

Cardiology

Complex Valvular Heart Disease: A Team Approach Brings Surgeons and Cardiologists Together in Clinic & in Surgery

In the rapidly evolving era of trans-catheter aortic valve replacements, Washington University heart specialists are working side by side, collaborating both in surgery and in multidisciplinary patient clinics. “The surgical and medical disciplines are no longer completely independent because patients with complex valvular disease often present with multiple comorbidities and we need to evaluate treatment options from all perspectives,” says interventional cardiologist **Alan Zajarias, MD**.

The patient clinic visits are longer (45-60 min.), and benefit not only patients, but also physicians. “All of us are interested in treating patients with valvular heart disease, but a lot of my time is spent focusing on the technical issues and avoiding the potential pitfalls associated with open heart surgery,” says cardiothoracic surgeon **Hersh Maniar, MD**. “Working alongside cardiologists, our evaluations have become much more thorough, improving our abilities to care for these patients.”

The team includes Drs. Zajarias, Maniar, surgeon **Ralph Damiano, MD**, interventional cardiologist **John Lasala, MD**, and cardiologist **Brian Lindman, MD**. Roadblocks to the establishment of similar collaborative environments include potential “turf” battles, challenges of coordinating specialists’ schedules, and even economics. At WU, the hurdles were cleared during participation in the PARTNER (Placement of AoRTic traNscathER valves) trial and the recent opening of the multidisciplinary Valvular Heart Disease Center.

“Every trans-catheter procedure we did during the PARTNER trial, we did together, which improved our understanding of each other’s abilities and enhanced our mutual trust,” says Dr. Maniar. “Examples of this

type of collaboration between cardiac surgery and cardiology continue to grow, most recently in collaborative efforts between surgeons and electrophysiologists in the treatment of atrial fibrillation.”

Dr. Lindman says current WU fellows see the value of shared decision-making. “Just because we can put in a new valve doesn’t mean that we should or that the person will benefit,” he says. “There are difficult decisions about whether to intervene, and when and how best to intervene in patients with complex valvular heart



Left to Right: John Lasala, MD, PhD, and Hersh Maniar, MD, perform a transcatheter aortic valve replacement.

disease. Decisions are best made when the surgeon and cardiologist can put their heads together. The multidisciplinary format for seeing, evaluating and treating patients has definitely helped me as a cardiologist.”

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The mission of the Washington University and Barnes-Jewish Heart & Vascular Center is to achieve excellence in patient care, research and education through seamless integration of heart and vascular care. The Heart and Vascular Center is committed to promoting heart and vascular health through education, prevention and treatment of heart and vascular disease.

The following new research awards were made to cardiology faculty from August 2011 through June 2012.

Peter Crawford: NIH RO1: Ketone Body Metabolism and Integrated Metabolic Nomenclature

Sharon Cresci: NIH RO1: Genomic Variants Associated with Angina and Health Status Outcome after MI

Abhinav Diwan: DRTC: Diabetes Research and Training Center

Slava Epelman: AHA: Angiotensin Converting Enzyme-2 is a Novel Regulator of Monocyte Recruitment Into Ischemic Myocardium

Gregory Lanza: US Army Medical Research Acquisition Activity: Treatment of Multiple Myeloma with VLA4-targeted Nanoparticles Delivering Novel c-MYC inhibitor Prodrug

Daniel Ory: NIH Contract: Cyclodextrin Therapy for Niemann-Pick C1 Disease

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MESSAGE FROM THE CHIEF

As you can see from our lead article, our multidisciplinary approach is re-defining how cardiologists and cardiovascular surgeons can collaborate together in both the OR and in clinic. The advantages to this approach are apparent already, as demonstrated by higher



patient satisfaction scores, and the excitement that is generated within the faculty when they work together on complex cases. This step forward also mirrors what we have been doing to enhance the training experience of our fellowship program. As more fellows express an interest in outcomes training and specialized cardiology niches, we have added several new cardiology multidisciplinary training tracks. This has allowed us to improve the training environment for our fellows.

In July 2012, we have two new faculty members joining our Division. **Babak Razani, MD**, currently is one of our advanced research fellows. He focuses his research efforts on diabetes and atherosclerosis. Presently, Dr. Razani is training in the laboratory of Dr. Clay Semenkovich. The research team recently discovered that the absence of a specific protein leads to atherosclerotic progression in mice. **Amit Amin, MD**, will work on outcomes research within the division. He currently is an interventional cardiologist and outcomes research fellow at St. Luke's Mid-America Heart and Vascular Institute in Kansas City and was a finalist for the national AHA ACOR Young Investigator Award in 2010. Dr. Amin was part of a team of researchers who identified therapies that could improve the safety of percutaneous coronary intervention (PCI) and reduce the risk of post-procedure bleeding. These two appointments will strengthen our efforts to advance understanding of heart disease in the Center for Cardiovascular Research (CCR) and the Center for Cardiac Outcomes Research (CCOR).

We also are close to announcing new directors for both the CCR and CCOR. We have excellent candidates that have applied for these positions and look forward to sharing that information with you in the next newsletter.

We're pleased that our second annual satellite symposium held during the annual AHA meeting last November continues to draw participants across the country. The topic, which focused on advanced therapies for patients with heart failure, was especially timely as there has been growing evidence to suggest that early implantation of mechanical assist devices could result in better outcomes for these patients.

Along with the symposium, a number of our current fellows presented at the AHA meeting. In addition, we're proud to report that one of our fellows also earned top honors at an abstract oral presentation competition sponsored by the Missouri & Kansas Chapters of the American College of Cardiology.

As always, I encourage you to keep in touch with the Division and to let us know of your career moves and accomplishments. Send us an email to cards_alumni@dom.wustl.edu or log onto our Facebook page by searching for **Washington U. Cardiovascular Alumni** and clicking "Like" at the top of the page. Continued best wishes to you and your family and I look forward to hearing from all of you!

Douglas L. Mann, MD
Chief, Cardiovascular Division



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Masthead image courtesy of Pamela Woodard, MD, Washington University Advanced Cardiac Imaging (CT/MR) Program.

ALUMNI News & Awards

Alumni Update: Joseph Rogers, MD

Currently: Associate Professor of Medicine and Medical Director, Duke University Heart Failure Program. Majority of time is devoted to patient care with a primary focus on heart transplantation and mechanical circulatory support. Also involved in research and administration at the Duke Clinical Research Institute. Primary research interest is focused on the clinical application of LVADs in the treatment of patients with advanced heart failure. Dr. Rogers received RO1 funding last year.

Favorite Leisure Activities: Since moving to North Carolina, I have taken up fly fishing, but I am impressively poor at nearly all aspects of this sport. I have also developed an unwavering devotion to NASCAR!

In his words: favorite fellowship memories:

- Rehearsals for national oral presentations in front of Dr. Sobel and other faculty. It was a true test of one's urinary sphincter tone.
- Joe Smith teaching me to correctly characterize a wide complex tachycardia with, "I know it is atrial flutter with aberrancy because I am an electrophysiologist."
- Time with influential collaborators outside of cardiology, such as Demetrios Lappas in cardiac anesthesia, Michael Pasque in cardiac surgery, and Jeff Saffitz in Pathology. They helped shape my knowledge set beyond formal cardiology training.

I continue to believe that WU is one of the premier training programs. I have fond memories of the fellows and a great appreciation for faculty who have a real passion for education of house officers and fellows.



New NASCAR fan Joseph Rogers, MD, with wife Katina.

Message from the Program Director



Program Update

by Andy Kates, MD
Fellowship Program Director

As interests and career objectives expand, we have worked diligently to provide more diverse opportunities for fellows. Recently, we enhanced the 3rd year to include customized pathways to provide fellows the opportunity to create specialized niches, such as cardiac imaging, advanced outcomes training, and valvular heart disease, to name a few. Fellows interested in outcomes training now have several options, where as recently as a few years ago, none existed. Last year, we added a Masters of Population Health Science (MPHS) advanced degree track. It complements the Masters of Science in Clinical Investigation (MSCI), Masters of Public Health (MPH), and career research programs already in place. To improve clinical training further, we hope to increase simulations to allow for extended hands-on training. These steps serve to strengthen critical thinking skills needed for our cardiology fellows. Along the same path, through the American College of Cardiology, we are collaborating with cardiology programs across the country to identify best teaching practices. The result here is a vigorous and dynamic educational atmosphere of which you would be proud.

Fellows Accomplishments

Kory Lavine, MD (2nd year), Awarded 1st Place, Fellow in Training, Abstract Oral Presentation Missouri & Kansas Chapters of the American College of Cardiology 3rd Annual Update in Cardiovascular Diseases, *Prognostic Value of Coronary Collaterals and Microvasculature in Patients with Transplant Vasculopathy*.

Four fellows made presentations at the November 2011 AHA meeting in Orlando, FL:

Alex Aquino, MD (1st year); *Regional Variation in the Relationship of Infarct Size to Left Ventricular Ejection Fraction: Implications for Risk Stratification for Sudden Cardiac Death*

Alok Bachuwar, MD (3rd year); *Bleeding After Discharge Following Hospitalization for Acute Myocardial Infarction*

Ajit Janardhan, MD, PhD (advanced research fellow); *Low-Energy Three-Stage Electrotherapy Delivered Through Implantable Leads Significantly Reduces the Cardioversion Threshold in a Canine Model of Persistent Atrial Fibrillation*; and *Low-Energy Three-Stage Electrotherapy Delivered Through Endocardial Leads Terminates Ventricular Tachycardia With Higher Efficacy Than Anti-Tachycardia Pacing*

Kory Lavine, MD (2nd year), *Prognostic benefit of collateral development and in coronary allograft vasculopathy*

Many fellowship activities, including vital research to further innovations in cardiovascular care, are funded in whole or in part through the generosity of our alumni. If you are interested in giving back to Washington University and future cardiology fellows, please contact Doug Mann, MD, or Andy Kates, MD, at **314-747-3031**

FACULTY

News & Awards

Satellite Symposium: “Recovering” the Failing Heart

For the second year in a row, heart specialists from Washington University/Barnes-Jewish Hospital hosted a satellite symposium during the annual meeting of the American Heart Association in Orlando, FL. The symposium focused on the latest therapies that allow the heart to recover after heart failure, including the use of newer medications as well as earlier intervention with mechanical heart assist devices. Currently the REVIVE-IT study is underway to evaluate whether patients with less advanced heart failure would be good candidates for LVADs versus waiting until their disease progresses further. “It could be the dawn of a new era if evidence supports the benefit of implanting mechanical assist devices earlier in the disease process,” says **Douglas Mann, MD**, chief of the WU cardiovascular division. Other WU presenters included: **Ralph Damiano, Jr., MD**, chief of cardiothoracic surgery; **Edward Geltman, MD**, professor of medicine; **Greg Ewald, MD**, chief of clinical cardiology and director of the heart failure and cardiac transplantation section; and **Scott Silvestry, MD**, associate professor of surgery. They were joined by Emma Birks, MBBS, PhD, BSc, FRCP, director of the heart failure, transplant and mechanical support program at the University of Louisville, and Keith Aaronson, MD, MS, medical director of the heart failure program at the University of Michigan and one of the principal investigators of the REVIVE-IT study.



Greg Ewald, MD, WU chief of clinical cardiology and director of the heart failure and transplantation section discusses patient selection, timing and outcomes related to mechanical circulatory support in advanced heart failure patients at the WU satellite symposium held in November.

John P. Boineau Memorial Lecture To Be Established



In his 27 years as a member of the Division, John Boineau, MD, spanned the worlds of cardiology and cardiothoracic surgery. A former director of the Department of Medicine's Pacemaker Center and co-director of the Cardiothoracic

Surgery Research Labs, Dr. Boineau was internationally recognized for contributions in the field of electrocardiography. He authored *The ECG in Multiple Myocardial Infarction and the Progression of Ischemic Heart Disease*, published in 2005. Dr. Boineau died Nov. 7, 2011 after a long battle with leukemia.

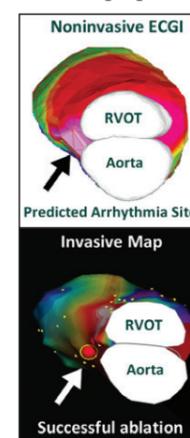
The Cardiovascular Division is in the process of establishing a memorial lecture and fund to honor Dr. Boineau. More details of the lecture, which will focus on treatments for cardiac arrhythmias, will be available soon. If you would like to send a contribution in memory of Dr. Boineau, please send it to:

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DIVISION RESEARCH HIGHLIGHTS

ECGI Beneficial in Mapping Ventricular Arrhythmias

Catheter ablation for ventricular tachycardia (VT) can be a long, arduous procedure for patients and physicians alike. In two recent publications from the *Journal of the American College of Cardiology* and *Science-Translational Medicine*, Washington University cardiologists have found that noninvasive electrocardiographic imaging (ECGI) accurately provides high resolution images of VT on the heart's surface in a single beat. More significantly, the advanced procedure, which is only performed in research protocols at WU, can pinpoint regions of the heart

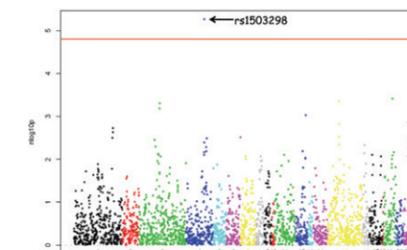


where VT occurs and areas that have been damaged by previous heart attacks. “ECGI images have been remarkably accurate in locating the origin for an arrhythmia,” says electrophysiologist **Phillip Cuculich, MD**. “The process takes just seconds to map when compared to the current catheter-based mapping, which is invasive and requires a long time in a stable arrhythmia to map it in a point-by-point fashion. This should translate into shorter procedures with better outcomes and safety profiles for patients.”

For more information, email pcuculich@dom.wustl.edu.

First Genetic Variant Discovered Associated with Extent of Coronary Artery Disease (CAD) in Diabetics

Washington University researchers have found the first genetic variant that correlates the extent of atherosclerosis in patients with diabetes. The research, published in *Circulation*, is significant because clinical factors alone don't explain why patients with diabetes often develop aggressive coronary artery disease (CAD). Researchers identified the gene, TLL1, after analyzing thousands of DNA samples from three large-scale health studies. “We now have a very early clue of the underlying mechanism that regulates how and why these patients develop CAD,” says researcher **Sharon Cresci, MD**. The team is analyzing additional DNA samples to determine if the gene variant is verified across multiple ethnic populations. Further study also will revolve around clinical outcomes. “What we'd like to know now is does this gene link to an increase in mortality or an increased need for bypass surgery,” says **Richard Bach, MD**. Read more at <http://news.wustl.edu/news/Pages/22734.aspx> or email: scresci@dom.wustl.edu



Researchers tested DNA samples against a customized microarray containing 3,351 nucleotide polymorphisms. *Circulation* 2011;124(10):2106-16.

Selected Publications

The Development of Myocardial Fibrosis in Transgenic Mice With Targeted Overexpression of Tumor Necrosis Factor Requires Mast Cell-Fibroblast Interactions. Zhang W, Chancey AL, Tzeng HP, Zhou Z, Lavine KJ, Gao F, Sivasubramanian N, **Barger PM, Mann DL**. *Circulation*. 2011 Nov 8;124(19):2106-16.

Small nucleolar RNAs U32a, U33, and U35a are critical mediators of metabolic stress. Michel CI, **Holley CL**, Scruggs BS, Sidhu R, Brookheart RT, Listenberger LL, Behlke MA, **Ory DS, Schaffer JE**. *Cell Metab*. 2011 Jul 6;14(1):33-44.

The electrophysiological cardiac ventricular substrate in patients after myocardial infarction: noninvasive characterization with electrocardiographic imaging. **Cuculich PS**, Zhang J, Wang Y, Desouza KA, Vijayakumar R, Woodard PK, Rudy Y. *J Am Coll Cardiol*. 2011 Oct 25;58(18):1893-902.

Myocardial oxygen consumption change predicts left ventricular relaxation improvement in obese humans after weight loss. Lin CH, Kurup S, Herrero P, Schechtman KB, Eagon JC, Klein S, **Dávila-Román VG**, Stein RI, Dorn II GW, **Gropler RJ, Waggoner AD, Peterson LR**. *Obesity (Silver Spring)*. 2011 Sep;19(9):1804-12.

A generalized strategy for designing (19)F/(1)H dual-frequency MRI coil for small animal imaging at 4.7 Tesla. Hu L, Hockett FD, Chen J, Zhang L, **Caruthers SD, Lanza GM, Wickline SA**. *J Magn Reson Imaging*. 2011 Jul;34(1):245-52.

Hepatic steatosis, inflammation, and ER stress in mice maintained long term on a very low-carbohydrate ketogenic diet. Garbow JR, Doherty JM, Schugar RC, Travers S, Weber ML, Wentz AE, Ezenwajaku N, Cotter DG, Brunt EM, **Crawford PA**. *Am J Physiol Gastrointest Liver Physiol*. 2011 Jun;300(6):G956-67.



Passing it On Jose Madrazo, MD, Helps Fellows Prep for Board Exams

Assistant Professor Jose Madrazo, MD remembers well the time he spent preparing for board examinations, with hours dedicated to studying near the end of his fellowship training and during the start of his career as faculty. “I thought the process would

Jose Madrazo, MD (seated, with pen), discusses cardiology topics with current fellows.

have been more useful at the beginning of my fellowship rather than condensed at the end,” he says. So when Dr. Madrazo joined the Cardiovascular Division in 2010, he decided to reach out to current fellows, conducting informal board review sessions focusing on core topics in cardiology almost every month for nine months out of the year. “I try to identify learning opportunities that are useful for patient care as well as things that are frequently asked in board-type examinations,” says Dr. Madrazo. “I build from the basics to try to make concepts as concise and as easy to remember as possible.”

For his efforts, Dr. Madrazo, who specializes in echocardiography and valvular heart disease, was awarded the Department of Internal Medicine's first “Attending of the Month” award. The award recognizes those who distinguish themselves with teaching, patient interaction, and mentoring. Among the comments he received: “Dr. Madrazo is an excellent role model for trainees.” He “provided extra teaching that went beyond immediate care needs.”

“I think doing this year-round will help improve our fellows' knowledge base as well as ease anxiety,” adds Madrazo. “Besides, it's a good excuse to socialize and eat pizza!”

Little Packages Deliver a Big Wallop — Nanomedicine

Within this decade, nanomedicine will advance breakthrough clinical methods to treat one of the leading causes of cardiovascular disease, atherosclerosis. After more than a decade, two WU heart specialists are honing in on ways to prevent strokes caused by build-up of plaque in the arteries. **Gregory Lanza, MD, PhD** and **Samuel Wickline, MD** are receiving worldwide attention after developing a targeted nanoparticle that enables noninvasive molecular imaging of plaque-associated angiogenesis. “We have developed the tool to precisely image angiogenesis,” says Dr. Lanza. “Coupled with the ability to image intraplaque hemorrhage in patients with atherosclerosis, we now have two markers that additively should accurately stage a patient’s risk for stroke and their responsiveness to antiangiogenic therapy.”

The synthesized nanoparticle, which can be injected into a patient intravenously, is of particular interest because plaque secretes enzymes to “recruit” more blood vessels as it builds up along the vessel walls. Because these newer vessels are initially fragile, they can rupture, causing an intraplaque hemorrhage. “Disease

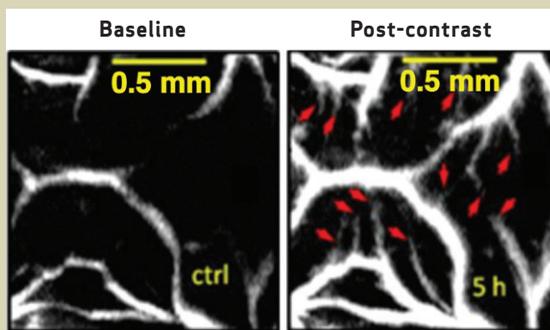


Gregory Lanza, MD, PhD

progression is slow until intraplaque hemorrhaging starts, and then it escalates, driving further angiogenesis,” says Dr. Lanza. “Our nanoparticle is filled with a fluorine-rich compound that can be seen binding to nascent vessels forming in active plaque with clinical MRI (¹⁹F MRI). Our laboratory studies suggest that if both markers were present, there is a high risk for stroke regardless of whether or not there was moderate or severe stenosis.”

On the heels of this diagnostic nanoparticle imaging agent, the team has also developed laboratory breakthroughs that extend the nanoparticle imaging system for drug delivery, a so-called theranostic agent. Because the nanoparticles can travel in vivo directly

to the location of angiogenesis, lower doses of potentially toxic medications can be used to attack where tumors or plaques are growing. “We patented the platform in 1995 and we’ve been pushing our way to the clinic ever since. In addition to cancer and cardiovascular disease, we now are researching the use of our nanoparticles to treat rheumatoid arthritis,” Dr. Lanza says. “The research has broad applications in medicine.”



Nanoparticles allow researchers to image angiogenesis.

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