

Cardiology

Honoring the Past: Cardiovascular Division Celebrates 65 Years

The Cardiovascular Division at Washington University has been at the forefront of advances in cardiology since it was founded in 1947. From the development of cardiac positron emission tomography (cPET) to the participation with the Division of Cardiac Surgery in the invention and assessment of the Cox-MAZE procedure and the establishment of a multidisciplinary valvular heart disease program, the Division has sought to distinguish itself through rigorous research and innovative clinical training. “We were first grounded in bedside teaching and research,” says **Robert Paine, MD**, who, in 1948, was the Division’s second fellow and later initiated the cardiology fellowship program at St. Luke’s. “We learned from distinguished faculty and I continued that tradition by ensuring young doctors were well-rounded and educated in heart disease.” This year the Division turns 65. It has trained more than 300 cardiology fellows as well as graduate students and postdoctoral research fellows and melded separate training programs originally based at Barnes Hospital and The Jewish Hospital of St. Louis. A large portion of that history was under the leadership of Burton Sobel, MD, head of the division for 21 years. “The primary theme of investigation pursued under Burt Sobel was ischemic heart disease,” says **Sandor J. Kovacs, MD, Ph.D**, a fellow from 1982 to 1985. “Tangentially the development of recombinant TPA began, and I was in the cath lab on the day it was first administered to a patient with an acute thrombotic occlusion of the left anterior descending artery by Phil Ludbrook, MD. It was standing room only.” Through it all, the hallmark of the fellowship program has been flexibility to pursue clinical

or research interests or to develop new programs and treatments. **Michael Cain, MD**, now Vice President for Health Sciences and Dean of the School of Medicine and Biomedical Sciences at the University of Buffalo, was a WU cardiology fellow from 1977 to 1980.

“Individualized research and clinical training programs were supported and encouraged,” says Dr. Cain, who focused on cardiac electrophysiology. “It enabled me to join the faculty and establish the investigative and

clinical cardiac electrophysiology lab and cardiac arrhythmia service at Washington University, which I directed from 1981- 1993.”

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Heart & Vascular Center



NATIONAL LEADERS IN MEDICINE

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 during January – May 2012.

Slava Epelman: K08: Regulation of monocyte recruitment into the ischemic myocardium by the ace2 axis

Gregory Lanza: NIH R01: Theranostic Approach to Asthma Using Anti-Angiogenic Nanomedicine

Gregory Lanza: NIH R01: Next Generation Approaches to Breast Cancer Using Image Guided Drug Delivery

Doug Mann/Victor Davila: U10: NIH Heart Failure Network

Doug Mann: NIH RO1: Cytoprotective effects of inflammation mediated membrane repair

Linda Peterson: NIH P20: Administrative Core: Lipid biomarkers for diabetic heart disease

Jean Schaffer: NIH P20: Lipid biomarkers for diabetic heart disease

Sam Wickline: NIH R01: Anti-Inflammatory Therapeutics for Cardiovascular Disease

Sam Wickline: NIH U54: Project 5: Antithrombin Nanoparticle Therapeutics in “Proteases in the Pathogenesis and Treatment of Thrombosis”

Sam Wickline: Bear Cub Fund: Antithrombin Nanoparticles for Diverse Thrombotic Microangiopathies

CONTACT INFORMATION

Cardiovascular Division

Washington University
School of Medicine
Campus Box 8086
660 S. Euclid Ave.
St. Louis, MO 63110

Administration Office

314-747-3031

Fellowship Office

314-362-1297

Ava Ysaguirre, coordinator
aysaguir@dom.wustl.edu

On the web:

cardiology.wustl.edu

Toll-Free Appointment Line:

888-210-8375

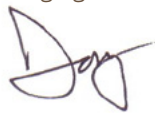
MESSAGE FROM THE CHIEF

I have had the utmost pleasure in meeting many alumni as I travel to annual meetings and conferences and delve into the division's files. It's hard to believe that the Cardiovascular Division is turning a healthy 65 years old this year. Bob Paine, who was the Division's second cardiology fellow (Albert Roos was the first) still recalls lively details of his own fellowship training in large hospital wards and of starting the fellowship program at St. Luke's, at the time just down the street from Barnes Hospital. I'm sure many of us are not fully aware of all of the innovative and significant contributions to the cardiology field from the faculty and researchers in the early days of our Division through present day. To celebrate these accomplishments and to honor the link between all of our alumni, we are planning a 65th Anniversary Celebration of the Cardiovascular Division near the end of the year. Look for details to come and I hope you have the opportunity and desire to return to St. Louis and celebrate with us.



In November, heart specialists from Washington University and Barnes-Jewish Hospital again will be holding our 3rd annual unofficial satellite symposium during the American Heart Association's 2012 Scientific Session, held this year in Los Angeles. Our symposium, titled "Update on Atrial Fibrillation: Mechanisms, Mapping, and Treatment," will feature the latest information on novel mapping techniques for atrial fibrillation as well as updates on both surgical ablation and novel hybrid approaches to treating this disease. We'll also discuss some of the clinical trials now under way.

We are looking forward to meeting the 2012 candidates for fellowship training this fall. And we look forward to telling them about the rich history of our Division and the wide-ranging accomplishments of our faculty and former fellows.



Douglas L. Mann, MD
Chief, Cardiovascular Division

65 Years

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Cain went on to serve as Chief of the Cardiovascular Division for 13 years. Now overseeing clinical electrophysiology, **Mitchell Faddis, MD, PhD**, remembers "reading 25-50 EKGs a day, five days a week for 12 months" during his fellowship from 1995 to 1997. And he laughingly recalls "the legend of the fellow in the year ahead of us who discovered that if he didn't read the EKGs, they were reissued to his classmates to read, hidden in the usual stream." Fellows consistently mention the camaraderie among each other along with

mentoring by faculty. "There were a lot of people at the cutting edge of their field and I respected them all," says **Linda Peterson, MD**, who switched from a clinical to a research-oriented pathway and now focuses on studying the effects of obesity and diabetes on the heart muscle. So did **Lisa de las Fuentes, MD**. "During the echocardiography rotation in my first year, I met a physician scientist studying hypertensive heart disease. Victor Davila-Roman's extraordinary mentorship and the opportunities here to train in clinical and quantitative research led me to develop my own career in academia."

*Want to read more? Visit cardiology.wustl.edu. You'll find reflections on our 65 years and funny fellowship memories. You can also send in your own reflections to cards_alumni@dom.wustl.edu or post them on Facebook under **Washington University Cardiology Alumni**.*

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

ALUMNI

News & Awards



Message from the Program Director

Program Update

by Andy Kates, MD
Fellowship Program Director

This fall, we will see the first round of fellowship candidates as a result of a significant change in the fellowship match process that takes effect this year. As many of you know, fellowship candidates used to determine their field of specialty early in the second year of residency. This led many students to feel undecided about a career path, resulting in a delay in applying and taking a year or two off from training, or at times requesting reference letters from faculty having minimal experience with a candidate they were asked to recommend. After discussions with program directors across the country, the application timeline for all medicine specialties was overhauled to begin at the end of the second year. Applications are submitted in July, interviews take place in the fall and then Match Day is held in December (this year-Dec. 5th). From our perspective, this is welcome change. The longer lead time will give applicants the time necessary to explore specialties so that they feel confident in their career plans. It also enables faculty to write stronger recommendations. I anticipate this will make for an exciting fall interview season.

Alumni Spotlight: Robert Paine, MD

Dr. Paine was the second fellow in Washington University's cardiology fellowship program in 1948. He joined the faculty soon after. In addition to his academic responsibilities, Dr. Paine joined the staff at St. Luke's Hospital, directing the section of cardiology and becoming Chief of Medicine there in 1963. He also established the training program for WU cardiology fellows at St. Luke's. During his long faculty tenure at Washington University, Dr. Paine was named "Teacher of the Year" three times by Washington University medical students.

Currently: At age 91, still volunteers and serves as co-chief for the preventive health organization he and his wife, Jane, founded in 2000. Called Health Protection & Education Services, the organization provides free health screenings and education monthly to the medically under-served.

Fellowship Memories: I was the first fellow at Washington University to receive a Rockefeller grant for fellowship training. It was \$3,000 a year. I told the department that my wife made more as a social worker, and convinced them to raise my salary to \$3,500/year! In the early days we were assigned to care for patients in the City Hospital ward. I'm amazed at the technology advancements in cardiology and still attend Grand Rounds, but I tell my colleagues that "the train has left the station!" and I relish my retirement. I'm proud of the distinguished fellows and faculty with whom I've trained and worked. My advice — even if you specialize, don't forget your roots in primary care. And LISTEN to your patients!



Dr. Paine and his wife, Jane

Fellows Accomplishments

Mohammed Saghir, MD, made a presentation at the March 2012 American College of Cardiology's conference on "Improvement of Heart Failure with Preserved Ejection Fraction in Obese Individuals Following Gastric Bypass Surgery."

Three fellows, along with faculty, made presentations at the International Society for Heart and Lung Transplantation meeting in Prague in April:

Kate Lindley, MD, "Antibody Mediated Rejection of the Heart in the Setting of Inflammatory Demyelinating Polyneuropathy"

Sarah Martinez, MD, "SLAM: A new echo parameter of LV unloading in patients with LVADs."

Ashwin Ravichandran, MD, "Hemolysis in LVAD: Harbinger of Doom?"

Jeremiah Depta, MD, gave a presentation at the Society for Cardiovascular Angiography and Interventions in May, 2012 on "Clinical Outcomes with the Use of a Modified Provisional Jailed-Balloon Stenting Technique for the Treatment of Coronary Bifurcation Lesions."

Several fellows received recognition for peer-reviewed published articles or books recently. Those that were listed as lead authors were:

Ajit Janardhan, MD, "Optical Mapping of the SA Node and A-V Node." *Cardiac Mapping* (Fourth Edition, 2012).

Scott Marrus, MD, "Characterization of a novel, dominant negative KCNJ2 mutation associated with Andersen-Tawil syndrome. *Channels* (Austin). 2011 Nov-Dec;5(6):500-9. Epub 2011 Nov 1.

Yogi Patel, MD, "Long-term Clinical Outcomes with the Use of Intravascular Ultrasound for the Treatment of Coronary Bifurcation Lesions." *Am J Cardiol* 2012; 109(7): 960-5.

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**

Cardiology Division Authors Two Publications

The first Washington Manual of Echocardiography® will be released in August 2012. The manual is filled with echocardiographic images and educational tips from cardiologists and sonographers regarding the interpretation of images and understanding of basic echocardiographic and Doppler physiology. The book was conceived and written by fellows to be an easy reference tool that would support their ability to perform and interpret echocardiograms. Editor Ravi Rasalingam, MD, says, “Echocardiography will always be a fundamental diagnostic tool in the care of cardiac patients. Our fellows have done an outstanding job at distilling their own learning experiences at a busy academic hospital into a book that is both practical and insightful.” Fellows in the Division interpret an average of 3,000 echocardiograms annually. “This book is an accumulation of knowledge that has helped us countless times on the wards, in clinic, and while on call,” says contributing writer Mohammed Saghir, MD, a third-year cardiology fellow. “We hope readers will share our enthusiasm in better understanding the application of this technology.”



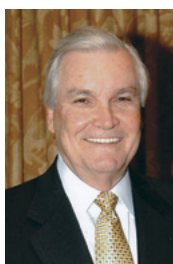
The Washington Manual of Echocardiography, Ravi Rasalingam, MD, editor, Department of Medicine, Washington University School of Medicine, 2012

Also debuting in early 2013 is the Washington Manual® Cardiology Subspecialty Consult, Third Edition. The popular book is a practical guide to the diagnosis and treatment of cardiovascular diseases. “We began work on this third edition a mere two years after the second edition, which speaks volumes about the quality of the Manual and the importance of keeping it current because the field of cardiovascular medicine is rapidly evolving,” says Phillip Cuculich, MD, co-editor with Andrew Kates, MD. Faculty members teamed with fellows to write every chapter, allowing opportunities for mentorship. Clinical fellow Jeremiah Depta, MD, worked on two chapters — one with Richard Bach, MD, on unstable angina/non-ST segment elevation myocardial infarction (UA/NSTEMI) and another with Craig Reiss, MD, on pericardial diseases. “We included important guideline recommendations on the antithrombotic agents available for the treatment of UA/NSTEMI, says Depta. “We also updated the chapter on pericardial diseases to include the latest diagnostic and management strategies for patients with diseases of the pericardium. The opportunity to work with esteemed faculty with a wealth of clinical knowledge was amazing.”

Cardiology Executive Health Program Established

In response to the growing public interest in healthy living and disease prevention, the Division has launched its Executive Health Program. The program is geared for busy individuals who want a comprehensive evaluation of their health beyond what is typically attained in the constraints of standard office visits. In addition to identifying immediate health risks, the program’s goal is to promote healthy aging with an emphasis on, but not limited to, cardiovascular disease prevention. “Each session is individually tailored, limited to 1 to 2 individuals, and offers a thorough evaluation of lifestyle, diet, adiposity, psychosocial stressors, along with comprehensive laboratory testing and assessment for subclinical atherosclerosis,” says program director Mohammad Ali Kizilbash, MD, MS, assistant professor of cardiology. “Results will be reviewed the same day. By the end of the evaluation, patients will leave having a clear understanding and be better educated about their own personal risk for heart disease and understand the hurdles they need to cross to achieve or maintain optimal health.”

James L. Cox, MD, Named First John P. Boineau Memorial Lecturer



James L. Cox, MD, emeritus Evarts A. Graham Professor of Surgery and emeritus Chief of the Division of Cardiothoracic Surgery, was the first speaker for the John P. Boineau Memorial Lecture, held in April. Dr. Boineau, who passed away last year, was internationally known for his contributions in the field of clinical electrophysiology. He worked closely with Dr. Cox to pioneer the Cox-Maze procedure for atrial fibrillation.

“Having spent the better part of 45 years with John Boineau, I suspect that I know and appreciate his unique and profound contributions to the understanding and treatment of cardiac arrhythmias better than most,” said Dr. Cox. “I delighted in being able to describe his numerous accomplishments and contributions to his former colleagues, many of who may not have appreciated what a giant John Boineau was in the field of cardiac electrophysiology. I will forever cherish this particular opportunity more than any other because of the unique experience that it provided to me personally.”

To contribute to the Boineau Memorial Lecture Fund, please send to:
**Cardiovascular Division, Washington University
 School of Medicine, Campus Box 8086, 660 S. Euclid Ave.,
 St. Louis, MO 63110**

Renal Denervation Study for Patients with Uncontrolled Hypertension

Washington University is one of 60 sites in the country participating in the Symplicity HTN-3 Trial evaluating the safety and efficacy of renal denervation for uncontrolled hypertension. The minimally invasive procedure uses low-dose radiofrequency energy to denervate renal sympathetic nerves encircling the renal artery. “There are nearly six million Americans who are unable to get their blood pressure under control despite treatment with three to five medications,” says interventional cardiologist and co-principal investigator **Jasvinder Singh, MD**. “Once the study is completed and the device is approved by the FDA, this novel approach to treatment-resistant hypertension may finally help address this public health challenge.” **Angela Brown, MD**, a hypertensive specialist, also serves as co-principal investigator. Earlier studies in both Europe and Australia found that this approach substantially reduced blood pressure. The U.S. study will enroll adult patients with systolic blood pressure > 160 mmHg despite treatment with three or more antihypertensive medication classes (including a diuretic). Results from the Symplicity HTN-1 and HTN-2 trials found that the reduction in blood pressure after the denervation procedure was sustained for at least two years. The study is sponsored by Medtronic, Inc., maker of the Symplicity Catheter System.

New Clinical Training Pathway for Heart Failure Research

The Cardiovascular Division is now offering a new clinical pathway for cardiology



Dr. Davila-Roman and fellow Justin Vader, MD

fellows in their final years of training focusing on clinical heart failure research. The subspecialty training is designed to increase the number of investigators who are dedicated to multidisciplinary research into the prevention, diagnosis and treatment of heart failure. The program dovetails with Washington University’s announcement earlier this year that it received a \$3.5 million, seven-year grant from the National Heart, Lung and Blood Institute to establish the WU Heart Failure Network, one of nine regional centers funded across the country. The consortium is comprised of five Regional Clinical Centers and is led by **Victor G. Davila-Roman, MD** and **Douglas Mann, MD**. “The HFN fellowship training program is designed to train the next generation of clinician-scientists that will be involved in clinical trials geared to enhance patient care,” says Davila-Roman. **Justin Vader, MD**, the first WU fellow selected for the research pathway, says, “In addition to exposing young physicians to the possibilities of multi-site collaboration, the goal is to take people who are passionate about patient care and provide them with the tools to focus on research that may ultimately enhance care across the entire heart failure field.”

Do Lysosomes Worsen Cell Death in Ischemia-Reperfusion Injury?

A study published in the March 2012 edition of *Autophagy* is challenging existing paradigms that suggest lysosomes worsen cell death in ischemia-reperfusion injury. The study examined whether enhancing lysosome biogenesis attenuates BNIP3-induced cardiomyocyte death. Researchers found that expression of BNIP3, a hypoxia-inducible protein, provokes mitochondrial permeabilization with release of multiple death-inducing mediators. This results in lysosome consumption and, ultimately, the impairment of an evolutionarily conserved pro-survival pathway termed autophagy, or “self-eating,” that hinders the ability to remove damaged mitochondria. Enhancing lysosome biogenesis restores the ability to remove the damaged mitochondria and prevent cardiac myocyte death. “The study establishes a framework by which conflicting roles of BNIP3, namely as an evolutionarily conserved receptor to target hypoxia-damaged mitochondria for autophagic removal and its pro-death effects may be reconciled,” says **Abhinav Diwan, MD**, one of the cardiovascular researchers. “It also implicates the ‘efficiency’ of the autophagic process as a critical determinant of whether the final outcome is cell survival or death.” Ongoing laboratory studies suggest that intermittent fasting may be a potent stimulus for enhancing lysosome biogenesis and autophagy, potentially pointing toward therapeutic implications for both primary and secondary prevention in individuals with ischemic heart disease.

Selected Publications

Autophagy links inflammasomes to atherosclerotic progression. **Razani B, Feng C, Coleman T, Emanuel R, Wen H, Hwang S, Ting JP, Virgin HW, Kastan MB, Semenkovich CF.** *Cell Metab.* 2012; 15(4):534-44.

Characterization of a novel, dominant negative KCNJ2 mutation associated with Andersen-Tawil syndrome. **Marrus SB, Cuculich PS, Wang W, Nerbonne JM.** *Channels (Austin).* 2011; 5(6):500-9.

Diagnosis of multiple infarcts from complex electrocardiograms during normal rhythm, left bundle-branch block, and ventricular pacing. **Boineau JP.** *J Electrocardiol.* 2011; 44(6):605-10.

Long-term outcomes with use of intravascular ultrasound for the treatment of coronary bifurcation lesions. **Patel Y, Depta JP, Novak E, Yeung M, Lavine K,**

Banerjee S, Lin CH, Zajarias A, Kurz HI, Lasala JM, Bach RG, Singh J. *Am J Cardiol.* 2012; 109(7):960-5.

Spatio-temporal attributes of left ventricular pressure decay rate during isovolumic relaxation. Ghosh E, **Kovács SJ.** *Am J Physiol Heart Circ Physiol.* 2012; 302(5):H1094-101.

Two-year outcomes after transcatheter or surgical aortic-valve replacement. Kodali SK, Williams MR, Smith CR, Svensson LG, Webb JG, Makkar RR, Fontana GP, Dewey TM, Thourani VH, Pichard AD, Fischbein M, Sze TO, Lim S, Greason KL, Teirstein PS, Malaisrie SC, Douglas PS, Hahn RT, Whisenant B, **Zajarias A, Wang D, Akin JJ, Anderson WN, Leon MB; PARTNER Trial Investigators.** *N Engl J Med.* 2012; 366(18):1686-95.

Building a Strong Cardiac MR Imaging Program

In the past decade, the use of cardiac magnetic resonance imaging (MR) has evolved to be the gold standard for quantifying left ventricular contractile function and as an effective tool to assess cardiomyopathy. As the number of patients who may benefit from the use of cardiac MR rises at Washington University, the Cardiovascular Division is teaming with the radiology department to increase awareness of the clinical applications of MR. “This is a clinical application that many physicians don’t have access to outside of a large academic medical center,” says Assistant Professor Anita Bhandiwad, MD, FACC, who has advanced training in echocardiography and cardiovascular MR. “We envision becoming a regional referral center for patients who need advanced cardiac imaging. We also recognize the importance of training physicians in order to make this technology more accessible to patients. We hope to grow the imaging training program for fellows and also for physicians outside of Washington University who are interested in learning how to perform and interpret cardiovascular MR.”

Dr. Bhandiwad says physicians should consider cardiac MR for patients with a new cardiomyopathy — either with ischemic (due



Cardiac MR image



Anita Bhandiwad, MD

to heart blockages) or non-ischemic causes—or in cases when an echocardiogram doesn’t provide enough detailed information. “We can use cardiac MR to help determine the extent of cardiac muscle damage after a heart attack or to under-

stand the mechanism of contractile dysfunction.” she says. “In addition to patients with cardiomyopathy, cardiac MR is useful when patients need to be followed serially and LV function needs to be quantified to track small changes.”

Dr. Bhandiwad sees broader applications for the use of cardiac MR. “This imaging modality has a role in multidisciplinary approaches for certain diseases that can have primary or secondary cardiac involvement,” she says. “Because of its high spatial resolution, I think we’ll see continued expansion of cardiac MR applications both clinically and in research as we delve into why people develop heart failure and cardiac dysfunction.”

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Cardiovascular Division
Washington University School of Medicine
Campus Box 8086, 660 S. Euclid Ave.
St. Louis, MO 63110

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