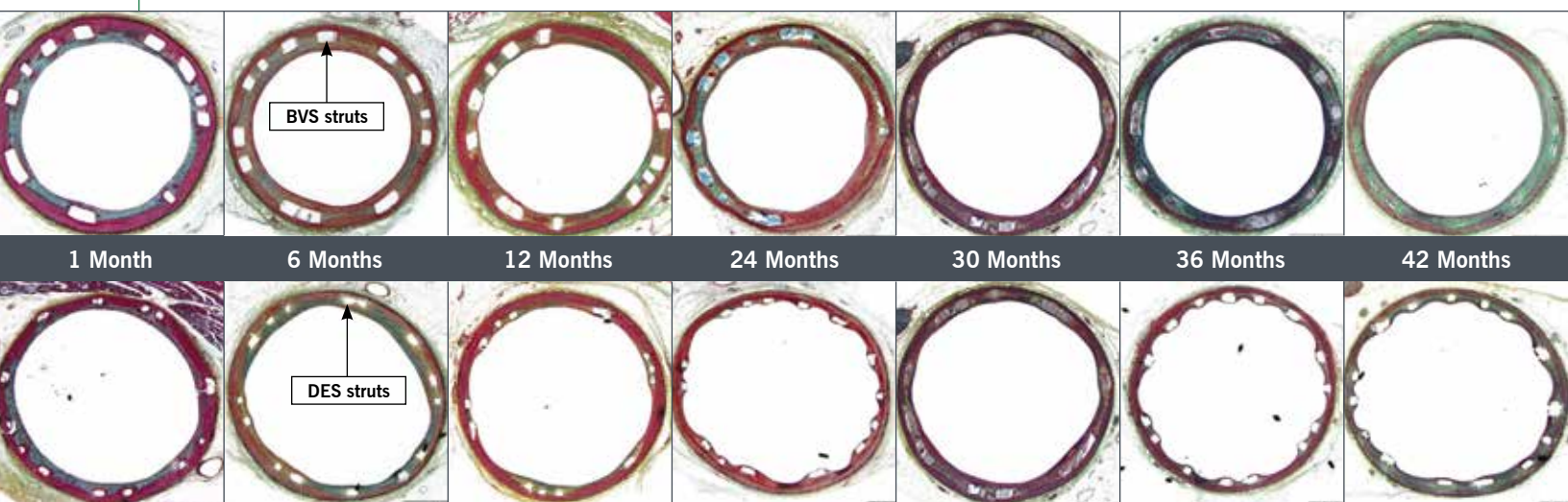
The first-generation scaffold dissolved too quickly and was withdrawn from evaluation. The second-generation Absorb scaffold uses a combination of polymers that addresses the problem of a bioabsorbable scaffold degrading too quickly, yet further improves on a restenosis rate that has decreased with the change from purely metal scaffolds to the current metal, polymer and drug devices.

“By providing a device that initially matches the performance of DES and then totally resorbs, we hope that the occasional long-term complications with standard stents will be eliminated,” says Dr. Ellis.

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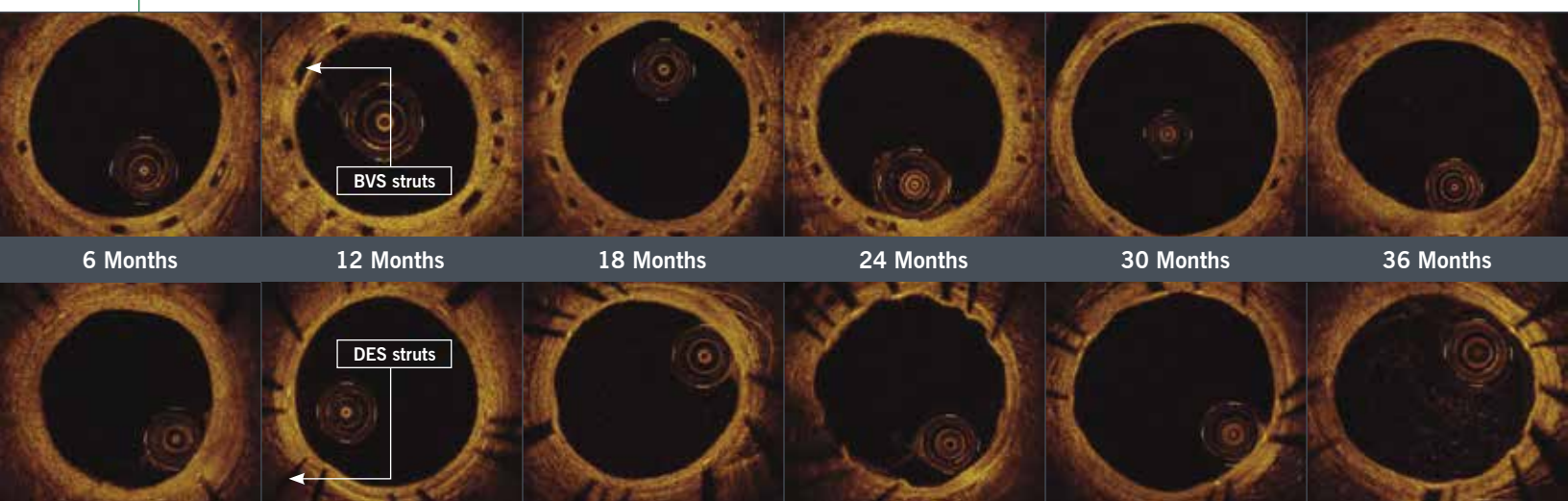
Absorb BVS stent shadow (top) VS. Xience V scaffold shadow (bottom) – Preclinical Safety

Representative photomicrographs of porcine coronary arteries (Movat's pentachrome stain, 2X magnification)



Absorb BVS scaffold shadow (top) VS. Xience V stent shadow (bottom) – OTC Imaging

Representative photomicrographs of porcine coronary arteries (Movat's pentachrome stain, 2X magnification)



Who They're Looking For

The study is enrolling patients at 180 sites across the country who have already been determined to be good candidates for stenting. To be enrolled they must not have more than two native coronary artery lesions in separate epicardial vessels, neither of which can be near a branch. Patients cannot have a known allergy to the polymers from which the scaffold is constructed. The limit for the scaffold length is 24 mm, and the area for treatment must be a simple lesion. Appropriate patients will be randomized 2-to-1 for scaffold vs. current DES.

What They're Looking For

Target lesion failure (death, heart attack or need to treat the site again) at one year is the primary endpoint of the

study; a subset of patients will be evaluated for other endpoints, such as vasomotion. Several five-year outcome measures will indicate how well the vessel remains open.

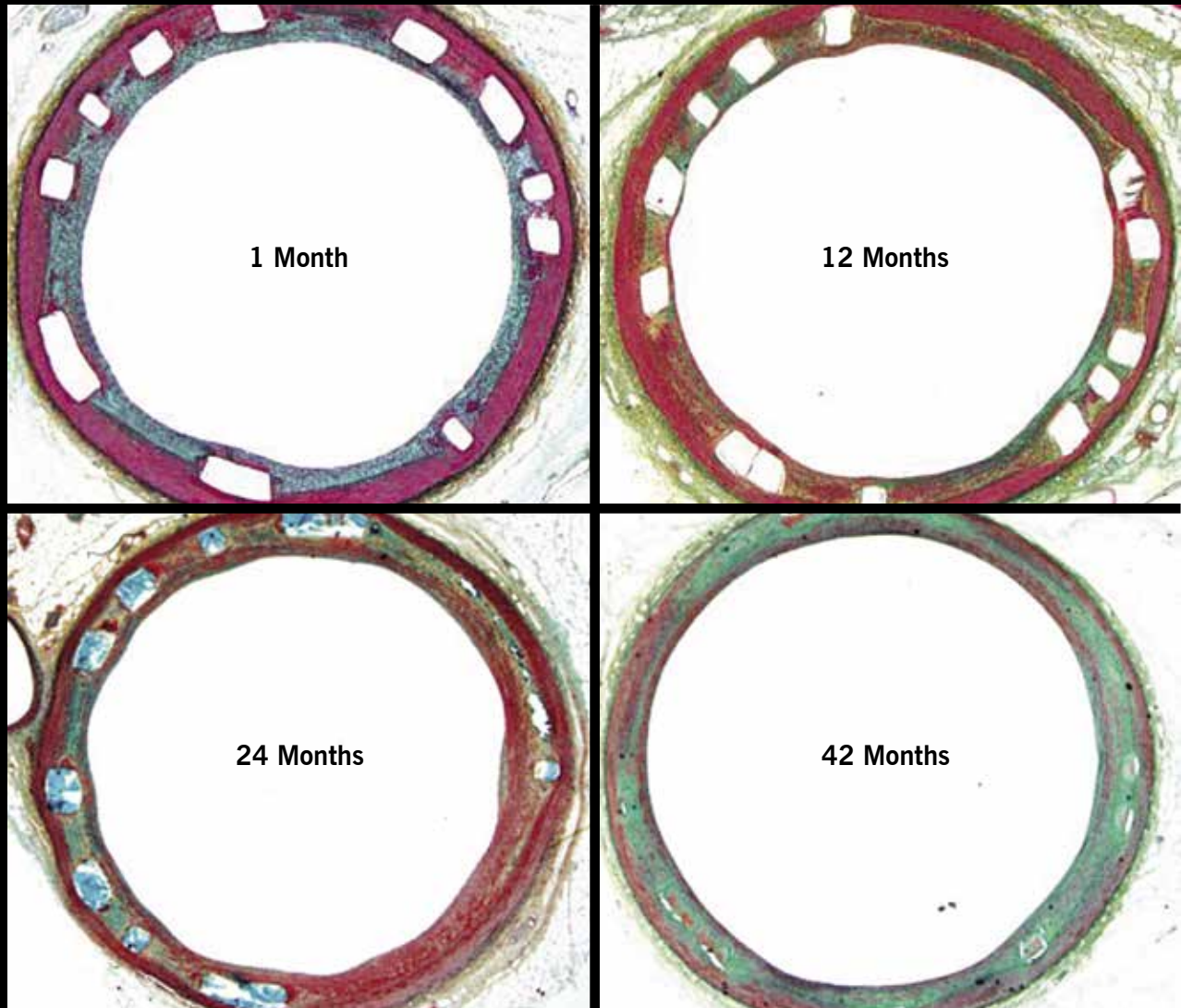
The estimated study completion date is March 2018, with primary outcome measure data collected by August 2015.

Absorb is available commercially in Europe, India and parts of Latin America and Asia. In June, a randomized, controlled study designed to enroll 400 patients was initiated in Japan. ■

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Image of the Issue

BY STEPHEN ELLIS, MD



GOING ... GOING ... GONE

This sequence of cross-sectional intravascular images shows how the drug-eluting Absorb bioabsorbable stent slowly loses its structural integrity over one, 12, 24 and 42 months. By the final image, the only discernable traces of the stent are residue from the metallic markers used to help in positioning the stent. Cleveland Clinic is helping to lead a new clinical trial of the device, which is intended to reduce restenosis rates, preserve natural vasomotion, and eliminate the occasional long-term complications of conventional stents.

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Mona LSA Branch Stent Graft

Implanted in First-in-Human FDA Pilot

As part of a U.S. Food and Drug Administration (FDA) early feasibility pilot program, a Cleveland Clinic cardiovascular surgeon recently performed the initial implants of a novel branch stent graft system. This new system is designed to enable the repair of aneurysms of the descending thoracic aorta (DTA) that encroach on the aortic arch.

The Valiant® Mona LSA branch stent graft system (Medtronic, Minneapolis, Minn.) could obviate the need for left subclavian artery (LSA) bypasses, allowing for the totally endovascular repair of some thoracic aortic aneurysms that currently require an additional open surgery. Endovascular repairs of the thoracic aorta are particularly challenging; about 40 percent of the cases involve an additional surgical intervention, as they involve coverage of the LSA. The Society for Vascular Surgery estimates that approximately 40 percent of patients with aneurysms of the DTA have insufficient seal zones for endovascular repair.

"There currently is a need for more patient and disease-specific devices to allow us to expand least-invasive repair techniques to patients with potentially devastating thoracic aortic disease," says Eric Roselli, MD, staff in the Department of Thoracic and Cardiovascular Surgery in the Miller Family Heart & Vascular Institute and national principal investigator for the trial.

This device is one of only nine approved for the FDA's new Innovation Pathway program, which have the joint goal of early clinical evaluation of devices to provide proof of principle and initial clinical safety data. The Mona LSA was approved for inclusion in this program in mid-2012. The devices included can be subject to further design modifications as a result of these trials. Generally, the devices are used in a small number of patients.

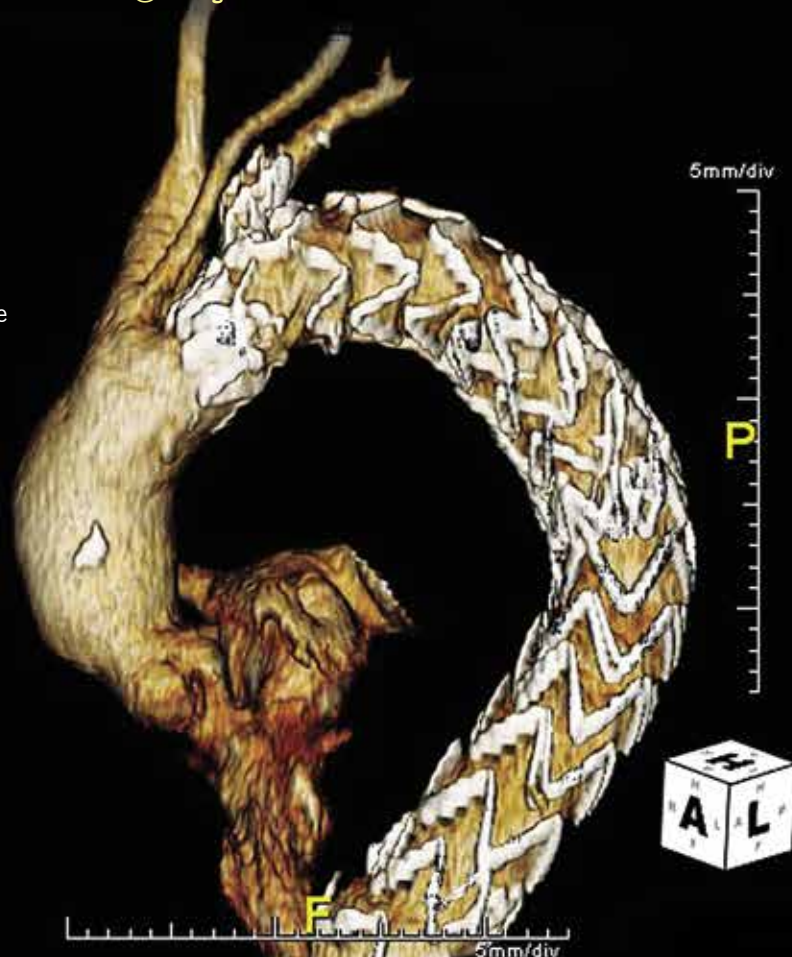
The pilot program for this branch stent graft system was approved for use in seven patients; all patients identified as eligible have received the device. Dr. Roselli implanted two of the devices this past spring, and a third patient underwent the surgery in August.

Cumulative major adverse events at one month are the primary safety endpoint for the study. Major adverse events may include aneurysm-related mortality, stroke, paraplegia and left arm/hand ischemia. Endoleak of all types from the

stent graft is the secondary endpoint, with a planned follow-up of five years.

The device seeks to address an important segment of the population that requires this type of repair. Because higher rates of adverse events such as spinal cord ischemia, arm ischemia and death are reported in patients when the LSA is covered, this new device seeks to provide preoperative revascularization to perfuse the LSA in patients who require endovascular repair when an adequate seal can be attained only by coverage of the LSA. ■

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Case Study

Iliocaval Venous Interventions

by Michael W. Park, MD



Venous disease is more prevalent than arterial disease and has a significant impact on patients' lifestyle and ability to work. Established treatments such as anticoagulation and compression therapy have limited efficacy in severe cases. Recent advances in interventional techniques have allowed for effective and durable treatments in these situations.

Presentation

The patient is a middle-aged man with a prior DVT/PE who developed stabbing back pain and near syncope. A CT scan at another hospital showed retroperitoneal hematoma and extensive femoral and ilio caval DVT, extending to his IVC filter. Bleeding stopped but leg pain and swelling worsened. AngioJet® (MEDRAD Inc., Warrendale, Penn.) thrombectomy and balloon venoplasty were attempted, but failed. A contrast nephropathy with a serum creatinine level over 6 mg/dL occurred. With worsening phlegmasia, the patient was transferred to Cleveland Clinic for treatment. On transfer, he had tensely swollen and tender legs. Noncontrast CT showed no increase in the size of the hematoma.

Treatment

Venography showed extensive femoral and iliac vein DVT with occlusion of the vena cava at the IVC filter (Figure 1, pre-lysis). Ultrasound accelerated infusion catheters were positioned via both popliteal veins to the IVC filter. Tissue plasminogen activator was delivered through each catheter.

The next day, venography showed clearance of thrombus in the ilio caval segment (Figure 1, post-lysis) with a chronic thrombosis of the IVC filter. A large self-expanding stent was deployed in the IVC from the confluence to the filter, and then a balloon-expandable stent was deployed across the IVC filter. This re-established flow through the IVC (Figure 2).

Both iliofemoral systems were opened with large self-expanding stents from the femoral veins to the iliac confluence (Figure 3). Intra-vascular ultrasound confirmed successful dilatation of the femoral-iliocaval venous system. The patient experienced immediate relief of the painful swelling in both legs. Dialysis was started for nonoliguric renal failure; at discharge, his creatinine level was 3.6 mg/dL.

Discussion

Several groups report excellent patency rates for ilio caval venous interventions of nearly 90 percent at one year and between 60 and 70 percent at five years. Technical aspects that are critical to success include generous stent sizing and ready availability of IVUS. Stenting across IVC filters and the inguinal ligament does not appear to degrade patency.

Contact Dr. Park at 216.444.6268 or parkm3@ccf.org.

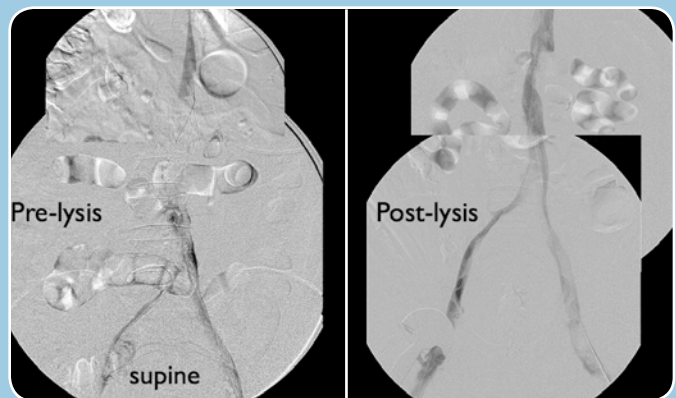


Figure 1. Venography

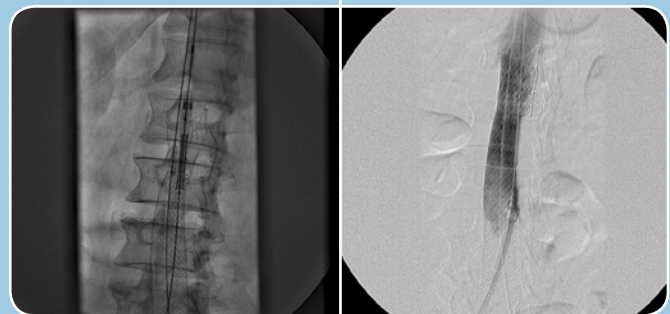


Figure 2. Stent across IVC filter

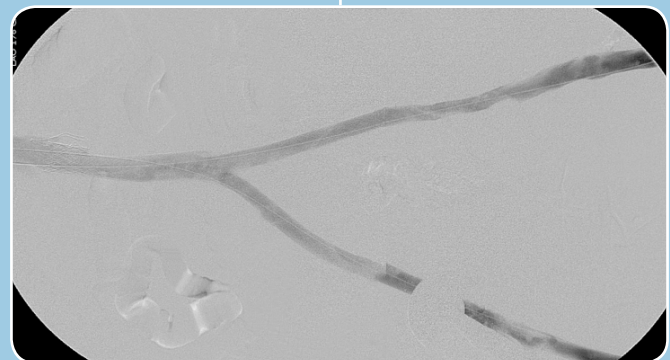


Figure 3. Final result



Save the Dates

For These Events and Conferences

9th Annual Pulmonary Hypertension Symposium: Translating Discoveries into Patient Care

Nov. 15 – 16, 2013

InterContinental Hotel & Bank of America Conference Center | Cleveland, Ohio

The Pulmonary Hypertension Symposium brings together leaders in the field of pulmonary hypertension to discuss recent advances and future directions in the diagnosis and management of this disease. The symposium will highlight the disease mechanisms and pathophysiology of pulmonary hypertension as well as the evaluation and medical management of the patient. Expert speakers will present the recent advances in the context of challenges faced by physicians and other healthcare providers caring for patients with this complex medical condition. Saturday will include a half-day patient-oriented session.

For more information, visit ccfcme.org/pulhyper13.

2013 Preceptorship in Carotid Ultrasound Interpretation

Dec. 2 – 6, 2013

Cleveland Clinic Miller Family Heart & Vascular Institute
Noninvasive Vascular Laboratory | Cleveland, Ohio

(class size is limited to six participants)

This intensive 4 ½-day program will train the participant to interpret carotid duplex ultrasound examinations through a series of activities, including didactic lectures, preceptored interpretation sessions with staff physicians from Cleveland Clinic's Noninvasive Vascular Laboratory, hands-on scanning sessions, and review of an extensive library of programmed-learning carotid cases with angiographic correlations.

For more information, visit ccfcme.org/carotid13.

17th Annual Diastology and Valve Summit

Feb. 27 – March 2, 2014

Eden Roc Hotel | Miami Beach, Fla.

The Diastology and Valve Summit provides a unique opportunity to interact with key clinical leaders and receive updates in heart valve disease, emerging imaging technologies, diastology and multimodality imaging. Expert speakers will highlight important controversies and interactive workshops for each of these topics: Heart Valve Disease and Diastology, which will incorporate “Read with the Experts” sessions through case presentations and a basic sonographer tutorial; New Echo Technologies, which will include 3-D echo, strain and TAVR cases, as well as a basic sonographer tutorial; and Multimodality Imaging, which will have a “Read with the Experts” session on CT and cardiac MR in various diseases.

For more information, visit ccfcme.org/echo.

CLEVELAND CLINIC RESOURCES

About Cleveland Clinic

Cleveland Clinic is an integrated healthcare delivery system with local, national and international reach. At Cleveland Clinic, more than 3,000 physicians and researchers represent 120 medical specialties and subspecialties. We are a nonprofit academic medical center with a main campus, eight community hospitals, more than 75 northern Ohio outpatient locations (including 16 full-service family health centers), Cleveland Clinic Florida, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Cleveland Clinic Canada, Sheikh Khalifa Medical City and Cleveland Clinic Abu Dhabi.

In 2013, Cleveland Clinic was ranked one of America's top 4 hospitals in *U.S. News & World Report's* annual "America's Best Hospitals" survey. The survey ranks Cleveland Clinic among the nation's top 10 hospitals in 14 specialty areas, and the top in heart care for the 19th consecutive year.

24/7 Referrals

Referring Physician Hotline

855.REFER.123 (855.733.3712)

Live help connecting with our specialists, scheduling and confirming appointments and resolving service-related issues.

Hospital Transfers

800.553.5056

New patients, in most cases, can be seen within one week of calling for an appointment.

On the Web at clevelandclinic.org/heart



Download Today! Physician Referral App

Contacting us is easier than ever before. With our new free "Physician Referral" app, you will be able to view all our specialists, transfer a patient and get in touch immediately with one click of your iPhone® or iPad®. Available at the App Store. Coming soon to Android™ phone and tablet.



Resources for Physicians

Physician Directory

View all Cleveland Clinic staff online at clevelandclinic.org/staff.

Track Your Patient's Care Online

DrConnect is a secure online service providing real-time information about the treatment your patient receives at Cleveland Clinic. Establish a **DrConnect** account at clevelandclinic.org/drconnect.

Critical Care Transport Worldwide

Cleveland Clinic's Critical Care Transport teams and fleet of vehicles are available to serve patients across the globe.

- To arrange for a critical care transfer, call **216.448.7000** or **866.547.1467** (see clevelandclinic.org/criticalcaretransport).
- For STEMI (ST elevated myocardial infarction), acute stroke, ICH (intracerebral hemorrhage), SAH (subarachnoid hemorrhage) or aortic syndrome transfers, call **877.379.CODE (2633)**.

Outcomes Data

View clinical Outcomes books from all Cleveland Clinic institutes at clevelandclinic.org/outcomes.

Clinical Trials

We offer thousands of clinical trials for qualifying patients. Visit clevelandclinic.org/clinicaltrials.

CME Opportunities: Live and Online

The Cleveland Clinic Center for Continuing Education's website offers convenient, complimentary learning opportunities. Visit ccfcmc.org to learn more and use Cleveland Clinic's myCME portal (available from the site) to manage your CME credits.

Executive Education

Cleveland Clinic has two education programs for healthcare executive leaders — the Executive Visitors' Program and the two-week Samson Global Leadership Academy immersion program. Visit clevelandclinic.org/executiveeducation.

Same-Day Appointments

Cleveland Clinic offers same-day appointments to help your patients get the care they need, right away. Have your patients call our same-day appointment line, **216.444.CARE (2273)** or **800.223.CARE (2273)**.



Cleveland Clinic

The Cleveland Clinic Foundation
9500 Euclid Ave./AC311
Cleveland, OH 44195

Cardiac Consult



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Cleveland Clinic Heart Care Ranked



For the 19th consecutive year, Cleveland Clinic has been ranked No. 1 in the nation for heart care, according to the 2013 *U.S. News & World Report* “America’s Best Hospitals” survey.

The survey, released in July, recognized Cleveland Clinic as one of the nation’s best hospitals overall, ranking it as No. 4 in the country.

Fourteen Cleveland Clinic programs were listed among the top 10 in the United States, including nine in the top five.