



David J. Pinsky, MD
Division Chief/Professor

Emeritus Faculty

- David R. Bassett, MD (active)
- Philip N. Cascade, MD
- Sunil K. Das, MD (active)
- Stevio Julius, MD, ScD (active)
- Bertram Pitt, MD (active)
- John T. Santinga, MD
- Andrew J. Zweifler, MD (active)

Professor

- William F. Armstrong, MD
- David S. Bach, MD
- Eric R. Bates, MD
- Robert J. Cody, MD
- James Corbett, MD (secondary)
- Mario Delmar, MD, PhD
- Wolf F. C. Duvernoy, MD
- Kim A. Eagle, MD
- José Jalife, MD
- Kenneth A. Jamerson, MD
- Fareed Khaja, MBBS
- Daniel A. Lawrence, PhD
- Michael H. Lehmann, MD
- Fred Morady, MD
- Robert S. Rosenson, MD
- Melvyn Rubenfire, MD
- Michael J. Shea, MD
- Alan B. Weder, MD

Adjunct Professor

- Richard D. Judge, MD
- Mauro Moscucci, MD

Associate Professor

- Keith D. Aaronson, MD
- Robert D. Brook, MD
- Yuqing E. Chen, MD, PhD
- Claire S. Duvernoy, MD
- Daniel T. Eitzman, MD
- James B. Froehlich, MD, MPH
- Alan D. Goldberg, MD, MBBS
- Todd M. Koelling, MD
- Vallerie McLaughlin, MD
- Joseph M. Metzger, PhD (secondary)
- John M. Nicklas, MD
- Hakan Oral, MD
- Frank Pelosi Jr, MD

Assistant Professor

- Justus M. Anumonwo, PhD
- Mark R. Benson, MD
- Omer Berenfeld, PhD, MSc
- Frank M. Bogun, MD
- Stanley J. Chetcuti, MD
- Aman Chugh, MD
- Sharlene M. Day, MD
- David B. Dyke, MD
- Matthew Ebinger, DO
- Eric D. Good, DO
- P. Michael Grossman, MD
- Hitinder S. Gurm, MBBS
- Peter G. Hagan, MD
- Elizabeth Jackson, MD, MPH
- Krit Jongnarangsin, MD
- Jerome Kalifa, MD, PhD
- Theodore J. Kollas, MD
- Brahmajee K. Nallamothu, MD
- Andrew Rosenblum, MD
- John A. Sallach, MD
- Ralph H. Stern, MD, PhD
- Karen L. Vikstrom, PhD
- Audrey H. Wu, MD, MPH
- Elina Yamada, MD

Research Assistant Professor

- Paul S. Changelian, PhD
- Hassan Musa, PhD
- Sandeep V. Pandit, PhD
- Sharon Zlochiver, PhD

Adjunct Assistant Professor

- Eduardo Bossone, MD

Instructor

- Kenneth J. Tobin, DO

Clinical Lecturer

- Sreedhar R. Billakanty, MBBS
- Nagib Chalfoun, MD
- Thomas C. Crawford, MD
- Sujoya Dey, MD
- Michael Kuhne, MD
- Jean-Francois Sarrazin, MD
- Adam B. Stein, MD
- Srikanth Veerareddy, MBBS
- Wai S. Wong, MD

Clinical Lecturer/Research Fellow

- Scott Hummel, MD
- Jennifer C. Mathews, MD

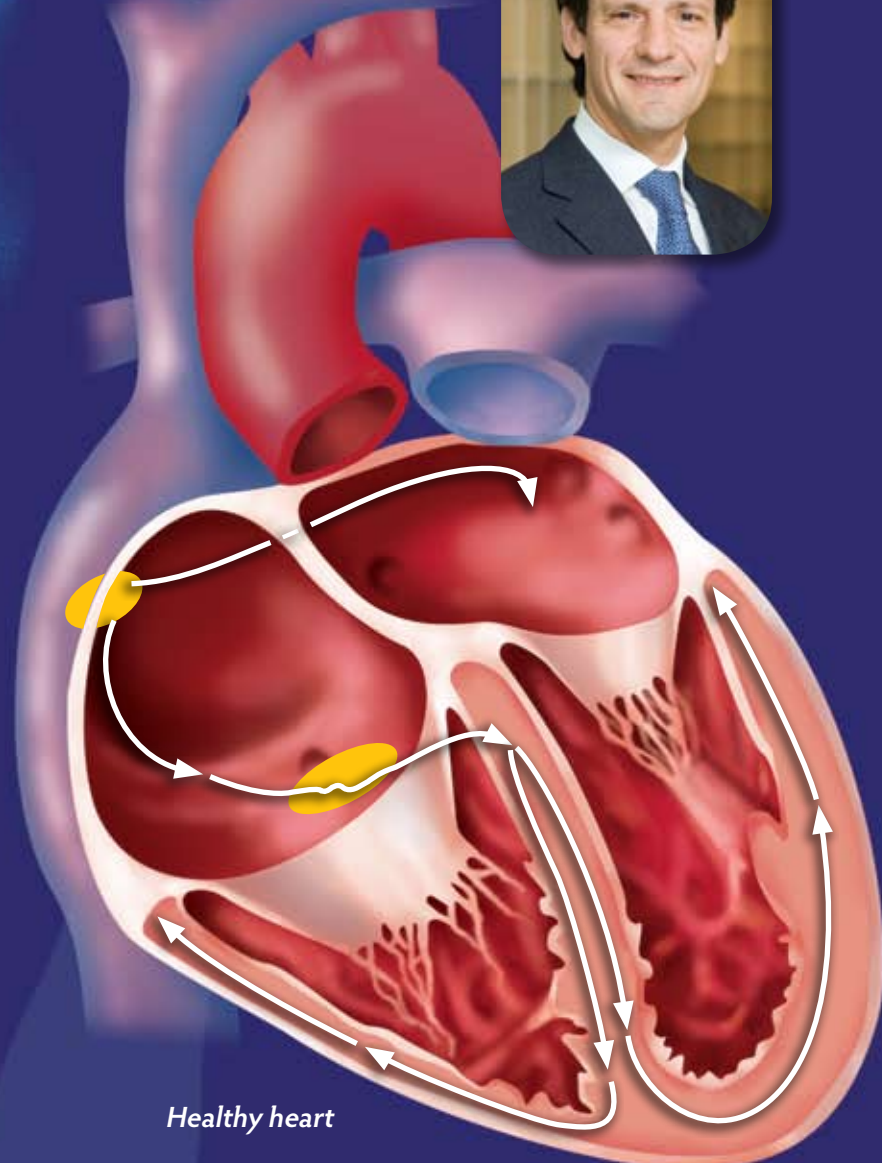
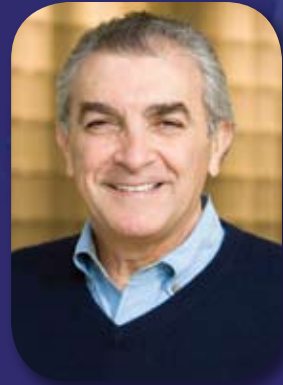
Research Investigator

- Tonya Corbin, MD
- Maria Carolina Delgado, MD
- Sergey Mironov, PhD
- Danica Petrovic-Djergovic, MD, PhD
- Gerald Schielke, PhD
- Enming (Joe) Su, PhD
- Kejie Yin, PhD
- Jifeng Zhang, MS

Adjunct Research Investigator

- Lillian K. Gleiberman, PhD

Atrial Fibrillation



Healthy heart

Basic Arrhythmia Research: Calming Electrical Storms of the Heart

Millions of Americans experience heart arrhythmias, electrical storms that disrupt the heart's beating and can lead to fatal results. Atrial fibrillation, or arrhythmias that affect the top chambers of the heart, are the leading cause of stroke; ventricular fibrillation, those arrhythmias affecting the lower chambers of the heart, can lead to sudden cardiac arrest. Numerous conditions both inherited and acquired can predispose individuals to arrhythmias of both types. Fortunately, work at the new U-M Center for Arrhythmia Research is yielding tremendous insight into the basic science of how and why these storms take hold—and how best to treat them.

Co-directors **José Jalife, MD**, (*upper left*) and **Mario Delmar, MD, PhD**, (*lower left*) established the center in late 2007, when they and a team of 33 other physicians, students and research staff arrived in Ann Arbor from the State University of New York Upstate Medical University in Syracuse. Three focus areas drive many of the center's collaborative investigations, explains Dr. Jalife: the mechanisms of atrial fibrillation; the mechanisms of ventricular fibrillation and the role of fibrosis in cardiac arrhythmias.

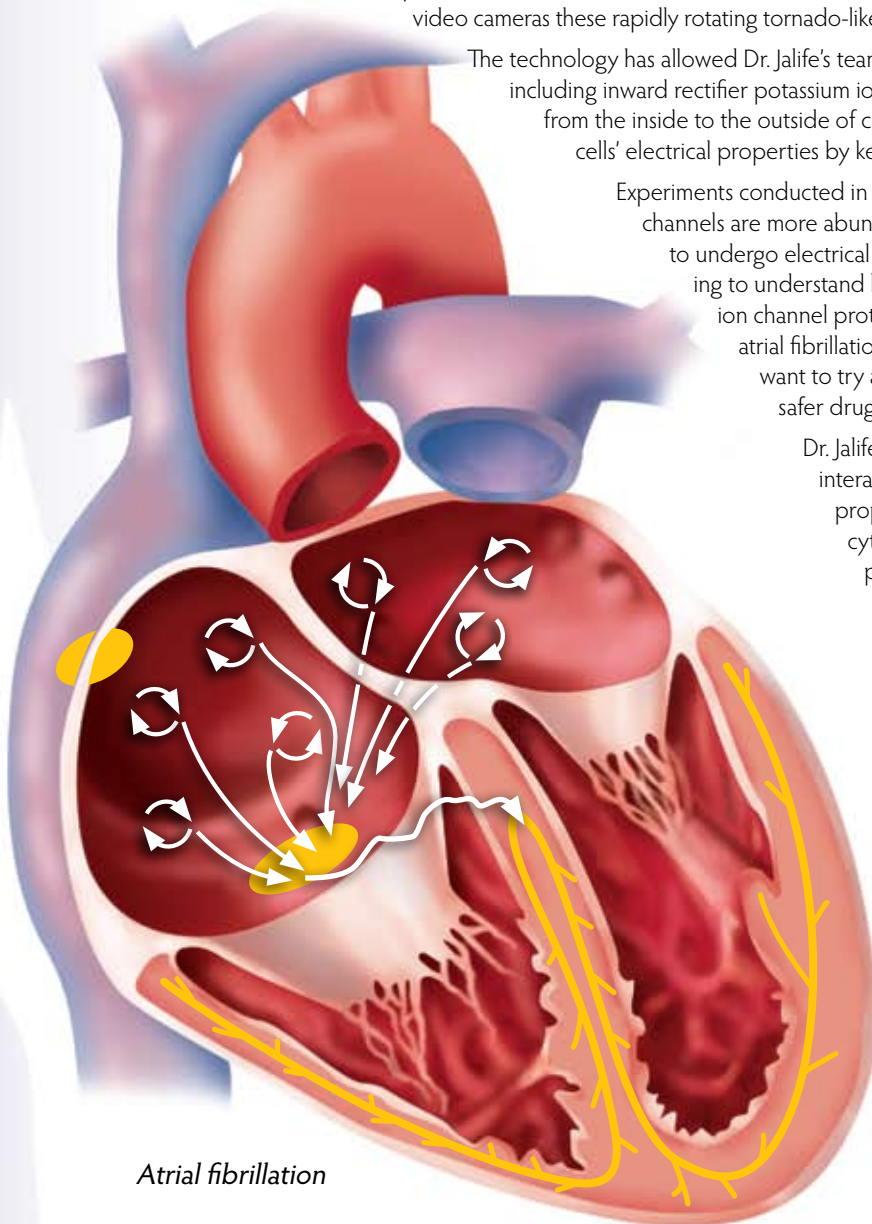
Using optical mapping technology previously developed by Dr. Jalife, his group has demonstrated that atrial fibrillation is "a problem of electrical waves rotating at very high speeds in the left atrium," he says. As a result of this prior work, scientists can now measure and visualize with fluorescent dyes and high-resolution video cameras these rapidly rotating tornado-like electrical waves found in rhythm disturbances.

The technology has allowed Dr. Jalife's team to focus in on sources of fibrillatory forces, including inward rectifier potassium ion channels, which allow potassium to move from the inside to the outside of cells in the heart. The channels help maintain cells' electrical properties by keeping them polarized.

Experiments conducted in Dr. Jalife's lab have shown that potassium ion channels are more abundant in the left atrium than the right, causing it to undergo electrical activity at higher frequencies. He is now working to understand how certain anti-arrhythmic drugs interact with ion channel proteins. While current medications can reduce atrial fibrillation, they can cause serious side effects. "We want to try and mimic that anti-arrhythmic effect by using safer drugs that more directly target the channel," he says.

Dr. Jalife also works at the cellular level to understand interactions among different cardiac cell types in propagating electrical impulses, including myocytes, or heart muscle cells, and fibroblasts, which produce collagen. Myocytes are embedded in a collagen matrix—a scaffolding of sorts—that allows them to develop electrical contacts with and mechanical anchors to one another. Some heart conditions, however, cause fibroblasts to proliferate and destroy myocytes. This causes scarring, which can lead to arrhythmias.

A novel experimental animal model and computer simulations of the interplay between these two cell types have been developed by Dr. Jalife and collaborators. In work published in *Biophysical Journal*, they found that fibrosis precedes atrial fibrillation and that a linear relationship exists between electrical frequency and the amount of fibrosis. "Eventually we'll be able to use our observations to explain many of the things we see in patients with atrial fibrillation," he adds.



Atrial fibrillation

Dr. Delmar also explores how cardiac cells convey electrical signals. Heart cells must contract in a coordinated way to maintain the heart's rhythm and pumping function. Mechanical connections—through structures called desmosomes—and electrical connections—through gap junctions—orchestrate the continuous process. In certain heart conditions these connections can close, potentially causing arrhythmia.

In work published in the journal *Circulation Research*, Dr. Delmar and his group found a large molecule that is able to hold the connections open. The 34-amino-acid molecule is too large to be feasible as a pharmacological agent, but "as a proof of principle, we've shown it's possible to modulate gap junctions," he says.

Dr. Delmar and his team have since reduced the molecule's size and weight significantly and, working with a Danish pharmaceutical firm, are getting closer to a drug that could be delivered orally to patients.

The destruction of myocytes by scar, as well as fat tissue also occurs in arrhythmogenic right ventricular cardiomyopathy (ARVC). This inherited, often silent condition can lead to sudden cardiac arrest. "The fact that this disease affects the desmosome made us think that perhaps there is crosstalk between molecules that anchor cells mechanically and molecules that allow the electrical communication," he says. Indeed further research, published in *Circulation Research and Heart Rhythm*, showed that when the integrity of mechanical connections is disrupted, integrity of the electrical connections is, too.

The research group continues to investigate the mechanisms involved. "We think the mechanism we're discovering for triggering arrhythmias in patients with ARVC could potentially be expanded to understand the mechanisms of arrhythmias in other inherited cardiomyopathies as well," says Dr. Delmar.

The collaborative basic science research at the center provides a better understanding of the precise mechanisms of atrial fibrillation and other arrhythmias, which will one day lead to effective treatment strategies for patients, says **Hakan Oral, MD**, (right) director of the division's electrophysiology service.

Dr. Oral has developed algorithms to measure frequencies in the right and left atria in order to locate sources of fibrillation. The information is used during radio-frequency ablation procedures, during which energy destroys small areas of the chamber that are conducting abnormal electrical signals. Under Dr. Oral's direction, physician-researchers continue to conduct clinical studies and refine techniques. More than 1,000 catheter ablation procedures are performed at the U-M Cardiovascular Center annually. The arrhythmia is eliminated in between 75 and 85 percent of patients.

"Our goal is to get that figure even higher," Dr. Oral says. "We're also trying to make these procedures much simpler and efficient so they can be done by more physicians in more settings. About five million people around the country have this condition and not all have access to a highly developed tertiary care center."

High-Tech Catheter Interventions

The division's interventional cardiology group strives to work at the leading edge of both scientific research and clinical catheter-based cardiac care. Research into novel areas and clinical practices that use new technologies to diagnose and treat many cardiovascular conditions, are complemented by a strong patient registry program. The Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2) is a statewide quality improvement collaborative related to percutaneous coronary interventions and peripheral vascular interventions. These sister registries are coordinated and directed by U-M interventional cardiologists. "Not only do these programs provide opportunities for qualitative improvement; they help us set new paradigms for where the field should go," says **Stanley Chetcuti, MD**, who directs the Interventional Cardiology Procedures Unit.

"The data gathered will allow us to ask and answer some very important questions related to peripheral vascular interventions," adds **Paul Michael Grossman, MD**, who leads the peripheral vascular interventions portion of the BMC2 initiative. Peripheral vascular disease (PVD) occurs when arteries carrying blood to the arms, legs or organs narrow or become blocked. Some patients are asymptomatic while others experience pain upon exertion, or claudication. Some develop more severe signs or symptoms, such as pain at rest and ulcers, and may eventually require amputation.

Percutaneous interventions to treat PVD have become more common in recent years as technology and techniques improve. "A large group of patients who couldn't be treated surgically before—because they may have been too sick for surgical revascularization or their symptoms weren't severe enough to warrant the risk—now can be," Dr. Grossman explains.



A comprehensive peripheral vascular disease management and revascularization program, run in partnership with the Section of Vascular Surgery, Division of Interventional Radiology and Section of Vascular Medicine, offers complete and efficient care to patients in a collaborative environment. This team approach also enables highly specialized training to fellows, who learn across disciplines and in a state-of-the-art simulation suite.

Dr. Grossman also conducts translational and clinical research on therapeutic angiogenesis to find ways to stimulate the growth of new blood vessels in patients with PVD. Using cell and gene therapy techniques, he combines endothelial and smooth muscle cells with growth factors to increase the vasculature in ischemic tissue—with the goal of improving blood flow and easing pain. A phase I study is underway, with promising initial results.

Other seminal research was conducted by **Hitinder Gurm, MBBS**, and published this year in the *New England Journal of Medicine*. Dr. Gurm's work focused on the effects of carotid artery stenting on stroke prevention. Stenting is done to improve blood flow to the brain in patients with carotid artery disease.

The interventional cardiology team also is developing a percutaneous valve program in conjunction with colleagues in Echocardiography and Cardiothoracic Surgery. "The University of Michigan is already seen as a leader in the field of valvular heart disease, having a thriving surgical program known as one of the premier programs in the country. It is critically important that we complement this with an active percutaneous program to ensure that patients with high risk features for surgical intervention have other options available to them," says Dr. Chetcuti.

Brahmajee Nallamothu, MD, has begun to offer balloon valvuloplasty for patients with mitral stenosis, an increasingly rare condition that typically results from rheumatic fever. While relatively uncommon in the United States, the inflammatory disease is common in less developed parts of the world. Dr. Nallamothu has traveled to India to gain additional experience. "The volume of cases in this country is low, so it's important for places like U-M to continue to offer the procedure so patients in the States have somewhere to go for treatment." He is planning to return to India in spring 2009 to continue with these efforts.

To complement U-M's active heart transplantation program the interventional group continues to offer a vibrant percutaneous assist device program. The group was an early leader in using the "Tandem Heart" pump and last year introduced a second pump that can also be inserted percutaneously. This offers another option for patients with severe heart problems and who may be awaiting transplant or a surgical assist device. Studies are also underway to evaluate newer generations of these devices.

Ongoing research into patient outcomes using the BMC2 databases helps the division set standards, melding new technology with guidelines for appropriate use. Several faculty sit on the guidelines and standards committees of professional groups, including the American Heart Association and American College of Cardiology.

To further improve patient care, the interventional cardiology group has made a commitment to all referring physicians that patients will be seen and receive a treatment plan within 24 hours, an uncommon promise in most subspecialty clinics. Dr. Chetcuti sums up the group's philosophy: "We believe it's our mission to collaborate with physicians in the community and offer to our patients easy access to the highest quality, most comprehensive and technologically advanced cardiovascular care."



FROM LEFT TO RIGHT: Drs. Chetcuti, Grossman, Nallamothu and Gurm.