An interdisciplinary approach to studying and treating rhythm disorders of the heart
ABOUT CBAC

CBAC is an interdisciplinary center set up to foster intellectual interactions and collaborations between researchers and clinicians from the Washington University Danforth and Medical School campuses in an effort to understand the heart’s irregular rhythms and to prevent their fatal consequences.

The CBAC center includes 29 faculty members from various departments in the Danforth and Medical School campuses. [CBAC Faculty member directory can be found on Pages 3-5].

CBAC publishes information about the center’s faculty members and their research through the CBAC website located at http://cbac.wustl.edu and the CBAC brochure which is distributed both in print and online in PDF format. The center also publishes educational dissemination materials that currently include the CBAC Video Archives (digital videos in MPEG and DIVX formats of the CBAC seminars that are made available online for public viewing; see Pages 6-7 for a current list), and the CBAC Newsletter which is also distributed both in print and available online in PDF format. To enhance education and outreach goals, CBAC sponsors a seminar series held throughout the academic year [the CBAC Fall 2006 seminar schedule is listed on Page 8]. If you would like a printed copy of either the CBAC brochure, or current or past issues of the CBAC Newsletter, please email Jennifer Godwin-Wyer at <jlgodwin@biomed.wustl.edu> with your name and mailing address.

An Overview of the CBAC center

The CBAC Mission Statement
The Cardiac Bioelectricity and Arrhythmia Center, CBAC, is an interdisciplinary center whose goals are to study the mechanisms of rhythm disorders of the heart (cardiac arrhythmias) and to develop new tools for their diagnosis and treatment. Cardiac arrhythmias are a major cause of death (over 300,000 deaths annually in the US alone; estimated 7 million worldwide) and disability, yet mechanisms are poorly understood and treatment is mostly empirical. Through an interdisciplinary effort, CBAC investigators apply molecular biology, ion-channel and cell electrophysiology, optical mapping of membrane potential and cell calcium, multi-electrode cardiac electrophysiological mapping, Electrocardiographic Imaging (ECGI) and other noninvasive imaging modalities, and computational biology (mathematical modeling) to study mechanisms of arrhythmias at all levels of the cardiac system. Our mission is “To battle cardiac arrhythmias and sudden cardiac death through scientific discovery and its application in the development of mechanism-based therapy”.

Research Goals
Research projects at CBAC cover the entire spectrum from molecular and cellular processes to mechanisms, diagnosis and treatment of arrhythmias in patients. The cross-disciplinary structure of CBAC promotes collaborations between researchers and clinicians and fosters a multiple-approach strategy to the study, diagnosis and treatment of cardiac arrhythmias. Approaches include molecular, single-cell and whole-animal experiments, mathematical modeling and computer simulations, and patient studies during imaging, catheterization and open-heart surgery. Among the state-of-the-art techniques employed are genetics, biomolecular structural analysis, patch clamp recordings from single ion channels, ion-selective electrode measurements, high resolution electrical mapping, optical mapping of cardiac activation and cell-calcium, Electrocardiographic Imaging, supercomputing and computer graphics, signal processing and image analysis.

Projects include:

• Molecular structure and electrophysiological function of cardiac ion channels
• Development of mathematical models of cardiac ion channels, cells and tissues
• Regulatory pathways in cardiac cells
• Mechanisms of hereditary cardiac arrhythmias
• Arrhythmias in myocardial ischemia and infarction

continued on Page 3...
• Cell-to-cell communication and action potential propagation in the diseased heart
• Structure and function of the atrio-ventricular node
• Mechanisms of cardiac (ventricular and atrial) fibrillation and new strategies for defibrillation
• Development and application of a novel imaging modality for cardiac arrhythmias
• Mechanisms of cardiac resynchronization therapy for heart failure

Education and Training Goals
An important goal of CBAC is to enhance and promote education and training in biomedical engineering, life sciences, and clinical medicine. The cross-disciplinary structure of CBAC facilitates a synergistic relationship between training, research and clinical medicine. The educational component of CBAC builds on graduate programs in the Department of Biomedical Engineering and the Medical School. Through CBAC, graduate students and scientists in engineering and life sciences can participate in clinical lectures, seminars, case presentations and clinical procedures such as diagnosis and treatment of arrhythmias in the catheterization laboratory. Similarly, post-M.D. clinical fellows can participate in lectures and seminars in the basic science departments and in research projects in the basic science laboratories.

Support and Facilities
Research is supported through grants to affiliated faculty. Funding agencies include: NIH, AHA, VA, Whitaker Foundation and NSF. A number of projects are funded through industrial support (pharmaceutical- and device-related studies). Facilities include state-of-the-art laboratories for genetics, molecular biology, cellular and subcellular electrophysiology, optical mapping of action potentials and cell-calcium, multi-electrode mapping of cardiac electrical activity, and theoretical and computer simulations using supercomputing. Studies can also be conducted in clinical facilities for MRI, CT and Ultrasound imaging, and for electrophysiology studies and arrhythmia treatment during cardiac catheterization and surgery.

CBAC Faculty Members

Director - Yoram Rudy, Ph.D., F.A.H.A., F.H.R.S.
The Fred Saigh Distinguished Professor of Engineering; Professor of Biomedical Engineering, Cell Biology & Physiology, Medicine, Radiology, and Pediatrics; Director of the Cardiac Bioelectricity and Arrhythmia Center (CBAC)

R. Martin Arthur, Ph.D.
Newton R. and Sarah Louisa Glasgow Wilson Professor of Engineering; Professor of Electrical and Systems Engineering; Professor of Biomedical Engineering

Philip V. Bayly, Ph.D.
Lilyan and E. Lisle Hughes Professor of Mechanical Engineering, Aerospace Engineering, and Biomedical Engineering

John P. Boineau, M.D.
Professor of Surgery, Medicine, and Biomedical Engineering

Michael E. Cain, M.D.
Tobias and Hortense Lewin Professor of Medicine; Director, Cardiovascular Division

Jianmin Cui, Ph.D.
Associate Professor of Biomedical Engineering on the Spencer T. Olin Endowment

Ralph J. Damiano, Jr., M.D.
John M. Shoenberg Professor of Surgery; Chief of Cardiac Surgery

Victor G. Davila-Roman, M.D.
Associate Professor of Medicine, Anesthesiology, and Radiology; Medical Director, Cardiovascular Imaging and Clinical Research Core Laboratory

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ABOUT CBAC cont.

CBAC Faculty Members cont.

Igor R. Efimov, Ph.D.
The Stanley and Lucy Lopata Associate Professor of Biomedical Engineering, Cell Biology & Physiology, and Radiology

Mitchell N. Faddis, M.D., Ph.D.
Assistant Professor of Medicine, Radiology; Clinical Cardiac Electrophysiologist, Barnes Hospital

Richard W. Gross, M.D., Ph.D.
Professor of Medicine, Chemistry, and Molecular Biology & Pharmacology; Director, Division of Bioorganic Chemistry and Molecular Pharmacology (Joint Appointment with the School of Medicine), Department of Internal Medicine, Department of Molecular Biology and Pharmacology and Department of Chemistry, Washington University School of Medicine

Patrick Y. Jay, M.D., Ph.D.
Assistant Professor of Pediatrics and Genetics

R. Gilbert Jost, M.D.
Elizabeth Mallinckrodt Professor of Radiology; Chairman, Department of Radiology; Director, Mallinckrodt Institute of Radiology

Daniel Kelly, M.D.
Alumni Endowed Professor in Cardiovascular Diseases; Professor of Medicine, Pediatrics, and Molecular Biology & Pharmacology; Director, Center for Cardiovascular Research; Co-Director, Cardiovascular Division, Department of Medicine, Washington University School of Medicine

Sándor J Kovács, Ph.D., M.D.
Associate Professor of Medicine, Physiology, Physics and Biomedical Engineering

Bruce D. Lindsay, M.D.
Associate Professor of Medicine; Director, Clinical Electrophysiology Laboratory at Washington University

Achi Ludomirsky, M.D.
The Louis Larrick Ward Professor of Pediatrics and Biomedical Engineering; Director, Pediatric Cardiology, Washington University School of Medicine and St. Louis Children’s Hospital

Arye Nehorai, Ph.D.
Chairman of the Department of Electrical & Systems Engineering; Eugene and Martha Lohman Professorship of Electrical Engineering

Jeanne M. Nerbonne, Ph.D.
Alumni Endowed Professor of Molecular Biology and Pharmacology

Colin G. Nichols, Ph.D.
Professor of Cell Biology and Physiology

Joseph A. O’Sullivan, Ph.D.
The Samuel C. Sachs Professor of Electrical Engineering; Professor of Radiology and Biomedical Engineering; Director of Electronic Systems and Signals Research Laboratory; Associate Director of Center for Security Technologies

Edward K. Rhee, M.D.
Assistant Professor of Pediatrics, Washington University School of Medicine; Director, Arrhythmia Services, St. Louis Children’s Hospital

Richard B. Schuessler, Ph.D.
Associate Research Professor of Surgery; Associate Research Professor of Biomedical Engineering; Director, Cardiothoracic Surgery Research Laboratory

Jean E. Schaffer, M.D.
Associate Professor of Medicine, Molecular Biology & Pharmacology

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CBAC Faculty Members cont.

Jinyi Shi, Ph.D.
Research Faculty, Biomedical Engineering

Timothy W. Smith, D.Phil., M.D.
Assistant Professor of Medicine

Jason W. Trobaugh, D.Sc.
Research Instructor in Medicine, Electrical and Systems Engineering

Samuel A. Wickline, M.D.
Professor of Medicine; Adjunct Professor of Physics and Biomedical Engineering; Co-Director of Cardiology

Pamela K. Woodard, M.D.
Associate Professor, Diagnostic Radiology, Cardiovascular Imaging Laboratory, Mallinckrodt Institute of Radiology

Kathryn A. Yamada, Ph.D., F.A.H.A.
Research Associate Professor of Medicine

CBAC Website

The Cardiac Bioelectricity and Arrhythmia Center (CBAC) website is located at http://cbac.wustl.edu.

The CBAC website consists of the following sections and content: • Overview <CBAC Mission, Research Goals, Education and Training Goals, Support and Facilities, Center Directory, CBAC brochure (pdf), CBAC Newsletter (pdf)>; • Director; • Faculty; • Research <Research Areas, Representative Publications, Work in Progress (password required)>; • Facilities; • Education <Course Listings, Seminars and Journal Clubs, Research Retreat, Video Archives>; • Bulletin Board <Announcements, News, Seminars and Journal Clubs, Upcoming Events, Recent Events, Faculty Meetings>; • Links; • Contacts.

The CBAC website is continuously updated, so check back often.

The CBAC Seminar Series has started its second year with the Fall 2006 schedule. With permission from the speaker we videotape the seminar talk, as well as the question & answer session that immediately follows, and place the videos online on our website at http://cbac.wustl.edu/pageEducationVideo.asp. We offer both MPEG (lower quality video but accepted more my various browsers) and DIVX (higher quality video: needs to have a plug-in installed in order to view the file) formats for each seminar video.

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The following is a list of the CBAC seminar videos we currently have available for online viewing or downloading:

Yasushi Okamura, M.D., Ph.D.
Professor, Okazaki Institute for Integrative Bioscience, National Institutes of Natural Sciences, Okazaki, Japan

Colin Nichols, Ph.D.
Professor of Cell Biology and Physiology, Washington University School of Medicine, St. Louis
Seminar titled “ATP dependent K+ channels and cardiac rhythm: Surprising findings from transgenic animals” given on September 12, 2005.

Richard Schuessler, Ph.D.
Associate Research Professor of Surgery and Biomedical Engineering; Director, Cardiothoracic Surgery Research Laboratory, Washington University School of Medicine, St. Louis
Seminar titled “Inflammatory Mechanisms in Postoperative Atrial Fibrillation” given on September 26, 2005.

Igor Efimov, Ph.D.
The Stanley and Lucy Lopata Associate Professor of Biomedical Engineering; Professor of Cell Biology & Physiology, and Radiology, Washington University, St. Louis
Seminar titled “Imaging Arrhythmias: Toward Painless Defibrillation” given on October 17, 2005.

András Varró, M.D., Ph.D., Dsc.
Chairman of the Dept. of Pharmacology & Pharmacotherapy, University of Szeged, School of Medicine, Szeged, Hungary
Seminar titled “Cellular Electrophysiology of Normal Human Myocardium” given on November 7, 2005.

Peter J. Schwartz, M.D.
Professor and Chairman, Dept. of Cardiology, University of Pavia, Italy
Seminar titled “The Long QT Syndrome: From Genes to Sudden Cardiac Death” given on November 21, 2005.

Yoram Rudy, Ph.D., F.A.H.A, F.H.R.S.
The Fred Saigh Distinguished Professor of Engineering; Professor of Biomedical Engineering, Cell Biology & Physiology, Medicine and Pediatrics; Director of the Cardiac Bioelectricity and Arrhythmia Center (CBAC), Washington University, St. Louis

Ralph Damiano, Jr., M.D.
John M. Shoenberg Professor; Chief of Cardiac Surgery, Cardiothoracic Surgery, Washington University School of Medicine, St. Louis

Geoffrey S. Pitt, M.D., Ph.D.
Assistant Professor of Pharmacology and Medicine, Columbia University Department of Pharmacology, New York, NY
Seminar titled “Modulation of Calcium Channels by Accessory Subunits” given on January 9, 2006.
CBAC Website cont.

Michael Cain, M.D.
Tobias and Hortense Lewin Professor of Medicine; Director, Cardiovascular Division, Washington University School of Medicine, St. Louis, Missouri

Daniel Kelly, M.D.
Alumni Endowed Professor in Cardiovascular Diseases; Director, Center for Cardiovascular Research, Department of Medicine, Washington University School of Medicine, St. Louis, Missouri
Seminar titled “PGC-1: A Physiologic Transducer Linked to Gene Regulatory Networks Controlling Cardiac Metabolism and Function” given on February 6, 2006.

Samuel A. Wickline, M.D.
Professor of Medicine; Adjunct Professor of Physics and Biomedical Engineering; Co-Director of Cardiology, Washington University School of Medicine, St. Louis, Missouri

William Gregory Stevenson, M.D.
Director, Clinical Cardiac Electrophysiology Program, Brigham and Women’s Hospital, Cardiovascular Division, Boston, Massachusetts
Seminar titled “Scar-Related Ventricular Arrhythmias” given on March 6, 2006.

Craig Henriquez, Ph.D.
W.H. Gardner Jr. Professor of Biomedical Engineering; Associate Professor of Computer Science; Co-Director of the Center for Neuroengineering, Duke University, Durham, North Carolina
Seminar titled “Multiscale Heart Modeling: Can you ignore interstitial space?” given on March 27, 2006.

Henk E.D.J. ter Keurs, M.D., Ph.D.
Professor of Physiology and Biophysics; Member of the Cardiovascular Research Group, University of Calgary, Canada
Seminar titled “Arrhythmogenic Calcium Release from Cardiac Myofilaments” given on April 10, 2006.

Albert Waldo, M.D.
The Walter H. Pritchard Professor of Cardiology, Professor of Medicine, and Professor of Biomedical Engineering, Case Western Reserve University, Cleveland, Ohio; Director of the Clinical Cardiac Electrophysiology Program, University Hospitals of Cleveland
Seminar titled “Mechanisms of Atrial Fibrillation” given on May 1, 2006.

Please note that each video comes with a strict Disclaimer: All material within each video file was filmed during a Cardiac Bioelectricity and Arrhythmia Center (CBAC) seminar at Washington University in St. Louis. It was made available on the website with permission from the speaker, who reserves and holds all rights. The video files are for educational purposes only and may not be reproduced, distributed or copied in any format.
The Cardiac Bioelectricity and Arrhythmia Center (CBAC) seminars are held on Monday afternoons at 5:30 PM, with refreshments served beforehand from 5:00 PM - 5:30 PM, in room 218 of Whitaker Hall on the Washington University Danforth Campus.

Contact Jennifer Godwin-Wyer (jlgodwin@biomed.wustl.edu) for more information, or visit the CBAC website at http://cbac.wustl.edu/pageBulletinBoardClubs.asp.
Bruno Taccardi. M.D., Ph.D.

Dr. Taccardi is a Research Professor of Medicine at the University of Utah School of Medicine, and Associate Director of the Cardiovascular Research and Training Institute (CVRTI), both located in Salt Lake City, Utah. He received his M.D. from the State University of Milan, Milan, Italy (with specialization in Cardiology), and two Ph.D. degrees in Physiology, one from the University of Brussels, Belgium and the other from the University of Pavia, Italy. He is an expert in cardiac electrophysiology with over 30 years of experience. Dr. Taccardi received an honorary doctorate from the University of Caen, France, was the winner of the gold medal of the President of the Italian Republic for scientific merit, and received the Professor Pierre Rijlant Triennial Prize for Cardiac Electrophysiology in Brussels. He is also a member of the Istituto Lombardo - Accademia di Scienze e Lettere and the Royal Academy of Medicine of Belgium. He invented the endocardial electrode, an instrument that allows measurements within the chambers of the heart.

Dr. Taccardi has held faculty positions at the University of Catania from 1964-1975, the University of Parma from 1976-1989, and the University of Utah from 1989-present. His research interests focus on biophysics of cardiac electric fields, three-dimensional mapping of potential and current distributions associated with excitation and recovery, and genesis of the electrocardiogram: Experimental study and computer simulation. His research is supported through two grants from the Nora Eccles Treadwell Foundation.

Dr. Taccardi has been an important collaborator at the University of Utah’s NCRR Center for Integrative Biomedical Computing since it was started and has provided the center with an archive of his research data on cardiac electrophysiology, as well as being a focal point for the center’s research and development initiatives through the work he does using their BioPSE and map3d modeling tools.

An example of the collaboration between Dr. Taccardi and the NCRR center is Dr. Taccardi’s use of the center’s computing of electrocardiographic forward solutions to measure electric potentials. These potentials are measured at 1,300 sites throughout the volume of a human shaped electrolytic torso tank in which they suspend a canine heart. In the heart they place multi-electrode needles to record from additional 1830 sites (from <http://www.sci.utah.edu/research/forward-sim.html>).

Excerpt from http://www.sci.utah.edu/cibc/collab/taccardi.html:

“Dr. Taccardi will continue to collaborate with the Center, especially in the use of forward problem simulation and visualization to understand the nature of cardiac currents. We have recently been able to provide Dr. Taccardi with the tools that allow him to create detailed three-dimensional images of the flow of current during all phases of the cardiac cycle throughout the volume conductor, which in humans is the thorax and in Dr. Taccardi’s experiments is a torso-shaped electrolytic tank in which he and his group suspend an isolated, perfused dog heart. Dr. Taccardi would like to use these tools to investigate data from past experiments in which he applied a wide range of interventions in order to understand the essential biophysics of electrocardiography under normal and pathological conditions. Success in this research would further both the understanding of mechanisms of cardiac activation and recovery and also the use of electrocardiography and cardiac mapping in clinical settings.”

Dr. Taccardi will be the September 18, 2006 seminar speaker and will give a talk on “Three-Dimensional Mapping of Intraventricular Excitation and Repolarization”. Go to Page 8 for a complete schedule of the CBAC Fall Seminar Series.
The first inaugural Cardiac Bioelectricity & Arrhythmia Center (CBAC) Research Retreat was held on Friday, May 12, 2006 in Whitaker Hall at Washington University.

Dr. Yoram Rudy’s first cardiac center, the Cardiac Bioelectricity Research and Training Center (CBRTC), Case Western Reserve University, Cleveland, Ohio, held annual research retreats, and the idea and form of the event carried over to Washington University when Dr. Rudy relocated here to become the Director of CBAC.

The CBAC Retreat was a full day of exciting lectures, informal talks and dialogue, and presentations from various CBAC faculty members whose interests range in both research and clinical studies.

The May 12, 2006 CBAC Retreat speakers included:

- **Thomas Hund, Ph.D.** from the Dept. of Surgery, “CaMKII Regulation of Cardiac Cell Excitation in Normal and Diseased Myocardium: A Computational Biology Approach”;
- **Patrick Jay, M.D., Ph.D.** from Pediatrics & Genetics, “Function Follows Form: The Role of Development in Cardiac Conduction”;
- **Bruce Lindsay, M.D.**, the Director of the Clinical Electrophysiology Laboratory, “Development of Magnetic Catheter Navigation for Ablation of Complex Arrhythmias”;
- **Jeanne Nerbonne, Ph.D.** from the Dept. of Molecular Biology & Pharmacology, “Molecular Insights Into Repolarization and Remodeling in the Ventricular Myocardium”;
- **Pamela Woodard, M.D.** from the Mallinckrodt Institute of Radiology, “Delayed Contrast-Enhanced Imaging of the Myocardium in Determining Cause and Source of Arrhythmogenic Foci”;
- with **Colin Nichols, Ph.D.**, Professor of Cell Biology and Physiology as the Morning Session Moderator, and **Michael Cain, M.D.**, Tobias and Hortense Lewin Professor of Medicine; Director, Cardiovascular Division as the Afternoon Session Moderator.

The keynote speaker was **Dan Roden, M.D.**, Professor of Medicine and Pharmacology, and the Director of the Oates Institute for Experimental Therapeutics at Vanderbilt University School of Medicine, “Hereditary and Drug-Induced Arrhythmias: From Gene to Bedside, and Back Again”.

Also during the Retreat were poster presentations given by various CBAC students, fellows, and laboratory members that emphasized important research occurring in the laboratories and facilities of the CBAC faculty members. A PDF version of the Poster Abstract Booklet can be downloaded at [http://cbac.wustl.edu/images/ResearchRetreat/Abstract_booklet_051206.pdf](http://cbac.wustl.edu/images/ResearchRetreat/Abstract_booklet_051206.pdf).

The CBAC Retreat focused on important and novel research by the CBAC faculty members. It highlighted the CBAC center’s interdisciplinary philosophy and showed how the center really does build a bridge in cardiology and cardiovascular research between the School of Engineering & Applied Science and the School of Medicine.

Below are some candid pictures taken during the retreat by Dr. Yoram Rudy’s wife, Hadas (unless otherwise noted). For more images please visit our website at [http://cbac.wustl.edu/pageEducationRetreat.asp](http://cbac.wustl.edu/pageEducationRetreat.asp).
New Members:

The CBAC center would like to welcome our newest member, Dr. Jean Schaffer.

Dr. Schaffer is the Associate Professor of Medicine in the department of Molecular Biology & Pharmacology, Washington University School of Medicine. She received her M.D. in 1986 from Harvard Medical School. Among her numerous other honors over her career, in 2006 Dr. Schaffer received the Burroughs Wellcome Clinical Scientist Award in Translational Research.

Dr. Schaffer's current research studies in her laboratory are aimed at understanding structure-function correlates and regulation of FATP1 and ACS1.

“While fatty acids are critical for many cellular functions, accumulation of excess fatty acids in non-adipose tissues leads to cell dysfunction and/or cell death. This lipotoxicity plays an important role in the pathogenesis of diabetes and heart failure. We are using genetic approaches to identify molecules that are important for channeling imported long chain fatty acids to specific cell fates, and to identify lipid metabolic and signaling pathways critical for fatty acid-induced apoptosis. Specifically, we have used a promoter trapping strategy to isolate mutant cell lines resistant to fatty acid-induced apoptosis. We are presently characterizing the disrupted gene that confers resistance in each mutant. We have also created transgenic mouse lines with tissue-restricted overexpression of proteins that facilitate fatty acid transport to understand the physiology of lipotoxicity. Our studies may provide insight to the pathogenesis of human disorders such as obesity, diabetes, and heart failure, in which fatty acid homeostasis is perturbed”.

Visit http://cbac.wustl.edu/pageFaculty.asp and http://cbac.wustl.edu/pageResearch.asp for more information on the CBAC Faculty members.

CBAC Alumni:

We would like to give a fond farewell to three of our original CBAC faculty members: Dr. Amir Amini, Dr. Kyongtae Bae, and Dr. Michael Cain. Dr. Amini and Dr. Bae are both leaving Washington University in the Fall 2006. We are grateful for their contributions to the center, as well as being a part of the first CBAC seminar series session which ran from September - December 2005.

Dr. Michael Cain has recently accepted the position of Dean of the School of Medicine and Biomedical Sciences at the University at Buffalo effective November 1, 2006. Dr. Cain presented a CBAC seminar during the Spring 2006 session, and was the Afternoon Moderator for the May 12, 2006 CBAC Research Retreat.

Other CBAC Alumni include:
• Vladimir P. Nikolski, Ph.D.
• Jeffrey E. Saffitz, M.D., Ph.D.

Faculty Honors:

We congratulate the following CBAC Faculty for their achievements and awards this year:

Michael Cain, Tobias and Hortense Lewin Professor of Medicine; Director, Cardiovascular Division
• Food and Drug Administration: 2003-2011 Consultant, Circulatory System Devices Panel, Medical Devices Advisory Committee;
• Heart Rhythm Society: 2006 Chairman, Publications Committee 2006 Fellow;
• Samoff Endowment, The Stanley J. Samoff Endowment for Cardiovascular Science, Inc.: 2006-present Chairman, Board of Directors.

Sándor J. Kovács, Associate Professor of Medicine, Physiology, Physics and Biomedical Engineering
• Cardiovascular Systems Dynamics Society (www.csdsorg): President-elect.

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Jean Schaffer, Associate Professor of Medicine, Molecular Biology & Pharmacology
• 2006 Burroughs Wellcome Clinical Scientist Award in Translational Research. See Pages 14-15 for details.

Yoram Rudy, Fred Saigh Distinguished Professor in Engineering and Director of CBAC
• In June, 2006, delivered two keynote presentations describing his work on noninvasive Electrocardiographic Imaging at the annual meetings of the International Society for Heart Research (Manchester, UK) and the International Congress on Electrocardiology (Cologne, Germany).

Faculty Research Support and Current Projects:

Michael Cain, Tobias and Hortense Lewin Professor of Medicine; Director, Cardiovascular Division

Government-awarded grants:
• 2006-11 Principal Investigator, Principles in Cardiovascular Research Training Program, (T32-HL07081). National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland, Amount: $1,999,987
• 2005-09 Core Director Clinical Research Skills Development Core NIH SCCOR in Cardiac Dysfunction and Disease, National Institutes of Health, Bethesda, Maryland, Amount: $471,004

Non-Government-awarded grants:
• 2006-07 Co-Investigator, Remodeling and novel biomarkers of cardiovascular disease in Type 2 diabetes. Washington University/Pfizer Biomedical Research Program Amount: $2,050,249.00

Daniel Kelly, Alumni Endowed Professor in Cardiovascular Diseases; Professor of Medicine, Pediatrics, and Molecular Biology & Pharmacology; Director, Center for Cardiovascular Research; Co-Director, Cardiovascular Division, Department of Medicine

Renewal NIH Grant Awarded:
2-R01-HL058493-09 (Kelly) 07/01/2006 - 06/30/2011 NIH
“Probing the cardiac PGC-1 regulatory cascade”

The major objective of this project is to identify and characterize upstream regulatory events relevant to the control of the PPARY/PGC-1 complex during physiologic and pathologic forms of cardiac hypertrophic growth.

Sándor J. Kovács, Associate Professor of Medicine, Physiology, Physics and Biomedical Engineering

Government-awarded grants:
• Barnes-Jewish Hospital Foundation 2005 – 2007 Kovács, PI “Real-time pressure-volume based assessment of cardiac function”.

Research projects:
• Successfully solved and published the solution to the “load independent index of diastolic function” problem.

Invited Presentations / Lectureships:

Michael Cain, Tobias and Hortense Lewin Professor of Medicine; Director, Cardiovascular Division
• Program Faculty, 2006, Heart Rhythm Society 27th Annual Scientific Sessions, Boston, MA
• International, 2006, 15th World Congress in Cardiac Electrophysiology and Cardiac Techniques, Nice, France

Yoram Rudy, The Fred Saigh Distinguished Professor in Engineering and Director of CBAC, delivered an invited presentation at Cardiostim – World Congress in Cardiac Electrophysiology and Cardiac Techniques (Nice, France) on the role of potassium ion channels in cardiac repolarization and its dependence on the channels’ mole-
Invited Presentations / Lectureships cont...

(Rudy cont.)...icular structure. In May, he participated as faculty in a Medtronic workshop for new leaders in cardiology and electrophysiology. He also gave a talk titled “Mathematical Modeling of Arrhythmogenic Cardiac Repolarization Abnormalities” at the Department of Pharmacology, College of Physicians and Surgeons of Columbia University, New York in April.

Daniel Kelly, Alumni Endowed Professor in Cardiovascular Diseases; Professor of Medicine, Pediatrics, and Molecular Biology & Pharmacology; Director, Center for Cardiovascular Research; Co-Director, Cardiovascular Division, Department of Medicine

Invited Lectureships:
- 50th Deuel Conference on Lipids, “The role of lipotoxic remodeling in diabetic cardiac dysfunction”, Monterey, CA, March 2006;
- Annual Blount Lectureship, University of Colorado, “Nuclear receptor signaling in the normal and failing heart”, Boulder, CO, April 2006;
- Seminar at Duke University, “Metabolic shifts in heart failure: A new target for pharmacotherapy”, Durham, NC, April 2006;
- Massachusetts General Hospital, Cardiovascular Cell and Gene Therapy Conference III, “Nuclear receptors as novel targets for cardiovascular therapeutics”, Cambridge, MA, April 2006;

Sándor J. Kovács, Associate Professor of Medicine, Physiology, Physics and Biomedical Engineering

Ed Rhee, Assistant Professor of Pediatrics, Washington University School of Medicine; Director, Arrhythmia Services, St. Louis Children’s Hospital, gave one invited talk, and two mini-course sessions at this year’s Heart Rhythm Society meeting, May 2006.

- Invited talk: “Arrhythmia Ablation in Congenital Heart Disease: When Is It the Best Option?”
- Session:
  - Mini-Course, MC02. The Evolving Role of Catheter Ablation for Arrhythmia Management in Patients with Heart Failure

Jean Schaffer, Associate Professor of Medicine, Molecular Biology & Pharmacology
- Lipotoxicity: getting to the heart of the matter. New England Medical Center Molecular Medicine Seminar Series, Boston, MA. May 2006;

The major goals of this research program are to identify novel biomarkers of diabetic cardiomyopathy and to test the specific hypothesis that cardiac remodeling occurs in the diabetic heart due to changes in lipid and glucose metabolism, resulting in altered electrical and mechanical functioning.

The Washington University participants are: Jeanne Nerbonne, P.I.; Colin Nichols, Co-PI; with Michael Cain, Yumi Kasai, Attila Kovacs, Dan Ory, Jean Schaffer, Reid Townsend, and Kathryn Yamada.

The Pfizer participants are: Mike Tones, Tony Bahinski, Eric Gulve, and Randal Numann.

Jeanne Nerbonne, the Alumni Endowed Professor of Molecular Biology and Pharmacology, and her colleagues at the Medical School, in collaboration with a group at Pfizer, St. Louis, have received a grant from the Washington University-Pfizer Biomedical Agreement. The title of the Award is “Remodeling and Novel Biomarkers of Cardiovascular Disease in Type 2 Diabetes”.

The Washington University participants are: Jeanne Nerbonne, P.I.; Colin Nichols, Co-PI; with Michael Cain, Yumi Kasai, Attila Kovacs, Dan Ory, Jean Schaffer, Reid Townsend, and Kathryn Yamada.

The Pfizer participants are: Mike Tones, Tony Bahinski, Eric Gulve, and Randal Numann.
NEWS AND ANNOUNCEMENTS

Faculty News cont...

Pamela Woodard, Associate Professor, Diagnostic Radiology, Cardiovascular Imaging Laboratory, Mallinckrodt Institute of Radiology, has been elected President-elect of the North American Society of Cardiac Imaging.

R. Martin Arthur, the Newton R. and Sarah Louisa Glasgow Wilson Professor of Engineering, has received a three-year, $818,414 grant from the National Cancer Institute for research titled “3D Non-invasive Temperature Estimation with Ultrasound”.

Philip V. Bayly, the Lilyan and E. Lisle Hughes Professor of Mechanical Engineering, Aerospace Engineering, and Biomedical Engineering, was the focus of a Washington People article in the April 28, 2006, Vol. 30, No. 31 issue of The Record, titled “Practicing What He Preaches” by Patricia Rice.

In the article, a more personal side of Dr. Bayly emerges: how he enjoys bicycling and soccer, and the love for his family. The article also emphasizes Dr. Bayly’s research in studying brain deformation and function.

Excerpt from http://record.wustl.edu/news/page/normal/7049.html:

“Grants from the National Institutes of Health and the McDonnell Center for Higher Brain Function are helping [Dr. Bayly] and his collaborators use costly magnetic resonance imaging (MRI) to examine brain deformation and function.”

“[Dr. Bayly’s] brain-dynamics team has observed how human brains respond to voluntary skull acceleration. Volunteers — almost always their subject is a member of the research team — experience about 1/10 the force of an adult player hitting a soccer ball with his or her head.”

“‘This research has uncovered explanations of unexpected brain-injury patterns. The front of the brain, even when the blow is to the rear, can be particularly deformed, as the brain pulls away from the skull,’ he says.”

“Bayly is awed by the MRI’s sensitivity, which can provide an image of the brain’s motion as shear waves at musical frequencies travel through it.”

“[Dr. Bayly] came to Washington University in 1993, and holds a joint appointment in the School of Engineering & Applied Science’s mechanical and aerospace engineering and biomedical engineering departments.”

Jean Schaffer, the Associate Professor of Medicine, Molecular Biology & Pharmacology, Washington University School of Medicine, received the 2006 Burroughs Wellcome Clinical Scientist Award in Translational Research to support her work on understanding how diabetes contributes to heart failure. The award offers $750,000 over five years for Dr. Schaffer to continue her research.

Excerpt from Washington School of Medicine Medical News, April 14, 2006, from “Work on Diabetes and Heart Disease Wins WU Researcher Award” by Gwen Ericson:

“According to Schaffer, diabetes increases the risk of heart failure even in the absence of heart valve abnormalities, high blood pressure or significant coronary artery disease. Evidence shows that high levels of fats in the blood and insulin resistance — factors commonly seen in diabetic patients — lead to an unusually large absorption of fat by the cells in heart muscle. The BWF award will...
Faculty News cont... (Jean Schaffer)

support a project exploring the toxic effects of excessive fat uptake by heart muscle in diabetes."

“This excess exposure of the diabetic heart to fats is associated with dysfunction and death of heart muscle cells, both of which contribute to heart failure in diabetic people. Schaffer’s laboratory team will focus on understanding the basic mechanisms of this toxic reaction to fats and how these processes contribute to heart failure.”

Also in the January 18, 2006 issue of the Washington School of Medicine Medical News, is an article on Dr. Schaffer’s research in fat-induced cell dysfunction and cell death titled “Fat overload kills mammalian cells - key culprit identified” by Gwen Ericson. The research identified a protein, EF1A-1, that triggers death in mammalian cells overloaded with saturated fat.

Excerpt from http://mednews.wustl.edu/news/page/normal/6398.html:

“When the researchers halted production of this protein, called EF1A-1, the cells were able to thrive in ordinarily damaging amounts of the saturated fat palmitate, a fat abundant in Western diets. At the same concentration of palmitate, normal cells still producing EF1A-1 rapidly died.”

“Other studies have linked the genesis of heart failure to fat-induced cell dysfunction and cell death in the heart.”

“With the discovery of EF1A-1’s role, this study is the first to identify a critical step in the pathway that leads from high cellular fat to cell death, according to Schaffer. EF1A-1 is an extremely abundant protein with several diverse functions within cells, including protein synthesis and maintenance of the cytoskeleton, the cell’s internal support structure."

“Schaffer’s laboratory earlier had developed a transgenic mouse that accumulates fat in its heart muscle cells resulting in the death of cells, heart failure and premature death. They found that EF1A-1 was increased nearly three-fold in the hearts of these animals.”

“In the process of identifying the role of EF1A-1, the lab members uncovered other proteins implicated in the toxicity of excess fats. They are now investigating each to find out what part it plays.”


John P. Boineau, Professor of Surgery, Medicine, and Biomedical Engineering, has published a book titled “The ECG in Multiple Myocardial Infarction and the Progression of Ischemic Heart Disease”.

The book was feautured in a write-up in The Record’s March 31, 2006, Vol. 30, No. 27 edition. Dr. Boineau writes:

“My book explains the mechanisms that cause complex ECG readings in ischemic heart disease and shows how and why the criteria for interpreting them were derived”.

Excerpt from http://record.wustl.edu/news/page/normal/6864.html:

“The ECG in Multiple Myocardial Infarction and the Progression of Ischemic Heart Disease” presents a unique view of the use of electrocardiograms (ECG) in diagnosing ischemic heart disease, which is caused by a reduced blood supply to the heart and results in the death of heart tissue,...at present the criteria for interpreting ECGs are relatively insensitive.”

“Boineau explains that if interpreted correctly, in many patients the ECG can be more useful than ultrasound in predicting the extent and distribution of tissue damage, known as infarction.”

Samuel A. Wickline, Professor of Medicine, Adjunct Professor of Physics and Biomedical Engineering, Co-Director of Cardiology, and R. Gilbert Jost, the Elizabeth Mallinckrodt Professor of Radiology, Chairman of the Department of Radiology, Director of the Mallinckrodt Institute of Radiology, took part in a March 3, 2006 University’s Board of Trustees meeting. The meeting focused on issues within the School of Medicine and included presentations by medical faculty and breakout sessions to discuss medical education, biomedical research and patient care. Dr. Wickline gave a presentation on the applications of nanotechnology to cancer and heart disease, and Dr. Jost spoke about the Center for Clinical Imaging Research. You can learn more about this meeting in the March 10, 2006, Vol. 30, No. 25 issue of The Record in the article titled “Trustees Discuss Medical School Priorities & Issues” <http://record.wustl.edu/news/page/normal/6751.html>.

Samuel A. Wickline also took part in the May 30-31, 2006 “21st Century Science: Foundation for Innovation” conference which was held at the Eric P. Newman Education Center on the Medical Campus. He was a lunch-time speaker at the conference, and is a co-founder of Kereos Inc. The conference’s purpose was to “bring together people interested in developing new enterprises in Missouri based on research discoveries”. Several notable persons spoke or were panelists at this conference and included Barry J. Marshall, the recipient of the 2005 Nobel Prize in physiology or medicine; Missouri Governor Matt Blunt; Chancellor Emeritus William H. Danforth; William B. Neaves, president and chief executive officer of the Stowers Institute for Medical Research; Roger N. Beachy, president and director of the Donald Danforth Plant Science Center; Dan Getman, vice president of global pharmaceutical research and development for Pfizer Inc.; and J.J. Stupp, co-founder and chief financial officer of Exegy, just to name a few. You can read more about this conference in the May 19, 2006, Vol. 30, No. 34 issue of The Record in the article titled “University to Host ‘Foundation for Innovation’ Symposium” <http://record.wustl.edu/news/page/normal/7214.html>, or on the Washington University Medical News website located at <http://mednews.wustl.edu/news/page/normal/7207.html>.

Sándor J Kovács, Associate Professor of Medicine, Physiology, Physics and Biomedical Engineering, was featured in a June 14, 2006 Washington University Medical News article titled “How do you measure a broken heart? Researchers find long-sought answer” by Gwen Ericson.

The question: “Is it possible to accurately measure the intrinsic filling function of the heart?”

Excerpt from http://mednews.wustl.edu/news/page/normal/7332.html:

“Consider that about half of people with heart failure have problems related to how well the heart fills with blood during the relaxation phase — referred to as diastole. Furthermore, these problems often develop earlier than problems with the contraction phase of the heartbeat — called systole. And consider that a person can have normal systole and yet have abnormal diastole. That fact, coupled with the lack of a reliable way to measure intrinsic filling function, has caused abnormalities of the filling process to be incompletely recognized.”

“‘Only in the last decade have physicians really become aware of the importance of the diastolic process and have come to recognize the syndrome of diastolic heart failure,’ says senior author Sándor J. Kovács, M.D., Ph.D., associate professor of medicine, of cell biology and physiology and of biomedical engineering and adjunct associate professor of physics. ‘When heart muscle loses its normal ability to simultaneously relax and spring back after contracting, it fails to move properly during filling. This causes blood to start backing up into the lungs with the patient developing life-threatening pulmonary edema (fluid in the lungs) and related symptoms.”

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“Echocardiograph machines obtain images of the heart using echoes from ultrasonic pulses. The machines also measure the velocity of the blood flow into and out of the heart’s chambers as the heart relaxes and contracts. This velocity measurement appears on the instrument’s screen as an image that takes on a wavelike shape (the velocity wave) with each heartbeat — the trough of the wave corresponds to the slowing of the blood flow, and the peak of the wave corresponds to speeding up of the blood flow.”

Their method is described in L. Shmuylovich L, S.J. Kovacs, “Load-independent index of diastolic filling: model-based derivation with in vivo validation in control and diastolic dysfunction subjects”. J Appl Physiol. 2006;101(1):92-101. They develop mathematical models that describe velocity wave during diastole by obtaining the heart’s velocity waves from a patient in two different positions (i.e., sitting up or laying down).

“This number is ‘load independent’ because it isn’t affected by the amount of blood reaching the heart... ‘We’ve shown what no one could before — that a load-independent index of diastolic function exists and that it has certain values in normal hearts and different values in abnormal hearts,’ Kovács says. ‘Our contribution will allow physicians to measure the filling process in a way that reflects the intrinsic capability of the heart to fill itself with blood — and this is a reflection of the relaxation and recoil properties of the heart muscle.’ ”

Support for their research is provided by Whitaker Foundation, the National Heart, Lung and Blood Institute, the American Heart Association, the Alan A. and Edith L. Wolff Charitable Trust and the Barnes-Jewish Hospital Foundation.

Ralph Damiano, John M. Shoenberg Professor of Surgery; Chief of Cardiac Surgery, was elected President of the Cardiac Surgery Biology Club for the term April 2006-present.

Yoram Rudy, the Fred Saigh Distinguished Professor in Engineering and Director of CBAC, and Achi Ludomirsky, The Louis Larrick Ward Professor of Pediatrics and Biomedical Engineering; Director, Pediatric Cardiology, Washington University School of Medicine and St. Louis Children’s Hospital, participated in a Washington University delegation to Israel. The delegation included, among others, Chancellor Wrighton, Dean Shapiro, Dean Macias, and Francis Slay - the Mayor of St. Louis City. The delegation visited several universities and academic institutions in Israel. As a result of the visit, the Technion-Israel Institute of Technology joined Washington University’s McDonnell International Scholars Academy, and Yoram Rudy will be the “ambassador” to Technion. Technion has a world renowned school of medicine and superb departments of biomedical and electrical engineering with a strong focus in cardiovascular research. We are looking forward to growing collaborations in research and education with the Technion.
FACULTY PUBLICATIONS

[Reference Cut-off Date: 03/01/2006 - 08/01/2006; References either received by author or retrieved from www.pubmed.gov]

In Press / Recently Submitted


Y. Rudy, J.R. Silva, “Computational Biology in the Study of Cardiac Ion Channels and Cell Electrophysiology”, Quarterly Reviews of Biophysics 2006 (in press but available online at the journal’s website).


Peer-Reviewed Publications

Narayan SM, Smith JM, Lindsay BD, Cain ME, Davila VG. “Relation of T-wave alternans to regional left ventricular dysfunction and eccentric hypertrophy secondary to coronary heart disease”, Am J Cardiol 2006;97:775-780.


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**Faculty News cont.; Contact Information**

**Faculty Research Support and Current Projects cont.:**

**Ralph Damiano**, John M. Shoenberg Professor of Surgery; Chief of Cardiac Surgery

**Government-awarded grants:**

- T32 HL007776-11 10/01/05-06/30/10
  NIH [Damiano, PI] $1,084,257
  “Basic Science Research Training: Cardiopulmonary Surgery”.

**Invited Presentations / Lectureships cont.:**

**Ralph Damiano**, John M. Shoenberg Professor of Surgery; Chief of Cardiac Surgery

- Program Director.  Atrial Fibrillation Course.  STS University.  Chicago, Illinois.  February 1, 2006;
- Management of Atrial Fibrillation in Patients with Valvular Heart Disease.  Invited Lecture.  5th Annual Recent Advances in the Management of Valvar Heart Disease.  Course Chair.  Washington University School of Medicine.  St. Louis, Missouri.  May 6, 2006;

**Want to Be Added to the CBAC Email List?**

If you would like to be added to the CBAC email list to receive information on upcoming seminars, events, and news, or to be added to the CBAC mailing list to receive future newsletters, email Jennifer Godwin-Wyer at jlgodwin@biomed.wustl.edu or call (314) 935-7887.

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This newsletter is produced on behalf of the Cardiac Bioelectricity and Arrhythmia Center (CBAC) by the CBAC office. Editors: J. Godwin-Wyer <jlgodwin@biomed.wustl.edu> and Y. Rudy <rudy@wustl.edu>.
Dr. Richard Schuessler is an Associate Research Professor of Surgery, an Associate Research Professor of Biomedical Engineering, and the Director of the Cardiothoracic Surgery Research Laboratory at Washington University School of Medicine, St. Louis, Missouri. He received his Ph.D. in Bioengineering in 1977 from Clemson University, Clemson, South Carolina. Dr. Schuessler was one of the first faculty members to join the CBAC center when it opened in 2004 and has been a constant supporter of the CBAC seminar series where you can almost always find him sitting in the second row and actively taking part in the question & answer session with the speaker. Dr. Schuessler’s collaborations with various faculty members and research projects spans both campuses (Danforth campus and the Medical School) and embodies the CBAC center’s motto: “To provide an “arch” in cardiology and cardiovascular research between the School of Engineering & Applied Science and the School of Medicine”.

“I have a long association with Washington University. My father was a graduate (ME, 1950). I grew up hearing stories of Wash U and would often go to engineering day events at the engineering school. When I was young I wanted to be an astronomer, but when I enrolled in college I decided that I would get an undergraduate degree in something marketable in case I didn’t go on to graduate school. I received a BS and MS in computer science and mathematics from the University of Missouri-Rolla. By this time my interest in astronomy had waned. At this point I considered three options. One was to go on and get my PhD in mathematics. I quickly dismissed this, as most mathematicians had made their major contribution by my age, and I felt that I didn’t have the smarts to make it. I considered getting a job, but college was way too much fun. I heard about a new field called Bioengineering. The applied nature of this discipline intrigued me and on a whim I enrolled in the program at Clemson University. Because of my background in finite element analysis I was assigned the task of performing stress analysis of artificial teeth. I found dentistry research to be exceedingly boring. However, this work was being done in collaboration with the Medical College of Georgia. On a visit there I had the good fortune to be introduced to the cardiac electrophysiologist, Dr. John Boineau. After talking with him for ten minutes, I knew what I wanted to do with my professional career. I continued to work with him during graduate school and after graduating in 1977 I did a postdoctoral fellowship in his laboratory. I then went to work with him. My initial research experience involved studies of naturally occurring atrial flutter in a dog. John then designed a series of studies in which we examined the role of the nonuniform distribution of conduction velocity, refractory periods and geometry. This was my initial training in electrophysiology and led me to appreciate the complexity and importance of the interaction of multiple substrates in the generation of arrhythmias. We then became interested in the generation of sinus rhythm and how multiple pacemakers in atria interacted with the nervous system to initiate atrial activation.”

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“In 1984, Dr. James Cox who had recently been appointed chief of the division of cardiothoracic surgery at Washington University, invited us to work in his lab. He had also trained in John’s lab when they were at Duke together. We arrived in St. Louis that November. Immediately the three of us started working on a surgical treatment of atrial fibrillation. With the help of Drs. Michael Cain and Peter Corr in Cardiology we went on to develop the Maze procedure. This was the first curative procedure for atrial fibrillation. Not only has it led to the widespread surgical treatment of AF, but the concept of the procedure was used to develop less invasive catheter procedures. Today, now under the direction of Dr. Ralph Damiano, we are still working to refine the procedure, but more importantly, we are trying to understand the basic causative mechanisms of atrial fibrillation. We are working with Dr. Yoram Rudy to use Electrocardiographic Imaging (ECGI) to non-invasively map AF. Working with Dr. Rudy, and also Dr. Igor Efimov, has returned me to my roots in the Washington University School of Engineering.”

**Drs. John Boineau, Michael Cain, Ralph Damiano, Igor Efimov, and Yoram Rudy are all CBAC faculty members. For a complete list of CBAC faculty see Pages 3-5 or visit our website at <http://cbac.wustl.edu/pageFaculty.asp>.**

Dr. Schuessler presented a CBAC seminar during the Fall 2005 session on September 26, 2005 titled “Inflammatory Mechanisms in Postoperative Atrial Fibrillation”. A video of his seminar presentation can be viewed or downloaded from the CBAC Video Archives section of the CBAC website located at <http://cbac.wustl.edu/pageEducationVideo.asp>; see Pages 6-7 for a complete list. He was also one of the invited speakers at this year’s inaugural CBAC Research Retreat held on May 12, 2006. He gave an afternoon presentation titled “Atrial Fibrillation: Revisiting The Critical Mass Hypothesis”. See Page 10 for more details.