

The Arrival of A-Fib Ablation

After more than a decade of development, Hopkins cardiologists have homed in on new solutions to atrial fibrillation.



Electrophysiologist Hugh Calkins has performed hundreds of atrial fibrillation ablations.

THE CASE: Except for hypertension, the 65-year-old executive had not suffered major health problems until four months ago, when she suddenly started noticing episodes of intermittent “heart pounding” that occurred without provocation. They happened two or three times weekly, did not appear to be precipitated by any identifiable cause, and lasted no more than five to 10 minutes. Then, early one morning after a cup of coffee, the patient noticed her heart was beating rapidly and irregularly, and it did not slow down after six hours of rest. She contacted her primary care physician, who encouraged her to come to the office, where an electrocardiogram showed atrial fibrillation with a rapid ventricular response. An echocardiogram showed the left atrium was slightly enlarged, the left ventricle and mitral valve were structurally and functionally normal, and no evidence of a thrombus in any of the chambers.

Though surprised that she had developed this very common form of heart disease, the patient and her husband were eager to learn

how atrial fibrillation might affect their plans for work and travel, and asked questions about treatment options.

TREATMENT DECISION: The patient has several friends with atrial fibrillation who take Coumadin for stroke prevention, so she is aware of this therapy and its risks and benefits. Her physician tells her about anti-arrhythmic drug therapy, and about anticoagulation and rate control. The patient mentions a relative with atrial fibrillation who recently underwent a “catheter procedure” that “cured” the condition. She wants to know if the same procedure might work in her case. Is it effective? Is it safe?

THE DISCUSSION: Over the past five years, catheter ablation of atrial fibrillation (AF) has evolved from an experimental procedure to one that is now performed in many large medical centers throughout the world. The Johns Hopkins Heart Institute performs an average of six AF ablation procedures each

week. The rapid and widespread acceptance of this procedure reflects the safety and efficacy of AF catheter ablation in experienced centers.

The first attempts at catheter ablation of AF were made more than 10 years ago. The goal then was to replicate the complex curvilinear lesions employed in the surgical “maze” procedure. These efforts showed that catheter ablation of AF was feasible, but the technique proved difficult, with a high incidence of complications.

Improved understanding of the mechanism of atrial fibrillation allowed the next major step forward, when French investigators showed that AF was caused by a rapidly firing single focus in a large proportion of patients. Later studies located the majority of these “trigger” sites for AF in the pulmonary veins, which carry oxygenated blood from the lungs to the left atrium.

Initial attempts to identify and apply radiofrequency ablation to these focal trigger sites for AF were encouraging, but limita-

Continued on next page

Consultation: Hugh Calkins

Director of Electrophysiology Service, Johns Hopkins Heart Institute



Which patients with AF are candidates for catheter-based pulmonary vein isolation?

In general, we would treat patients who have symptomatic AF and are unresponsive to one or more antiarrhythmic drugs. It is important for patients to recognize that techniques for catheter ablation of AF continue to evolve and improve. Some patients may elect to continue antiarrhythmic therapy to allow more time for AF ablation to advance before undergoing this procedure. For many other patients, however, catheter ablation of AF represents an excellent therapeutic option. The results of catheter ablation of AF are best among patients who have paroxysmal rather than persistent or permanent AF and among younger patients with smaller atrial size. Although catheter ablation is used today primarily for patients with symptomatic AF who have failed at least one antiarrhythmic drug, a recent study by Wazni and colleagues (*JAMA* 2005; 293:2634) suggested that it may soon be a feasible firstline approach for treating symptomatic AF patients.

tion of AF represents an excellent therapeutic option. The results of catheter ablation of AF are best among patients who have paroxysmal rather than persistent or permanent AF and among younger patients with smaller atrial size. Although catheter ablation is used today primarily for patients with symptomatic AF who have failed at least one antiarrhythmic drug, a recent study by Wazni and colleagues (*JAMA* 2005; 293:2634) suggested that it may soon be a feasible firstline approach for treating symptomatic AF patients.

Are surgical approaches ever required now?

In patients with atrial fibrillation who require cardiac surgery (for

coronary bypass or valve repair or replacement), Johns Hopkins surgeons can perform a pulmonary vein isolation (by applying radiofrequency energy from the epicardial surface, as opposed to the endocardial approach to catheter ablation) and this adds only a few minutes to the operation.

One area of active investigation now is using minimally invasive thoroscopic techniques to perform pulmonary vein isolation and ligation of the atrial appendage. I think this approach will be particularly suited for patients who cannot take Coumadin, since endocardial lesions are not created, and the appendage is the most common site of dangerous thrombus formation.

What about studies of rate control vs. anti-arrhythmic therapy?

Studies comparing these two strategies have shown that anticoagulation and rate control is a reasonable approach for patients who are asymptomatic or minimally symptomatic. For patients who have symptoms when in AF, a strategy to maintain sinus rhythm is required, and this is generally with either anti-arrhythmic drugs or a procedure.

What else do you see for the future in AF?

At Hopkins we are looking at several alternative approaches to creating the ablative lesions, including cryoablation, focused ultrasound ablation, and irrigated ablation catheters. We are constantly enhancing techniques of image integration, and **Dr. Henry Halperin's** lab has made major strides with the development of ablation procedures guided by real-time MRI. We are also exploring vagal ablation (mapping and ablating areas of the left atrium that have a high concentration of vagal stimulation) and rotor ablation (identifying and ablating regions in the left atrium that are sources of rapid, circular, re-entrant pathways). ■

A-Fib Ablation

Continued from previous page

tions to this approach soon arose. For instance, in many patients with intermittent atrial fibrillation, trigger sites are not active at the exact time of the ablation procedure, making it impossible to locate the optimal site for therapy. Some patients have multiple foci, arising from more than one pulmonary vein. When foci were identified in the pulmonary vein, ablation done within the pulmonary vein itself led to some cases of stenosis, or occlusion, of the vein.

Efforts to solve these challenges spawned three new pulmonary vein strategies for AF ablation. One involved the creation of radiofrequency lesions to ablate 20 percent to 60 percent of the pulmonary vein circumference, a procedure called “segmental pulmonary vein isolation.” This technique has largely been abandoned because of an unacceptably high rate of AF recurrence. A second strategy involves the delivery of radiofrequency energy around the entire circumference of all pulmonary veins by creation of circular lesions just outside each pulmonary vein ostium. This technique is referred to as “circumferential pulmonary vein ablation.” A third technique involves the creation of radiofrequency lesions en-

circling the pulmonary veins with the explicit goal of achieving pulmonary vein isolation. This technique is referred to as “circumferential pulmonary vein ablation with isolation.”

THE HOPKINS APPROACH: The physician referred his patient to the Electrophysiology Service at Hopkins, where she saw **Hugh Calkins** for consultation regarding her candidacy for AF ablation. Hopkins cardiologists have performed 800 catheter ablation procedures for AF over more than a decade. Taking into account the patient's active lifestyle and travel plans, Calkins offered the patient a catheter-based procedure, circumferential pulmonary vein ablation with isolation—the technique preferred by the Hopkins group for its safety and efficacy.

Drawing on Hopkins' cardiac imaging, Calkins starts his procedural technique with a CT or MRI study to evaluate the size of the atrium and the anatomy of the pulmonary veins. These images are used in real time to guide the catheter ablation. After performing an atrial transeptal puncture, a circumferential 10- to 20-pole electrode catheter is positioned at each of the pulmonary vein ostia. Characteristic electrical activity (“pulmonary vein potentials”) arising from muscle strands within the pulmonary veins is identified.

Using the cardiac CT scan image in conjunction with a three-dimensional anatomic mapping system, Calkins is able to combine the patient's own left atrial and pulmonary vein anatomic image with the electrical map. He delivers radiofrequency lesions around the entire circumference of all four pulmonary veins (see image on page 4). When the pulmonary veins are electrically isolated, Calkins confirms this by demonstrating elimination of pulmonary vein potentials with a “lasso” catheter placed within each vein.

OUTCOME: Following her procedure, the patient spends one night in the hospital. Coumadin anticoagulation is prescribed for three months, during which time the radiofrequency ablation sites will heal. She is advised that she may experience AF episodes for a few weeks, and that most patients are free of AF within one month of their procedure.

A number of studies have evaluated the safety and efficacy of the pulmonary vein isolation approach. Long-term success is achieved in 83 percent of AF patients. The risk of a major complication has been reported to be 3.2 percent, including stroke, cardiac tamponade and pulmonary vein stenosis (0.5 percent to 1 percent each), and esophageal injury (0.1 percent.) ■

Inherited Cardiac Arrhythmias—A Window into Mechanisms of Arrhythmia

Ventricular tachycardia and ventricular fibrillation sometimes result from inherited mutations in the genes encoding ion channels. “These are called ion channelopathies,” says Hopkins electrophysiologist/molecular biologist **Gordon Tomaselli**. Tomaselli says these channelopathies are important causes of sudden cardiac death in and of themselves—particularly in young people—but have also provided unique insights into the mechanisms of more common, acquired arrhythmias.

The most well-described of these disorders is the long QT syndrome (LQTS). It’s characterized by abnormal repolarization or electrical recovery of the heart, and manifests as prolongation of the QT interval on the ECG. At present, mutations in six genes have been implicated in the heritable form of the LQTS.

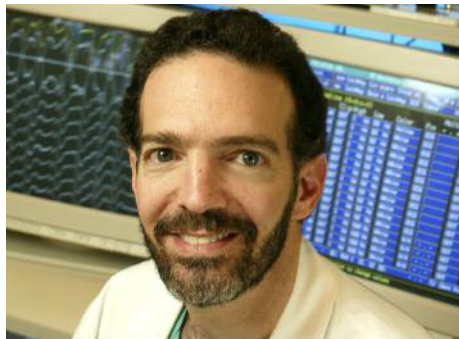
Prolongation of the QT interval may be fleeting and modest in patients with LQTS, rendering the diagnosis difficult. The channel mutations that produce QT interval prolongation are associated with other ECG abnormalities such as bradycardia. The most feared manifestation of the LQTS, however, is the curious polymorphic VT called torsades de pointes (TdP). TdP may be preceded by heralding arrhythmias such as persistent bigeminy and/or time-varying abnormalities of the QT interval that are particularly prominent after pauses.

A commercially available genetic test is now available for the mutations in the ion channel subunits associated with LQTS. Hopkins electrophysiologists can provide information regarding the test and the international registry of congenital LQTS patients. ■

Teaching Rounds

Mechanisms of Ventricular Tachycardia, and Implications for Catheter Ablation of VT

There are basically two types of ventricular tachycardia (VT), explains Hopkins electrophysiologist **Ronald Berger**. One type develops in people who have myocardial scarring, typically from prior myocardial infarction. It is due to a re-entry mechanism and often causes symptoms such as palpitations, dyspnea, chest pain, lightheadedness or syncope. Since this form of VT is an important cause of sudden cardiac death, patients who have this arrhythmia and who have depressed left ventricular systolic function—or who have survived a cardiac arrest—should be protected from sudden death with the placement of an implantable cardioverter defibrillator (ICD).



Ron Berger

The other type of VT is seen in people with structurally normal hearts that include an island of cells—usually located in the right ventricle—with increased automaticity that causes rapid heartbeat,

often during or after physical exertion. This type is called idiopathic VT and is associated with a much lower risk of sudden cardiac death, though patients are often highly symptomatic and may be limited by palpitations.

Both VT types can be suppressed or eliminated with catheter ablation. In idiopathic VT, ablation of the abnormal focus can be curative, requiring no further therapy. In patients with a pre-existing myocardial scar, other types of arrhythmia may develop even after the ablation eliminates the VT. This makes the protection of an ICD important, and antiarrhythmic medications may be required as well.

Patients requiring left ventricular mapping and ablation usually stay overnight after the procedure, while patients with idiopathic VT usually have the procedure performed on an outpatient basis. ■

The Biological Pacemaker

While electronic pacemakers are highly effective, they are not perfect, says **Eduardo Marbán**, chief of the Division of Cardiology, who cites infection and expense as just two of the limitations of these devices. Marbán’s laboratory has been pioneering the development of “biological pacemakers” that could one day replace the electronic devices. The idea, Marbán explains, is to convert part of the atria or ventricles into spontaneously active pacemaker tissue, without the use of implantable hardware.

Marbán and colleagues are exploring two general approaches. The first is the focal injection of a gene that releases an electrical “brake” in the ventricle, liberating latent pacemaker activity. The second approach is to deliver into the heart genetically engineered cells that will function as pacemakers. Prototypes are currently being tested in animals, Marbán says, with human application possible within five years.



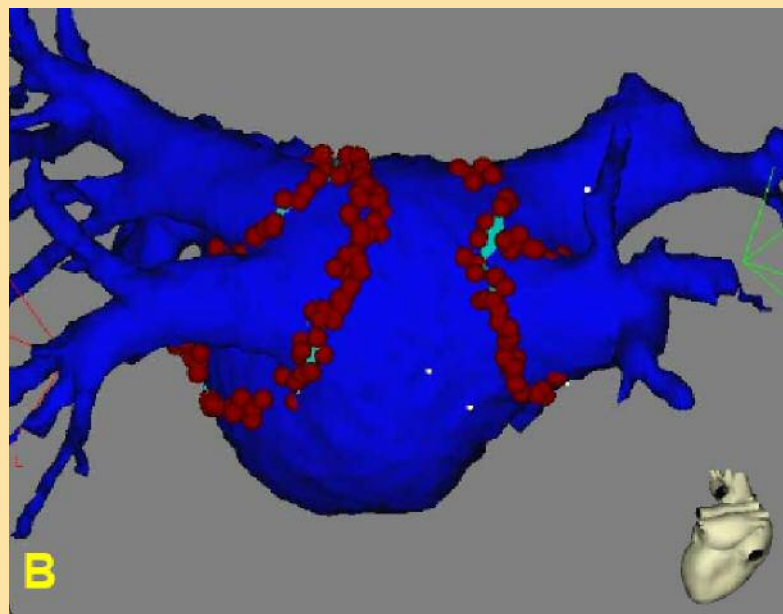
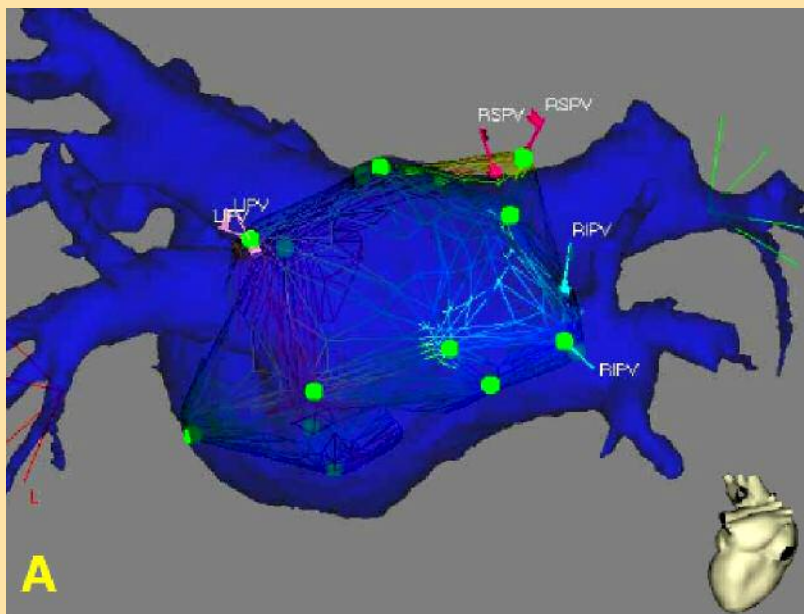
Eduardo Marbán

Gene Therapy Targets A-Fib

Breakthroughs in working with genetic materials have absorbed the interests of cardiac electrophysiologist **Kevin Donahue**, who is exploring gene therapy for a number of diseases. Donahue describes “an explosion in availability and ease of use” in new tools that help identify, characterize and manipulate genetic material.

Donahue says genetic therapy’s promises are twofold. First, such therapy might improve the specificity of actions of anti-arrhythmic drugs to reduce the side effects of pharmacotherapy. Second, genetic therapy might also provide a more directed response to an underlying problem—such as the replacement of underactive genes or dominant-negative suppression of overactive genes.

By painting gene transfer vectors onto the atria, Donahue’s laboratory has demonstrated the ability to treat atrial fibrillation in animal models; by delivering genes to the atrioventricular node, the ventricular response rate to atrial fibrillation has been controlled. Similar techniques can be used, Donahue believes, to deliver genes to the infarct border zone and treat ventricular tachycardia. ■



CT images can guide complex anatomic-based atrial fibrillation strategies. Contrast-enhanced axial slices of the chest obtained with a 64-slice CT scanner have been reconstructed and imported into an electroanatomic mapping system. In Panel A, the posterior view of the left atrium is shown, and the right superior (RSPV), right inferior (RIPV), and left inferior (LIPV) pulmonary veins are identified.

In Panel B, radiofrequency ablation lesions (in red) encircling the individual pulmonary veins were created via guidance from the registered left atrial CT image, which provided details of the complex left atrial anatomy in relation to the pulmonary veins. Image guidance improves the efficacy and safety of the ablation, while reducing procedure time. ■

Contact Information

Hopkins Access Line (HAL)

24/7 connection between a referring physician and Johns Hopkins full-time faculty in any subspecialty
410-955-9444 or 800-765-5447

Cardiology Access Line (CAL)

For physicians or their agents to refer an outpatient to cardiology
410-502-0550

Cardiac Surgery

410-955-2800

CME courses

For details on cardiovascular CME courses, go to www.hopkinscme.org or call 410-955-3169

Mark Your Calendar

Cardiovascular Topics at Johns Hopkins

February 23–25, 2006

www.hopkinscardiologycourse.com

CardiovascularREPORT

The quarterly Johns Hopkins Heart Institute *Cardiovascular Report* is one of many ways the Institute seeks to recognize and enhance its partnership with its thousands of referring physicians. Comments, questions and thoughts on topics you would like to see covered in upcoming issues are always welcome. © The Johns Hopkins University, 2005

Cardiovascular Report
Office of Referring Physicians
901 S. Bond St.
Baltimore, MD 21231

Editor
Alan W. Heldman, M.D.
aheldman@jhmi.edu; Phone: 410-614-3192; Fax: 410-614-1685

Contributing Editors
Ramsey Flynn
Luca Vricella, M.D.

Contributing Writers
Hugh Calkins, M.D.
Ronald Berger, M.D.
Gordon Tomaselli, M.D.
Eduardo Marbán, M.D., Ph.D.
Kevin Donahue, M.D.
Rick Lange, M.D.

Contributing Photographers
Bill McAllen
Keith Weller
Will Kirk

**CHANGE SERVICE REQUESTED
NO FORWARDING OR RETURN**

Non-Profit Org
U.S. Postage
PAID
Baltimore, MD
Permit No. 5415