



UNIVERSITY OF MARYLAND MEDICINE ROUNDS

Clinical and Research Updates from the *University of Maryland School of Medicine* and the *University of Maryland Medical Center*

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EARLY ACCESS TO NEW TREATMENTS FOR AORTIC DISEASE

A healthy aorta supplies the rest of the human body with blood the way the Mississippi River sends its waters through tributaries into the heartland. But an aneurysm or a penetrating ulcer can make patients so ill that the very surgery to cure them is risky.

At the University of Maryland Center for Aortic Disease, patients with acute aortic disease, including those too sick for open surgery, can receive treatments not yet available elsewhere.

Because of their vast experience in aortic disease, surgeons at the University of Maryland Medical Center (UMMC) serve as investigators on a clinical trial for the first thoracic aortic endograft available in the United States that seals off lesions in a neighboring artery, as well as for another trial for a device with four side branches for arteries that supply the abdominal organs.

The Center for Aortic Disease treats both acute and chronic aortic syndromes, including aneurysms, dissections, penetrating ulcers and intramural hematomas. The co-directors of the center are University of Maryland School of Medicine faculty **Shahab Toursavadkahi**, MD, assistant professor of surgery, and **Bradley Taylor**, MD, MPH, associate professor of surgery.

In a collaborative model seen at just a few centers in the country, Dr. Toursavadkahi, a vascular surgeon, collaborates with Dr. Taylor, a heart

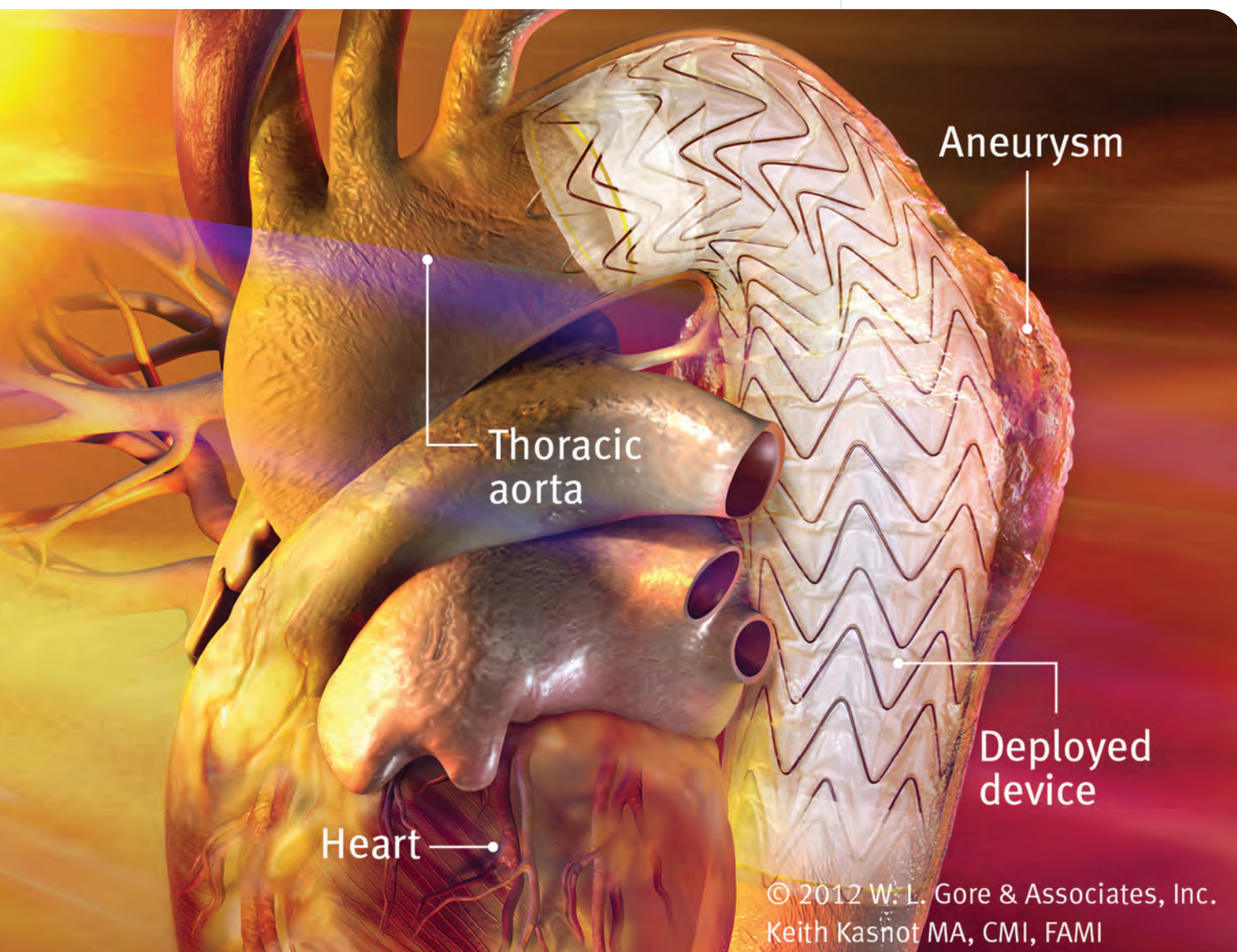


“Together, we can treat very complicated aortic diseases that other places are likely not capable of doing...”

COVER IMAGE: A 3D reconstruction of a patient's CT scan, showing the Gore Excluder AAA endoprosthesis with Gore Excluder iliac branch endoprosthesis. Image courtesy of Brian Peterson, MD, St. Anthony's Medical Center, St. Louis, Mo. BELOW: Artist's rendition of the delivery of a conformable Gore TAG thoracic endoprosthesis allowing for endovascular repair of a TAA

surgeon, to fix complex aortic problems. The two bring complementary strengths to the operating table. Dr. Taylor supplies expertise on organ perfusion and the heart, and Dr. Toursavadkahi's subspecialty is endovascular reconstruction and minimally invasive surgery.

“Together, we can treat very complicated aortic diseases that other places are likely not capable of doing,” Dr. Toursavadkahi says. The Center for Aortic Disease is also part of the University of Maryland Heart and Vascular Center, which has a national reputation for treating even the most complex conditions.



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Keith Kasnot MA, CMI, FAMI



KEY POINTS

- The University of Maryland Center for Aortic Disease offers endovascular treatment for weak or torn aortas, preventing ruptures in patients unlikely to survive open surgery.
- UMMC is among the few in the country where surgeons successfully mend Type A aortic dissections using minimally invasive means.
- Newer stent grafts, which seal off the damaged part of the vessel, come in sizes and shapes designed to more closely fit each patient's anatomy.
- Patients can gain access to novel devices, including those with branching, by participating in clinical trials at UMMC.

"The main thing that can impact the outcome is early treatment in a high-volume center by high-volume medical teams," Dr. Toursavadkahi notes, with a multidisciplinary "army of people" treating some of the most challenging aortic conditions nearly every day.

WHEN OPEN SURGERY IS TOO RISKY

For patients with Type A aortic dissections — tears in the wall of the ascending or arching part of the aorta — the standard fix involves open surgery. However, Dr. Toursavadkahi notes that affected patients tend to be older,

with multiple comorbidities and barely pumping hearts, making surgery risky.

"Typically, these people will go on medical management and hospice, and their outcome is extremely poor," Dr. Toursavadkahi says.

Nonetheless, blood can escape through the tears and become trapped. Downstream tissues may starve. Trapped blood could weaken and burst the aorta.

Seeking better outcomes, the Center for Aortic Disease is pioneering the use

THE LATEST TREATMENTS FOR AORTIC DISEASE

of minimally invasive techniques to fix these dissections.

The repair starts with a cut into the groin, through which surgeons thread the catheter used to send guide wires and a stent graft to the injured spot. Once positioned, the endograft lines the weakened part of the aorta, bolstering it and rerouting blood.

If the lesion sits near the heart, the organ might pump away the endograft before it reaches its destination. Therefore, surgeons medically increase the heart to about 200 beats per minute, so that it quivers without moving blood.

"We then drop the blood pressure to almost no pulsatility," he says. "That gives you a few seconds to land the graft precisely where you need to."

He and Dr. Taylor have performed about 10 of these procedures, including in an older woman whose ejection fraction had dropped to 10 percent.

"These people are extubated the next day, and they feel good," Dr. Toursavadkahi says. "So far, we haven't had any mortality."

Similar considerations underlie the treatment of large and fast-growing aneurysms. With those as well, a stent graft inserted through a small portal makes a fix possible in patients who cannot tolerate open surgery.

CLINICAL TRIAL OPPORTUNITIES FOR PATIENTS

To reinforce the aorta with no leakage, an endograft must fit properly.

"One of the issues that we have is, if you don't have a graft specifically designed for a particular segment of the aorta, then the size is not going to match," says Dr. Toursavadkahi. A graft that is too long might block blood flow to side vessels fed by the aorta, perhaps causing a stroke. Too short, and the surgeon might have to piece together something

from materials on hand, a process that takes time when every moment counts.

To meet such challenges, medical device makers have been developing new stent grafts and testing them in clinical trials. The UM Center for Aortic Disease aids

those efforts by serving as a test site. For example, two years ago, the center finished testing the Gore Excluder iliac branch endoprosthesis (IBE). Approved by the US Food and Drug Administration in 2016, it gives surgeons a ready-made option for patients with aortic aneurysms

involving the iliac artery, which supplies the legs and pelvis.

Before the IBE became available, many patients who had undergone endovascular repair experienced pain when walking, from ischemia caused by a poorly sealing graft. The new device addresses that problem by preserving blood flow to the iliac arteries.

“We were the only center that had access to that graft for about two years,” recalls Dr. Toursavadkahi. To date, the IBE

remains the only branching aortic device sold in the United States.

In 2014, the UM Center for Aortic Disease became the first to implant the Gore TAG thoracic branch endoprosthesis (TBE) into a patient, launching a big multicenter clinical trial. The first endoprosthesis in the United States to offer branching for the thoracic aorta, the TBE mends aneurysms and dissections in the aortic arch and descending thoracic aorta.

“By using this device, we avoid doing open surgery in these patients, and yet we are doing a complete endovascular repair,” says Dr. Toursavadkahi.

Additionally, he looks forward to testing the Gore Excluder thoracoabdominal multibranch endoprosthesis (TAMBE). W.L. Gore & Associates, which also makes Gore-Tex fabric, granted UMMC preliminary access to the device for early feasibility study.

The TAMBE isolates aortic aneurysms and dissections that affect vessels that feed the viscera. It comes with four side-branching tubes, enabling treatment of multiple vessels at the same time without opening the ribcage. The TAMBE comes in a range of sizes to ensure a better seal. Since these lesions would otherwise require a more invasive and risky surgery, Dr. Toursavadkahi says, the TAMBE might provide a safer alternative.

“This is an opportunity for us to treat these people and save lives,” he says.



Clinicians who suspect that a patient has acute aortic pathology may consult a University of Maryland vascular surgeon by calling **410-371-9578** any time, any day, or call the Division of Vascular Surgery at **410-328-5840**.

TOP PHOTO: The conformable Gore TAG thoracic endoprosthesis

BOTTOM PHOTO: The Gore Excluder AAA endoprosthesis with iliac branch prosthesis

POST-TREATMENT LYME DISEASE SYMPTOMS CALL FOR INTEGRATED APPROACH

Symptoms that persist after Lyme disease treatment can leave patients wondering whether they'll ever feel normal again. University of Maryland Medical Center (UMMC) offers a unique program that helps these patients reclaim their quality of life.

Carla Alexander, MD, and Kalpana Shere-Wolfe, MD, assistant professors of medicine at the University of Maryland School of Medicine, began the Integrated Lyme Disease Program in October 2017. They treat patients at UMMC and University of Maryland Faculty Physicians Inc. offices in Baltimore and Columbia.

Dr. Alexander and Dr. Shere-Wolfe use a holistic, multidisciplinary approach to find the cause of patients' symptoms, whether Lyme-related or not. Treatment depends on the diagnosis but may mix traditional and complementary therapies, as needed, to mitigate symptoms and improve patients' quality of life.

"We offer a unique approach to treating patients who have post-treatment Lyme disease syndrome, or PTLDS," says Dr. Shere-Wolfe, who is director of the Integrated Lyme Disease Program at UMMC.

"It's been terrible for those patients, because some of them have gone for

years without finding anyone who would agree that the symptoms they were having might be related to tick-borne illness," Dr. Alexander says. "What we're trying to convey with this clinic is that we do believe that people have some combination of signs and symptoms that ought to be addressed."

Many of their patients have received antibiotic treatment at least twice before coming to the program. Still, chronic pain, fatigue, cognitive issues, sleep trouble, and other symptoms disrupt their lives. Some have suffered for more than 10 years.

NOT CHRONIC LYME

Dr. Shere-Wolfe, an infectious-disease specialist, disagrees with calling PTLDS "chronic Lyme disease."

"A lot of infectious disease physicians will not use that term, because we don't feel that there is a chronic infection involved," Dr. Shere-Wolfe says, adding that clinical trials have shown that repeated or prolonged courses of antibiotics do not improve PTLDS symptoms over the long haul.

Some patients do, however, feel better on antibiotics. Dr. Shere-Wolfe explains that certain antimicrobials that have been used to treat Lyme disease, such as doxycycline, curb inflammation. She believes PTLDS may arise from an immune response that triggers inflammation or pain.

"Long-term antibiotics are harmful," she says, and can put patients



Carla Alexander, MD



Kalpana Shere-Wolfe, MD

at risk of developing *Clostridium difficile* colitis, sepsis from peripherally inserted catheters, or liver problems. "Antibiotics have a significant effect on the microbiome, and the microbiome is very important in terms of our immune system."

PINPOINTING THE PROBLEMS

"When we see new patients, we make

"These modalities can control some of the anxiety that comes from having an illness where you don't know what exactly is causing it and why it won't get better," Dr. Shere-Wolfe says.

KEY POINTS

- UMMC recently launched the Integrated Lyme Disease Program to evaluate and treat patients with acute Lyme-related illness using conventional oral and intravenous antibiotics, as well as patients with persistent symptoms despite antibiotic treatment.
- Long-term antibiotic use does more harm than good, and traditional treatments often fail PTLDS patients.
- The physicians find that some patients have been misdiagnosed with Lyme, and actually had other illnesses, including multiple sclerosis, or in some cases a more treatable condition.
- Dr. Shere-Wolfe uses integrative medicine to relieve patients' symptoms and bolster their immune systems; Dr. Alexander optimizes patients' quality of life and functioning.
- Even patients with severe, stubborn symptoms after Lyme disease treatment can improve with the proper care.

sure that nothing has been missed," says Dr. Shere-Wolfe. New patients receive a thorough workup, including lab tests and possibly neuropsychological testing to probe any cognitive complaints. To ensure the best working diagnosis, Dr. Shere-Wolfe and Dr. Alexander might both see the same patient.

Sometimes this reveals treatable conditions wrongly tied to *Borrelia* bacteria, as well as more serious diseases that were misdiagnosed. For instance, Dr. Shere-Wolfe has found sleep apnea, rheumatoid arthritis, multiple sclerosis and amyotrophic lateral sclerosis misdiagnosed as Lyme disease.

WHEN USUAL METHODS FAIL

The physicians first tackle any newly diagnosed conditions using standard treatments. After that, they identify which symptoms are disrupting patients' lives the most and focus treatment on where they can achieve the biggest impact.

"We try to implement symptom management that will at least improve the person's quality of life, whether or not we are treating their underlying illness," says Dr. Alexander.

Many patients have tried traditional treatments — not just antibiotics, but also sleeping pills and pain medications — without success.

"When they've tried all these things, and they didn't work, you have to think of a different approach," says Dr. Shere-Wolfe. She turns to integrative modalities to subdue remaining symptoms and improve patients' health.

Those modalities include acupuncture, which she has prescribed for patients who are in pain, with very good results. She tailors treatment to individual patients. For example, she might teach those who fear needles to do breath work and meditation instead. She finds such practices very helpful for improving muscle and joint pain.

"These modalities can control some of the anxiety that comes from having an illness where you don't know what exactly is causing it and why it won't get better," Dr. Shere-Wolfe says. She refers some patients for biofeedback, massage, or Reiki.

Dietary changes may help, too. Dr. Shere-Wolfe explores whether patients

have problems digesting certain foods, such as gluten, dairy products or refined or heavily processed foods.

"When certain foods are consumed, they can be improperly digested, particularly in people who are not well, and you can get substances that can cause an inflammatory response in the body," she explains. She might also urge patients, even those without digestive issues, to try eliminating refined sugars or other highly processed foods.

Sleep-related problems plague many PTLDS patients.

"They'll get up several times during the night, or they won't feel refreshed in the morning, even though they slept many, many hours," says Dr. Shere-Wolfe.

To Dr. Shere-Wolfe, the pervasive symptoms seen in PTLDS signal a whole-body problem.

"Taking a pill isn't going to fix that; what you need is for that whole system to function better." Accordingly, she tries to shore up patients' overall health.

PRESCRIPTION FOR BETTER LIVING

Dr. Alexander takes a different tack, using medication and other resources to help patients function better and achieve their best quality of life. A specialist in hospice palliative medicine, she, like others in her specialty, believes that palliative care can enhance the lives of people with chronic nonlethal illness as well as it does for patients at the end of life. Toward that goal, she explores what PTLDS patients and their families are experiencing and what they need for support.

If needed to control patients' anxiety

"The physicians first tackle any newly diagnosed conditions using standard treatments. After that, they identify which symptoms are disrupting patients' lives the most and focus treatment on where they can achieve the biggest impact."

“Sometimes you have to retrain your brain to control the symptom,” Dr. Alexander says.

or depression, she prescribes mood stabilizers or adjusts their dosage. Even when a symptom won't respond to treatment, the doctors and their holistic approach can often help people function better. For patients who are fatigued, for instance, there are exercises and ways that people can learn to conserve energy and do things more efficiently.

Dr. Shere-Wolfe examines a new patient.

“Sometimes you have to retrain your brain to control the symptom,” Dr. Alexander says. She tries to understand the psychological, social and spiritual issues that shape how patients cope with their symptoms. For that, she may refer patients to spiritual counselors or other experts.

Through innovative, real-life solutions, the Lyme disease program addresses the unmet needs of patients with PTLDS. Most importantly, the program gets patients back to living their lives.

“A lot of their symptoms really do either improve or go away,” says Dr. Shere-Wolfe. “We have some dramatic results.”

“Most importantly, the program gets patients back to living their lives.”



*Dr. Shere-Wolfe and Dr. Alexander are available for second opinions when needed. To reach them or to refer a patient, call **410-328-9102**.*

UM HEART AND VASCULAR CENTER PIONEERS A NEW CLASS OF AORTIC VALVE IMPLANT

Physicians often face a dilemma when choosing the best strategy for patients in need of a new aortic valve: a mechanical valve and a lifetime of blood thinners on the one hand, or a tissue valve that might need to be surgically replaced in about seven years. An innovative valve from Edwards Lifesciences could solve this dilemma. Called the Inspiris Resilia, the new aortic valve seems likely to outlast prior-generation tissue valves, lessening the need for repeat surgeries, and free patients from warfarin-linked worries.

Bartley Griffith, MD, was among the first heart surgeons in the US to implant the new device in January when he operated on a male patient in his early 40s at the University of Maryland Medical Center (UMMC). Dr. Griffith is a professor of surgery and the Thomas E. and Alice Marie Hales Distinguished Professor in Transplantation at the University of Maryland School of Medicine.

After that first successful prosthetic valve implant in January, at least another six patients at UMMC have had the surgery and are doing well.

Since the 1960s, surgeons have tried to replace or repair faulty valves with some success, while continuing to develop solutions for the more difficult-to-repair cases.

"Decalcification of the stenotic aortic valve has not worked well," says Dr. Griffith, a cardiothoracic surgeon at the University of Maryland Heart and Vascular Center. Surgeons have had more success mending leaky aortic valves that let blood return to the left ventricle (when that oxygenated blood should normally be surging out to the body).

Repairing the patient's own valve is not always an option, however, and so a prosthetic valve is the better option for many patients with aortic stenosis and some with aortic valve regurgitation.

Still, Dr. Griffith notes, "There's no perfect valve replacement."

Surgeons recommend the next-best option — prosthetic valves made either from metal or from sterilized and treated animal tissue. The decision

between metal valve or tissue valve depends on the patient's age, condition, history and other factors.

THE DRAWBACKS OF METAL VALVES

In the early days of valve replacement during the late 1960s to early 1970s, valves made of metal featured ball-and-cage designs or tilting discs. A series of refinements led to the mechanical valves used today, typically bileaflet designs.

Dr. Griffith says today's metal valves last indefinitely but require patients to take a blood thinner, warfarin, every day. The drug prevents clots from forming around the valves. Such clots could trigger a stroke or heart attack. Often, clots will cause the valve to become stuck in an open or closed position.

Yet, warfarin can be difficult to prescribe for some patients, says Dr. Griffith. Certain foods, such as leafy vegetables and alcohol, can change the drug's effects, so patients who take it must watch what they eat. Furthermore, warfarin's narrow safety margin means patients must take it exactly as directed and undergo periodic blood tests to check their clotting time. That's because high levels of warfarin can cause internal bleeding, whereas too little might raise the risk of clots.

In fact, Dr. Griffith says, warfarin treatment carries a cumulative 1 to 2 percent risk of internal bleeding or other major complication each year. That adds up, especially for younger patients.

"If you're 40 and you take a mechanical valve, and you want to live to age 85, there's a pretty good chance you're going to have an issue along the way because you're taking the blood thinner," he says. A run-of-the-mill fall or head bump could cause big problems.

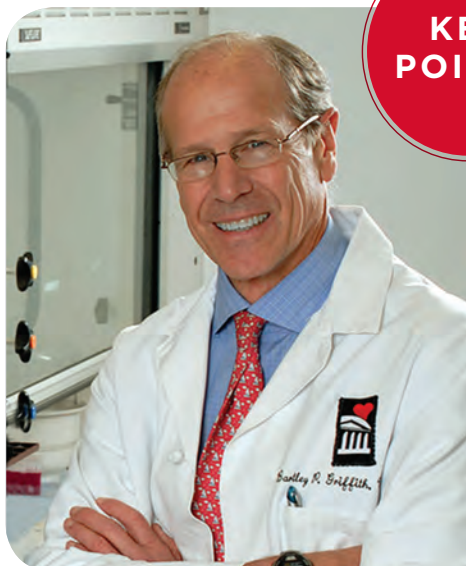
THE DOWNSIDE OF TISSUE VALVES

"Personally, I like to use tissue valves in

Dr. Griffith prepares to implant the new valve.



KEY POINTS



- UMMC was among the first centers in the nation to implant a next-generation aortic tissue valve from Edwards Lifesciences.
- The Inspiris Resilia valve frees patients from a lifetime on blood thinners and may last longer than previous generations of tissue valves, enabling them to delay replacement surgery.
- The valve may particularly help younger patients with calcium-hardened aortic valves.
- In animal studies, the valve's specially treated tissue resists calcium buildup better than typical valve tissue does.
- The ring holding the valve can expand, avoiding the diminishing circumference created by successive valve-in-valve replacements in the past.

Bartley Griffith, MD

Unlike their metallic counterparts, valves made of biological tissue spare patients from having to forever walk the blood-thinner tightrope.

young patients because I think that the blood-thinning can be a real problem," says Dr. Griffith.

Unlike their metallic counterparts, valves made of biological tissue spare patients from having to forever walk the blood-thinner tightrope. Tissue valves also offer a solution for patients who cannot or choose not to take blood thinners, those who exercise vigorously, and women who want to become pregnant.

Early aortic tissue valves consisted of actual aortic valves harvested from a pig, and then sewn into a cloth and metal stent before being implanted into patients. Eventually, valves made of pericardial tissue from pigs or cattle replaced them. The current market

leader, the Edwards Magna Valve, is made from bovine pericardium, which is sewn to form a 3-flap, 1-way valve. With that valve, "the outcomes have been excellent in terms of reduced blood clotting or stroke," Dr. Griffith says. "I have implanted more than 700 of these valves."

Nonetheless, tissue valves come with a big snag: Just like the valves humans are born with, they wear out.

"They take on calcium, but they do so at an accelerated rate, and the younger you are, the more quickly they can wear out," Dr. Griffith says. He explains that patients who are under 60 years old might get only seven years out of a tissue valve, while those 75 and older might get 15 years or more. In other words, some patients will outlive their valves, requiring repeated surgical replacement.

A NEW CLASS OF VALVE

To address these problems, Edwards Lifesciences created the Inspiris Resilia aortic valve. Implanted surgically, it heralds a new class of resilient heart valves that could outlast traditional tissue valves. Inspiris valves feature Resilia tissue, made by treating bovine pericardial tissue with a proprietary process to keep calcium from sticking to it. That tissue is mounted on the long-used Carpentier-Edwards Perimount

valve design.

A glycerol coating means the valves can be stored dry, instead of in glutaraldehyde as with other bioprosthetic valves. Dr. Griffith explains that glutaraldehyde preserves tissue valves, but at a cost. It etches cracks into them, perhaps compromising their longevity.

Inspiris valves feature another innovation: The ring into which the valve is sewn can expand, facilitating future valve-in-valve placements. When the valve wears out and the patient needs another, the surgeon can expand the ring by placing a high-pressure balloon inside the valve. The patient can then receive a new valve through a catheter inserted through the groin.

The new design avoids what Dr. Griffith calls the "Russian doll problem," whereby each valve is set inside another valve, making the opening smaller and smaller.

"We know if you can put a bigger valve in, it's probably better," says Dr. Griffith.

PROMISING EARLY RESULTS

As promising as these innovations sound, the data speak louder. Dr. Griffith says animal studies show that Resilia tissue resists calcium deposits "remarkably better" than the usual valve tissue.

In humans, two prospective, one-arm studies of similar valves made with



The novel Inspiris Resilia valve in the OR at UMMC

***Dr. Griffith,
one of the
COMMENCE
investigators,
implanted more
of these devices
than almost
anyone else in
the trial.***

RIGHT: Placement of the valve involves meticulous surgical technique.

Resilia tissue suggest how well the valve might work. A European study of 133 patients found good blood flow and safety outcomes one year after implantation. The larger COMMENCE trial looked at two-year outcomes in 689

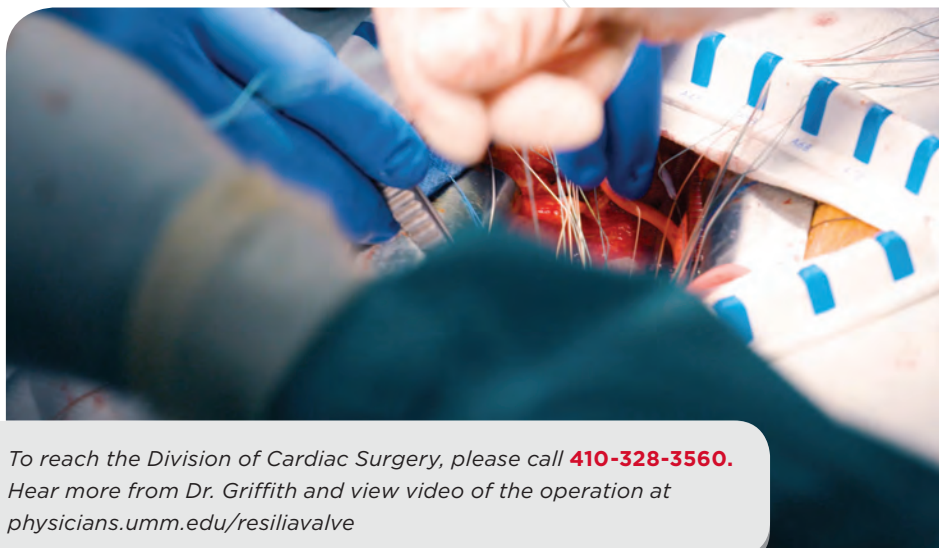
patients at 27 sites in the United States and Poland. Dr. Griffith, one of the COMMENCE investigators, implanted more of these devices than almost anyone else in the trial. The results of the trial show high survival rates and no loss of valve function, which Dr. Griffith finds encouraging.

"It's too early to judge whether the new valve has an advantage," he says. Even so, as the medical world awaits longer-term data, due out later this year, Dr. Griffith thinks the Inspiris valve may be the best option for many patients.

Not only is the UMMC one of the first centers in the United States to implant the new valve, Dr. Griffith considers it one of the top implant centers in the Mid-Atlantic.

"We have worked hard at the University of Maryland to build experience with aortic valve replacement," he says. In fact, UM performs at least 200 surgical implants and 200 catheter-based treatments a year.

If clinical trials back up the buzz about the new valve, Dr. Griffith thinks it will particularly benefit younger patients with calcified aortic valves. He hopes Inspiris will enable them to go longer between implantations and move the standard of care closer to "one patient, one surgery."



To reach the Division of Cardiac Surgery, please call **410-328-3560**.
Hear more from Dr. Griffith and view video of the operation at
physicians.umm.edu/resiliavalve

ROBOT MAXIMIZES PRECISION IN COMPLEX SPINE SURGERY

Spine surgeons at the University of Maryland Medical Center (UMMC) have a new helper in the surgical suite to guide their hands to the exact perfect spot on the patient's spine.

The latest robotic technology is particularly useful in complex spine surgery because it enables surgeons to place hardware with better-than-ever accuracy, lessening complications and the potential need for a repeat surgery. UMMC is the only hospital in Maryland that performs complex thoracolumbar and pelvic reconstruction with a robot.

University of Maryland orthopaedic surgeons are part of the R Adams Cowley Shock Trauma Center team, the world leader in trauma care, and also the official medical provider for the athletes of the University of Maryland Terrapins.

"There's never been a sector in any industry where a robot has not enhanced it," says **Steven Ludwig**, MD, professor of orthopaedics and head of the Division of Orthopaedic Spine Surgery at the University of Maryland School of Medicine (UMSOM).

Even so, robots came to spine surgery later than to other surgical specialties. Their use by spine surgeons blossomed over the past three years, spurred by improvements in the software that directs the robot arm.

Dr. Ludwig describes the difference between UMMC's new robot and the type of robots that assemble cars on a General Motors assembly line.

"This is almost like a cobot, where it's sort of a collaboration between the robot and the human surgeon," Dr. Ludwig says. The robot guides the surgeon's placement of the pedicle screws used to attach spinal segments to a rod, but it neither drills holes nor drives screws in. "It acts as an accurate aiming guide, but the surgeon does the actual procedure."

HELP WITH TRICKY CASES

So far, spine surgeons at UMMC have used the robot not for routine cases, but

for uber-complex ones. For instance, it facilitates surgery on patients who have had previous spine surgeries.

"Their anatomy is a little bit skewed by the fact that previous fusion surgery has been done, and very often what happens is it's harder to correctly place the hardware into their spine," explains **Charles Sansur**, MD, associate professor and director of spine surgery in the Department of Neurosurgery at UMSOM. "Having the robot basically perfects our ability to precisely place the hardware."

Moreover, the robot helps with surgery on adults and children who have badly deformed spines, trauma patients who have severe spine damage, patients who need reconstruction due to a tumor and other challenging cases. It aids minimally invasive surgery, making it an option for some patients who otherwise would have needed open surgery. That may mean a speedier recovery, a shorter hospital stay, and less pain.

ROBOT AT WORK

The robot can be used for open as well as minimally invasive procedures. In essence, robotic spine surgery works similarly to stereotactic surgery. It starts with the patient undergoing a computed tomography (CT) scan, the results of which the surgeon feeds into the robot's computer. The software then builds a 3-D model of the patient's spine, enabling the surgeon to plan the procedure before the patient arrives in the operating room.

Before robotic surgery, planning would proceed in a cruder way, says Dr. Sansur. Surgeons could only estimate the width and length of screw needed; now, robotic software helps them determine the precise screw size and trajectory. The software also helps them figure out the correction needed to improve the patient's alignment.



Charles Sansur, MD

With the planning done and the patient on the operating table, a mounting platform for the robot is attached to the patient's spine. Two fluoroscopic scans, fewer than usually needed for complex spine surgery, follow. Through a process called registration, the robot matches the vertebrae on the X-rays to those on the preoperative CT scan. After the software merges the two imaging technologies, the robotic arm moves up and down the spine, and from side to side, pointing out where to place the screws per the surgeon's plan.

MAKING SPINE SURGERY SAFER

"There are a lot of danger zones near where we operate," says Dr. Ludwig. In particular, surgeons must take care to avoid harming the spinal cord, nerve root and blood vessels.

"Being off by just a few millimeters could potentially create a devastating problem," says Dr. Sansur. Place a screw too medially or too close to the nerve root or spinal cord, and the patient might end up in worse pain or paralyzed. Place it too laterally, and it might break loose from the vertebra.

Both surgeons say the robot's accuracy of hardware placement enhances patient safety. Studies estimate its accuracy at over 99 percent, better than standard techniques.

“The robot doesn’t necessarily make really excellent surgeons even better, but it allows them to do things more efficiently and to avoid potentially preventable complications that can occur even in the best of hands,” Dr. Ludwig says.



**KEY
POINTS**

Stephen Ludwig, MD

- Robot-guided spine surgery improves the accuracy of hardware placement in children and adults with hard-to-treat anatomy, such as changes resulting from prior surgeries, traumatic injury, arthritis or scoliosis.
- UMMC is the only hospital in Maryland to perform complex thoracolumbar and pelvic reconstruction with a robot.
- Use of the robot minimizes radiation exposure, shortens the procedure time and length of stay, lowers infection risk and reduces injury to tissue and muscle.
- The robot simply guides surgeons to place hardware in the precise spot specified in the preoperative plan; surgeons still plan and perform the whole surgery.
- Robotic spine surgery enables more patients to have minimally invasive rather than open surgery, setting them up for an easier recovery.



*For more information
or to refer a patient,
call **410-448-6400**
or visit umortho.org.*

“This robot is the most well-established spine robot in the industry, and there’s a lot of literature that supports its accuracy,” Dr. Sansur says.

In another boon for safety, the robot helps surgeons see tough-to-see anatomy, as in cases where arthritis has worn down the spine or bone has grown around it after previous fusions. That “prevents us from seeing the standard anatomical landmarks that guide us,” explains Dr. Sansur. In addition, the robot enhances visibility when doing surgery through a small portal and minimizes radiation exposure for everyone in the operating room.

Dr. Ludwig sees other advantages as well. He believes the robotic technology improves workflow in the operating room, which benefits patients.

“When you’re in the operating room for a shorter period of time, there’s less anesthetic risk, there’s less blood loss, and there are lower transfusion rates,” he says. “The robot doesn’t necessarily make really excellent surgeons even better, but it allows them to do things more efficiently and to avoid potentially preventable complications that can occur even in the best of hands.”

Fixing tough spinal problems at UMMC involves collaboration between orthopaedic surgeons and neurosurgeons. Besides Dr. Sansur, the neurosurgery part of the team includes **Kenneth Crandall, MD**, clinical assistant professor. Orthopaedic surgery faculty on the team include **Kelley Banagan, MD**, assistant professor; **Eugene Koh, MD, PhD**, associate professor; and **Daniel Gelb, MD**, professor and vice chair for the department.

“We have a multidisciplinary team,” Dr. Sansur says, “and very often we’re able to make things better even in patients who have been told that there’s nothing further that can be done.”

Spine surgeries are performed at UMMC, but consults and post-op visits are scheduled at convenient practice locations around Maryland.

LESS-INVASIVE PLACEMENT OF LEFT VENTRICULAR PUMP AIDS RECOVERY

When medical therapy is no longer effective for patients with advanced heart failure, left ventricular assist devices (LVADs) can help them live longer and better, sometimes as a bridge to heart transplant. Most patients who receive an LVAD must undergo open-chest surgery, but the University of Maryland Medical Center is among the few hospitals in the United States to routinely implant them through less-invasive surgery. Smaller incisions should speed recovery and reduce the risk that the right ventricle will fail.

LVADs help the heart pump blood to the body. The device consists of a pump, driveline, controller and batteries. The pump is implanted near the heart and connects to the driveline, which goes through the skin on the abdominal wall. The driveline attaches to a controller and batteries worn outside the body. The pump moves blood from the left ventricle to the aorta, assisting the function of the heart.

THE NEXT STEP AFTER MEDICATION

"A left ventricular assist device is generally considered when patients have been receiving medical therapy, and the medical therapies are no longer working," says **David Kaczorowski, MD**, assistant professor of surgery at the University of Maryland School of Medicine (UMSOM). He joined UMSOM last July, having been recruited to grow the LVAD program, which is part of the UM Heart and Vascular Center and the UM in the Division of Transplantation. He received his cardiac surgery training at the University of Pennsylvania, where he focused on treating heart failure and performing heart transplant surgery.

Dr. Kaczorowski says that medications, the mainstay of treatment for heart failure, eventually may be limited by side effects or become less effective as heart failure progresses.

"Many of the medicines that we use to treat heart failure lower blood pressure, and if the heart failure progresses, the blood pressure may become so low that we can no longer use these medications," he says. Furthermore, as the patient's kidneys start to fail, side effects of these drugs may become intolerable. At

that point, consideration turns to heart transplantation, LVADs, or palliative care.

MORE TIME FOR THOSE WITH WEAK HEARTS

Heart transplants remain the best treatment for advanced heart failure, but a shortage of donor hearts often forces patients to wait years for a match. That problem has spurred the growing use of LVADs to bolster barely working hearts until a donor heart becomes available. In short, they serve as bridges to transplantation.

"As opposed to a heart transplant, we can essentially take an LVAD off the shelf and use it whenever we need it," Dr. Kaczorowski says.

In 2001, the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) study showed that, compared to the best medical management, LVADs kept patients with serious heart failure who were ineligible for transplant alive longer. Soon after that, the US Food and Drug Administration granted its first



David Kaczorowski, MD

approval of an LVAD as "destination therapy." That gives patients who cannot get a transplant due to recent cancer, smoking, or other issues a long-term option besides palliative care.

When it comes to achieving good results for patients with advanced heart failure, these devices outdo optimal medical therapy.

"It's been well-documented in large, randomized controlled clinical trials that left ventricular assist devices improve survival for patients with end-stage heart failure, and they also improve their quality of life," says Dr. Kaczorowski.

"A left ventricular assist device is generally considered when patients have been receiving medical therapy, and the medical therapies are no longer working," Dr. Kaczorowski says.

SAFER LVAD THERAPY

LVADs have come a long way since they were too big to fit inside most women and many men. Early devices mimicked the heart's pulse, but today's LVADs release blood continuously. As a result, most patients who carry them show no discernible pulse.

"Over the years, the devices have gotten better and safer and smaller, and we've learned how to use them in a safer way," says Dr. Kaczorowski. For instance, the implantation process has evolved.

"The University of Maryland has a long history with mechanical support devices and has always explored innovative strategies for using these devices," the surgeon says.

Most centers implant LVADs by opening the chest and splitting the entire breastbone.

"We've adopted a less invasive approach, which we think has been beneficial to patients and has resulted in exceptional outcomes," Dr. Kaczorowski says. To lessen patients' physical trauma, he divides just part of the breastbone and makes a short cut between the ribs. Almost all LVAD patients at UMMC receive minimally invasive surgery; out of the last 50 patients, only two underwent open surgery, and in those cases it was for reasons other than implanting the LVAD.

Dr. Kaczorowski explains that any sort of minimally invasive surgery helps patients recover faster than they would with a bigger operation. To clarify how the less invasive approach benefits LVAD patients, he and his colleagues have been retrospectively analyzing their data.

"We think that it'll facilitate their recovery, allow them to more easily be extubated and up on their feet and, hopefully, get out of the hospital more quickly," he says. Moreover, they expect it will reduce the need for blood transfusion and cause less scarring, which should allow a smoother transplantation surgery and recovery later.

Their data further suggest that the minimally invasive approach may help prevent right ventricle failure, too.

"Right ventricular failure can be a major problem and, in fact, it can carry up to a 50 percent mortality risk if the right side fails after placement of a left ventricular assist device," says Dr. Kaczorowski.

Blood clots pose another risk, so LVAD recipients require blood thinning. Therefore, the LVAD team at UMMC has developed protocols to prevent clots. Clinicians monitor various parameters so they can hone treatment to hit the sweet spot between clotting and bleeding.

PATIENT EDUCATION AND TEAMWORK AT THE HEART OF SUCCESS

The team includes not just surgeons, but also heart-failure cardiologists, VAD engineers, nurse practitioners, and VAD coordinators. Dr. Kaczorowski describes them as a "great team" of highly specialized and well-trained people. They make sure the equipment is maintained properly and teach patients how to use it.

Of course, treatment starts with assessing patients' condition. To that end, Dr. Kaczorowski recommends that all patients with

advanced heart failure be evaluated for advanced therapies, such as heart transplants and LVADs, particularly when drug therapy starts to falter.

"We have a fairly innovative approach to taking care of these patients that's resulted in excellent outcomes that are equal to or better than anyone else in the nation," he says.



"The University of Maryland has a long history with mechanical support devices and has always explored innovative strategies for using these devices. We've adopted a less invasive approach, which we think has been beneficial to patients and has resulted in exceptional outcomes," says Dr. Kaczorowski.

ROUNDING OUT CARE & RESEARCH

UMGCCC TREATING BLOOD CANCER PATIENTS WITH NEW GENETICALLY ENGINEERED IMMUNOTHERAPY

NEW LABORATORY TO FOSTER IMMUNOTHERAPIES

The University of Maryland Marlene and Stewart Greenebaum Comprehensive Cancer Center (UMGCCC) is now certified to offer a groundbreaking treatment for non-Hodgkin lymphoma in which a patient's own immune cells are genetically engineered to recognize and attack the cancer.

Last October, the US Food and Drug Administration (FDA) approved Yescarta, a chimeric antigen receptor (CAR) T-cell therapy, to treat adults with certain types of large B-cell lymphoma.

By this spring, Kite Pharma Inc., which makes Yescarta (axicabtagene ciloleucel), had certified 34 cancer centers nationwide to offer its new treatment. UMGCCC is the only authorized center in the Baltimore-Washington-Virginia region.

"We are very excited to offer this customized gene therapy to non-Hodgkin lymphoma patients who have not been helped by other treatments, such as chemotherapy or bone marrow transplants," says **Aaron P. Rapoport**, MD, the Gary Jobson Professor in Medical Oncology at the University of Maryland School of Medicine (UMSOM).

Dr. Rapoport's research has focused on using a patient's own genetically engineered immune cells to treat blood cancers. Since 1998, Dr. Rapoport has led six major clinical trials, with more than 150 patients. The results of his latest study, from 2015, showed significant success using genetically modified

T cells to treat patients with multiple myeloma.

"Having the ability to reprogram a patient's immune cells to attack their cancer is a powerful new tool, which will help many patients who have few treatment options," Dr. Rapoport says.

Of the patients with large B-cell lymphoma who participated in a multi-center clinical study, 54 percent showed no evidence of cancer after treatment, even though they had received two or more previous therapies that had failed.

Dr. Rapoport, a hematologist and oncologist who directs the Blood and Marrow Transplant Program at UMGCCC at the University of Maryland Medical Center (UMMC), notes that the treatment can cause serious side effects, including neurological problems and a life-threatening condition known as cytokine release syndrome (CRS), a systemic inflammatory response that causes high fever and flu-like symptoms.

"The FDA has mandated that cancer centers be specially certified to administer this treatment and their staff trained to recognize and manage side effects, particularly CRS and serious nervous system symptoms," Dr. Rapoport says. "Our staff has completed the training, and it has been an extraordinary team effort to be able to offer this treatment to lymphoma patients who might benefit from CAR T-cell therapy."

The customized therapy involves removing immune cells, or T cells, from the patient and shipping them to a laboratory, where they are genetically modified to produce receptors on their surface called chimeric antigen receptors, or CARs. The receptors enable the T cells to recognize a protein on the surface of the patient's cancer cells. The modified cells are infused back into the patient, where

they increase rapidly, and seek out and destroy lymphoma cells.

The FDA approved Yescarta for use in adults with large B-cell lymphomas who haven't responded to, or have relapsed after, at least two other kinds of treatment.

Meanwhile, UMGCCC's newly dedicated Fannie Angelos Cellular Therapeutics Laboratory will open this summer as a state-of-the-art laboratory producing cell-based therapies and cancer vaccines for immunotherapy research conducted by physician-scientists from UMSOM.

Until now, UM researchers relied on outside facilities for genetically modified cells to treat cancer patients in clinical trials.

The laboratory will also be used to study and develop regenerative medicine, engineering cells to treat other illnesses, including diabetes and heart disease. However, this lab will not be involved in the CAR T-cell therapy, which is a treatment specific to Kite Pharma.

The new lab is made possible by a \$1 million gift from lawyer and Orioles owner Peter G. Angelos, as well as donations from other benefactors, and named in honor of his sister, Fannie, who died in 2015 of complications from a bone marrow disorder. She had been a patient of Dr. Rapoport.

The opening was part of a daylong event in April focused on cancer immunotherapy, attended by Gov. Larry Hogan, who in 2015 received treatment for lymphoma at UMMC.

"Having our own cell-processing laboratory will increase our ability to offer novel and promising cell-based therapies to our patients," says Dr. Rapoport.



Whether you want to transfer a patient to UMGCCC immediately, or refer a patient to a UMGCCC physician for an outpatient appointment, One Call is all you have to make: **1-800-373-4111**.

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