

Rethinking Atrial Fibrillation

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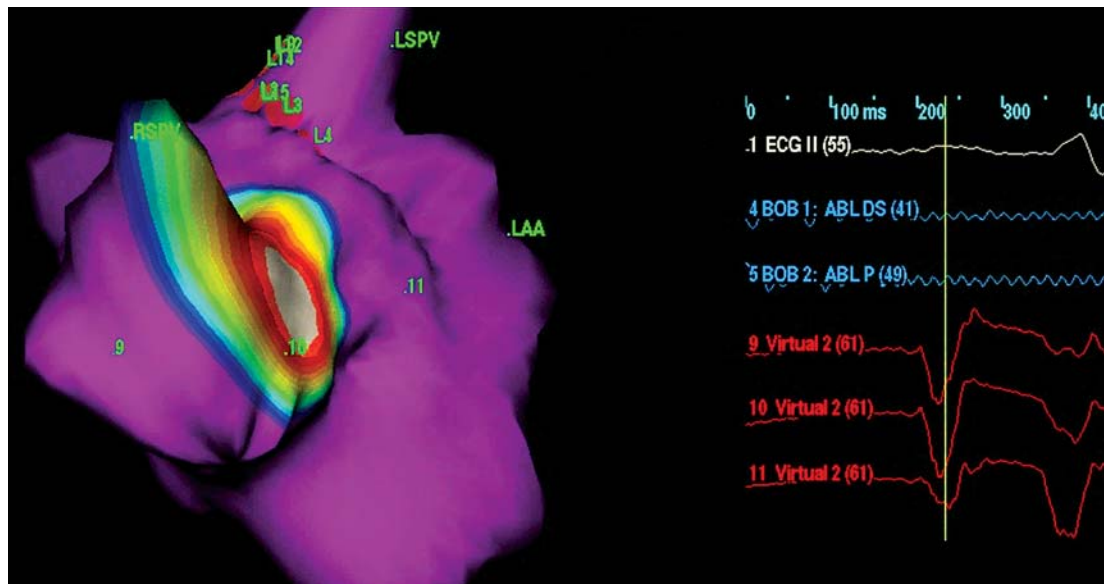
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The gray region indicates the area of the left atrium activated by a sinus beat. The wavefront is seen entering the pulmonary vein. Electrical connections between the atrium and the pulmonary vein, which can be identified with non-contact electroanatomical mapping, are targeted for ablation.

Atrial fibrillation (AF), one of the most common cardiac arrhythmias, affects the quality of life of over 2 million Americans. Its myriad forms and manifestations frequently elude definitive treatment despite increasingly advanced therapeutics, with recurrence rates of about 75%. Moreover, the presence of concomitant conditions in the majority of patients with AF further complicates treatment, and pharmacologic therapy is associated with adverse effects in a significant proportion of patients.

Long-sought, yet unrealized breakthroughs in treatments for AF clearly would have the potential to improve the lives of many people. Moderate progress has kept a sure and steady pace during the last 20 years, yielding incremental improvements in ablation options, antiarrhythmic agents, and anticoagulation.

But 2002 might be regarded as a “big” year for AF research and innovation. The landmark AFFIRM trial, published in December 2002, now challenges physicians to rethink long-held assumptions about AF treatment. Weill Cornell research in new waveforms for electrical cardioversion technology has identified biphasic waveforms as superior to the standard now used for electrical restoration of sinus rhythm. Columbia’s leading research into the mechanisms of clotting has opened an important door towards the development of selective anticoagulation.

The following sections highlight these and other important recent achievements at NewYork-Presbyterian Hospital, advances that will benefit patients with both secondary and lone AF.

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Rethinking Atrial Fibrillation

Advances in Cardioversion Technology

Biphasic defibrillators are now replacing monophasic defibrillators as the standard cardioversion technology for atrial fibrillation. This marks the first advance in transthoracic cardioversion's 40 year history.

Since electrical cardioversion for atrial fibrillation was first described in 1962 by Bernard Lown, MD, transthoracic cardioversion technology has remained essentially the same, relying on monophasic shock forms. The approximate 20% failure rate of this technology was

simply accepted as an unfortunate but unavoidable reality.

Until recently, there were only two non-pharmacological alternatives in patients who failed cardioversion: dual external defibrillators using an orthogonal electrode array, resulting in a 720 J defibrillator discharge, and internal catheter-based cardioversion. These alternatives were limited, however, by the risk of potential muscular damage from high-energy shocks and the inherent inconvenience and risks of the invasive internal catheter-based approach.

Meanwhile, the superiority of biphasic waveforms has been recognized in applications such as implantable cardioverter defibrillators (ICDs), and research has confirmed the efficacy of transthoracic biphasic shocks for ventricular fibrillation.

Research at Weill Cornell now demonstrates that biphasic waveforms are also superior to monophasic shock

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Surgical Options

Columbia offers a minimal access modified Maze procedure for the treatment of atrial fibrillation.

Of the 2.2 million people with atrial fibrillation, many would forego required surgical treatment rather than endure the trauma of an invasive operation – or if they suffer concomitant conditions, would prefer to wait until the need for an operation presents the opportunity to address both problems simultaneously. Innovations at Columbia's Surgical Arrhythmia Program are changing this trend, however, as minimal access – and even closed chest – operations are providing far less traumatic options.

When he founded the Surgical Arrhythmia Program in 1998, Mehmet C. Oz, MD embraced the challenge of improving therapeutic options for his cardiac patients. The fruits of his multidisciplinary efforts have included numerous innovations in minimal access cardiac surgery. As the newly appointed Director in 2000, Michael Argenziano, MD continued the pursuit of better minimal access approaches and, where appropriate, the use of surgical robots, to enhance patient outcomes.

“The surgical Maze operation has been the most reliable and most successful treatment for AF,” Dr. Argenziano explains. “But it involves many incisions, the use of the cardiopulmonary bypass machine, and significant operating time. Catheter-based approaches are still being developed, and success rates can vary depending upon the operator's experience and the chronicity of the patient's arrhythmia,” says Dr. Argenziano. “Through minimal access and thoracoscopic approaches, we are trying to bring these two worlds together and deliver the success rates of a surgical operation without the trauma.”

Since 1999, Columbia has performed a simplified version of the Maze operation – the left atrial modified Maze – for AF in patients having other cardiac operations. As one of several centers in the world to develop this procedure for AF, Columbia now stands as one of the leaders in performing it. In a step beyond the successes achieved elsewhere, however, Dr. Argenziano's team, led by senior research fellow Mathew Williams, MD, has

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Catheter-Based Approaches

In many patients, atrial fibrillation is initiated by triggers in the pulmonary veins. By isolating these foci through ablation, recurrences in AF may be prevented. Innovations in catheter-based techniques and in mapping technology have greatly enhanced non-surgical treatment options for both paroxysmal and chronic AF.

Cardiologists and cardiac surgeons are working together to provide AF patients with a wide spectrum of options, standardizing the management of these patients and tracking their outcomes.

In the Cardiac Electrophysiology Laboratories, cardiologists at Weill Cornell and Columbia are offering their patients a non-surgical, catheter-based approach to AF control. Through careful mapping of the electrical pathways between the pulmonary veins and the left atrium, physicians are able to terminate conduction along these pathways with radiofrequency energy, thereby preventing pulmonary vein triggers from reaching the atrium. In many cases, this strategy is successful in preventing further AF.

While pulmonary vein isolation procedures initially focused

on patients with paroxysmal AF, a similar but more extensive procedure is now being used for selected patients with persistent AF as well, according to Anthony Magnano, MD. The primary risk associated with the catheter-based approach, pulmonary vein stenosis, occurs infrequently, and

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Clinical Trials

In the world of atrial fibrillation, AFFIRM represents the landmark research event. As many readers are by now aware, AFFIRM (and its counterpart study in the Netherlands, RACE) has undermined long-held assumptions about rhythm control for asymptomatic AF.

Traditionally, it has been assumed that restoration of normal sinus rhythm would improve survival rates among patients with persistent atrial fibrillation, regardless of symptom level. In patients whose condition was acceptable following rate control, rhythm control (by drugs or ablation) was the standard approach to further improving symptoms and quality of life, and possibly, duration of life.

Published in December 2002, the results of AFFIRM and RACE now challenge this long-held supposition, showing instead that rate control alone may be as good a strategy as rhythm control regarding length of life, and that rhythm control should not be so aggressively pursued in many patients, especially those whose quality of life is reasonable following attainment of rate control.

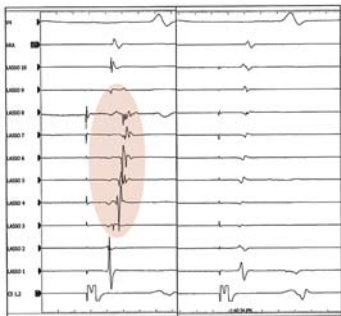
These studies, along with three smaller studies that also confirmed their results, revealed that medical or electrical restoration of sinus rhythm was in fact no better, and possibly slightly worse, than achieving rate control among patients with mild or no symptoms. Specifically, they found: 1) no difference in survival between those whose normal sinus rhythm was restored and those who remained in fibrillation; 2) slightly increased mortality and hospitalization among those receiving antiarrhythmic drugs in the rhythm control groups; and 3) that maintenance of sinus rhythm did not reduce the risk of embolic stroke.

Says James A. Reiffel, MD, "If natural sinus rhythm is teleologically better than being in fibrillation, then its benefits must be relatively small compared to rate control and anticoagulation, or offset by the side effects of antiarrhythmic drugs and procedures."

Furthermore, these studies found that even when normal sinus rhythm is restored, patients remain at risk for blood clots and stroke, just as they would if left in atrial fibrillation. Until recently, anticoagulation has been typically discontinued after restoration of normal sinus rhythm. Yet if anticoagulation is discontinued, the new studies show, the risk of clotting recurs when unrecognized AF recurs. Since recurrent AF is very common and is missed by patients as often as 70% of the time, the implications are clearly important. According to Dr. Reiffel, "Anticoagulation is recom-

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Elimination of Pulmonary Vein Electrical Signals



Before Ablation After Ablation

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Biventricular Pacing for Congestive Heart Failure

For the 30% of moderate to severe congestive heart failure patients who have intraventricular conduction disturbances, biventricular pacing can improve functional status, quality of life, and mortality rates.

Approved by the FDA in August 2001, biventricular pacing is quickly becoming adopted as a standard therapy for certain patients with congestive heart failure.

Sometimes referred to as cardiac resynchronization therapy, or CRT,

with about 10% requiring an open chest procedure due to poor target veins, venous tortuosity, or other complications.

Once programmed to optimize the A-V delay, the pacemaker improves the efficiency of ventricular contractions such that the heart's normal output is restored. In addition to increasing left ventricular filling time, biventricular pacing can also reduce mitral valve regurgitation and decrease septal dyskinesis. According to Kenneth Stein, MD, "This essentially treats a plumbing problem with electrical therapy. It is a totally new application for something we never envisioned."

The increase in cardiac output translates into a consistent improvement in one functional class in symptoms, on average. Explains Dr. Stein, "Someone who is very symptomatic won't become asymptomatic – severe symptoms may become moderate, or moderate may become mild. But," he adds, "I've had people on the transplant list who have come off the list."

Biventricular pacing is appropriate for patients with class III or IV congestive heart failure who have intraventricular conduction delays as identified by EKG – about 30% of patients with moderate to severe heart failure.

Research to date indicates that risks of implantation are extremely low, and there are no long-term disadvantages to biventricular pacing. Undergoing the implantation procedure presents some risk and discomfort. Insertion of the lead is the most difficult part of the procedure, and technically more difficult than inserting a regular

Rhythm – ICD Trial Enrolling Patients

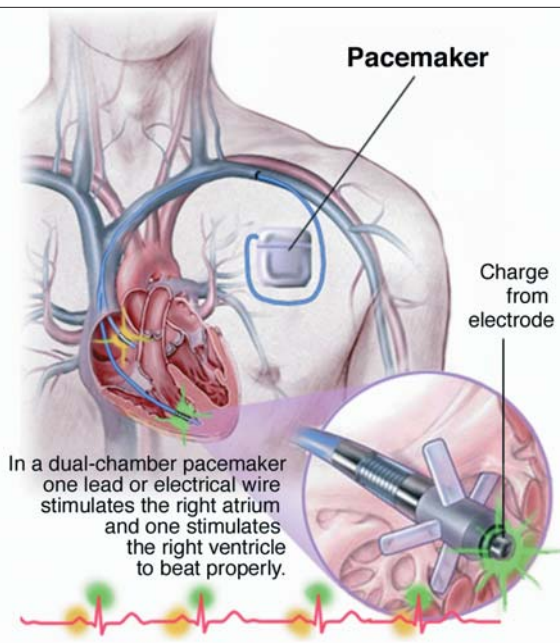
Weill Cornell is currently enrolling patients in a research trial of biventricular pacing–defibrillation for heart failure. Sponsored by St. Jude Medical, the study is designed to assess the efficacy of the Epic HF biventricular pacer-defibrillator.

Eligible patients are those with an FDA-approved indication for implantation of a defibrillator (AICD) who also have moderate to severely symptomatic heart failure with an LVEF $\leq 35\%$, and a wide QRS on an ECG (QRS ≥ 150 msec). All patients enrolling in the trial will have a device implanted. Patients will be randomized (in a 2:1 ratio) to have biventricular pacing therapy turned either on or off for the first six months. After six months, patients with pacing turned off can opt to have it turned on.

pacemaker. However, lead technology is evolving rapidly, notes Dr. Stein, and ongoing research promises to further optimize lead design and facilitate lead placement in the near future.

The concept of applying pacing to congestive heart failure originated from observations that patients with pacemakers experienced the type of ventricular conduction delay that occurs naturally in heart failure. Furthermore, heart failure patients with significant mitral regurgitation

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courtesy of www.heartcenteronline.com

biventricular pacing represents a totally new application for pacing devices originally designed to treat arrhythmias.

Biventricular pacing requires surgical implantation of the pacing device under X-ray guidance, usually through the posterior lateral cardiac vein. This method of lead insertion is successful in about 90% of patients,



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Perspectives in Aortic and Mitral Valve Surgery

The NewYork-Presbyterian Heart Institute is known for its expertise in valve surgery, particularly valvular repair. Continued evaluation and refinement during the past two decades has led to increasingly sophisticated, effective techniques and improved outcomes.

During the past 20 years, a resurgence of valvular heart disease has accounted for an exponentially rising percentage of deaths in the U.S. While due attention is paid to the ubiquitous presence of cardiovascular disease in the U.S. (coronary disease accounts for 530,000 deaths per year in women and 490,000 in men in the U.S.), diseases of the aortic and mitral valves represent

a silently growing threat. In particular, the incidence of calcific aortic stenosis is becoming increasingly prevalent.

Despite the important diagnostic improvements yielded by echocardiogram, patients still remain asymptomatic for years, and valvular disease frequently progresses unrecognized and untreated until the disease is severe. According to

Recommendations for Treating Mitral and Aortic Valve Disease

Aortic stenosis – once the gradient across the aortic valve reaches 50 mm Hg, or the calculated valve area is less than 1.0 square cm, the risk of sudden death is high. By the time patients become symptomatic (angina, shortness of breath on exertion, syncope), survival rate is 50% in 2½ years, if untreated.

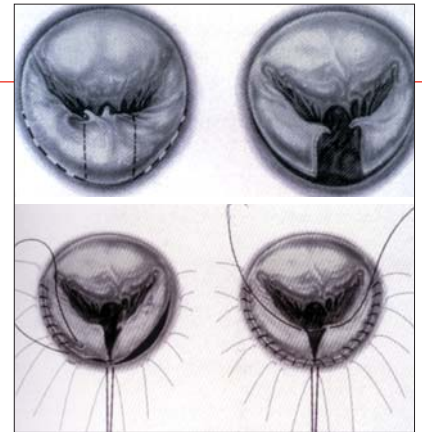
Aortic insufficiency – may be present for years without symptoms or need for surgery. Once the left ventricle begins to dilate or has any impairment of pumping function, valve repair or replacement should usually be done within 3 – 6 months, even in the absence of symptoms.

Mitral stenosis – is most often acquired, and a sequela of rheumatic fever, although about 50% of patients have no known childhood history of rheumatic fever. Diagnosis with a stethoscope is difficult, but may be made easily with echocardiogram. Typically, the first symptom is shortness of breath on exertion. Upon symptoms or disability, repair or replacement surgery should be performed. Urgency of surgery is not as great as with aortic stenosis.

Mitral insufficiency – like aortic insufficiency, may be present and asymptomatic for years, and repair should be performed within 3 – 6 months if the left ventricle begins to dilate or has impaired pumping ability, even if the patient is asymptomatic.

O. Wayne Isom, MD, “Once patients become symptomatic, mortality from surgery is markedly increased and the chances of rehabilitation are reduced.”

Physicians at NewYork-Presbyterian Hospital have focused intensively on perfecting mitral valve techniques during the past decade, and today their progress is evident. Surgeons now repair rather than replace the mitral valve in about



Sliding Annuloplasty Repair

60 – 80% of patients with primary regurgitation, a rate that is higher than at most U.S. institutions. The team has also become increasingly adept at repairing complex problems in anterior, posterior, and bi-leaflet pathology. In most cases, says Craig R. Smith, MD, “Good repairs are better for patients than replacements.”

According to Dr. Smith, “Even after years of experience with mitral valve repair we’re still refining what we do. We’ve learned that flexible annuloplasty rings are ideal in most patients, but there is still a place for more rigid rings in certain situations. By using sliding annuloplasty techniques in patients with abundant posterior leaflet tissue, the complication of systolic anterior motion (SAM) has been virtually eliminated.” In addition, Dr. Smith explains, “We’ve modified previous methods for connecting to the heart-lung machine to make these approaches safer and applicable to a larger number of patients undergoing minimal access mitral valve operations.”

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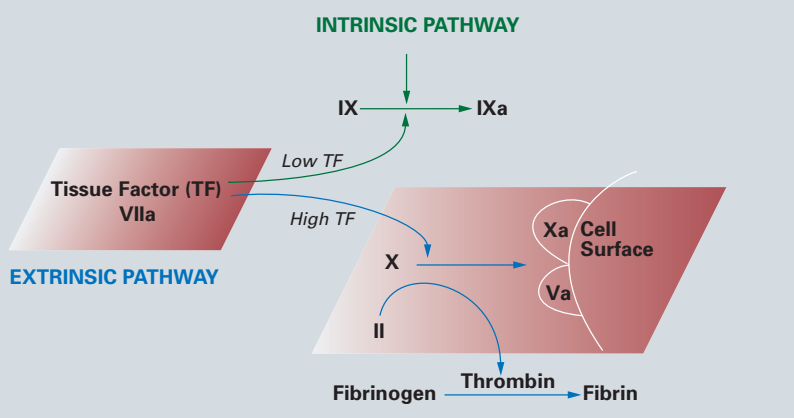
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New Selective Anticoagulant Targets Early Clotting Factor

Research at Columbia has provided a critical foundation for the development of a selective anticoagulant agent that works by inhibiting Factor IXa, a factor in the procoagulant pathway. Because targeted Factor IXa inhibition may result in diminished extravascular bleeding while maintaining intravascular anticoagulation, potential applications for cardiopulmonary bypass, extracorporeal circulation, stroke, and other uses are significant.

Factor IX and the Procoagulant Response



Blockade of Factor IXa selectively limits thrombosis in low tissue factor sites, but does not inhibit clotting in high tissue factor environments such as surgical wounds.

While heparin is routinely used for anticoagulation during cardiopulmonary bypass, it is associated with bleeding complications in 20% of patients undergoing heart surgery. Patients who are elderly or who have serious heart disease would be served better with a different type of anticoagulant – one that would thin blood in the vessels while suppressing extravascular bleeding sequelae.

Yet most current therapeutic agents function too late in the clotting cascade to be selective. Drugs that

block Factor Xa or thrombin, for example, act in the final stages of the clotting pathway. When the clotting pathway is interrupted at this late stage, no endogenous mechanisms remain for preventing broad spectrum anticoagulation, and, thus, the potential for extravascular bleeding.

Inhibiting Factor IXa with so-called IXai (active site-blocked Factor IXa), however, targets a more subtle and proximal factor in the procoagulant cascade. According to Eric A. Rose, MD, “We are hoping to

add a degree of safety with a comparable degree of effectiveness.” With Factor IXai, where there is high tissue factor (as in cases of injury or in the surgical wound), Factor VIIa will still activate Factor X and lead to clotting in those areas, while simultaneously maintaining anticoagulation in the low tissue factor intravascular space. While some experimental agents have targeted earlier stages of the clotting pathway, the ability of other factors in the clotting cascade to be activated (and thereby bypass the experimental blockade) has impeded the anticoagulant effects of these agents. Factor IXai, however, is not derailed in this manner.

Led by Ann Marie Schmidt, MD and David Stern, MD (who has since left Columbia), the Columbia team hypothesized that interrupting the coagulation pathway at Factor IXa could prove effective in models of cardiopulmonary bypass.

Jonathan Chen, MD used Factor IXai during cardiopulmonary bypass in canine and baboon subjects, and met with success – the agent achieved targeted intravascular anticoagulation and simultaneously maintained extravascular hemostasis. Thus, bleeding from the surgical wound,



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Advances in Cardioversion Technology

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particularly at the sternum, was largely nonexistent. The strategy was equally successful in hemodialysis and peripheral vascular surgery as well.

Moreover, the research team led by David J. Pinsky, MD and colleagues hypothesized that selective blockade of Factor IXa-driven coagulation might offer a unique advantage in the setting of stroke. Stroke represents a particularly difficult therapeutic challenge: while it is essential to rapidly prevent clots from forming or extending within brain blood vessels, standard anticoagulants present the profound risk of increasing hemorrhage into the brain. In a mouse model of stroke, administration of IXai was cerebroprotective, but did not lead to increased intracerebral hemorrhage (ICH), even when given after the onset of stroke. This unique advantage – of reducing the burden of flow-interrupting clot formation within brain blood vessels without increasing the tendency to bleed in the brain – may represent a particularly attractive therapeutic target for the treatment of the most common form of stroke.

Based on these promising results, recombinant human IXai (rhIXai) was given to select patients at Columbia, with IRB approval, for compassionate use. Several patients needed to undergo cardiopulmonary bypass but could not withstand heparin, and another required extracorporeal membrane oxygenation (ECMO). In these experimental cases, inhibiting Factor IXa worked exceedingly well – IXai allowed them to get through bypass surgery and to remain on the ECMO circuit without clotting, but inhibited extravascular bleeding.

Despite the success of these compas-

sionate use cases, the expense and difficulty of producing rhIXai prohibit its development as a marketable drug. But a low molecular weight inhibitor that mimics the mechanism of the large protein is likely to advance to the clinical realm, according to Dr. Schmidt. Based on the Columbia team's research, TransTech Pharma is now developing a low molecular weight analog that is expected to be deliverable in both oral and intravenous forms. According to Dr. Schmidt, data thus far indicate that the small molecule compound targeting Factor IXa will be as effective as the recombinant form. "This is a very wonderful approach," Dr. Schmidt says.

With respect to stroke, Dr. Pinsky states that "Development of any agent which reduces clot formation in brain blood vessels without exacting the price of intracerebral hemorrhage would represent a major advance in a field in which new therapies are urgently needed." IXai may represent one such new approach.

"I think Factor IXai is going to revolutionize the way clinicians anticoagulate patients," says Dr. Rose. Immediate and important potential uses include cardiopulmonary bypass, ECMO, cases of heparin-related thrombocytopenia, and patients with bleeding disorders who can not take heparin. In addition to providing selective anticoagulation, oral and intravenous delivery options of IXa-targeted agents could prove extremely valuable for patients who require long-term anticoagulation therapy. Animal trials are currently underway to test the experimental agent for toxicities. If animal studies progress well, human clinical trials could begin within 1 – 2 years. ■

waves for transthoracic cardioversion of AF. In addition, the routine use of biphasic waveforms significantly reduces the need to resort to the available alternatives, which are clearly less desirable.

A team of investigators led by Suneet Mittal, MD and Bruce Lerman, MD, principal investigator for the project, randomly assigned 174 patients undergoing cardioversion of AF to receive either a monophasic or biphasic shock. They determined that biphasic waveform defibrillators succeeded in 94% of AF patients – a significant improvement over the 79% success rate associated with the monophasic waveform defibrillators. Moreover, this success required significantly less energy (170 J versus 360 J in monophasic defibrillators), which may reduce both cardiotoxicity and potential skin burn. The biphasic waveform was especially effective in patients with high transthoracic impedance, a group that has traditionally fared poorly with monophasic shocks.

"This 15% difference in success rate means that for every seven patients needing cardioversion, one will succeed rather than fail," explains Dr. Mittal.

Two types of biphasic shock forms are currently available, rectangular and truncated exponential, which differ in the shape of their waveforms. Although the Weill Cornell team used rectangular waveforms in their study, some literature suggests that truncated exponential shock forms may be effective as well. A new Weill Cornell study (led by Drs. Mittal and Lerman) is now recruiting patients for a multi-center, head-to-head comparison of the two types. ■

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Catheter-Based Approaches

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refinements in the technique continue to minimize this risk. Reductions in power and temperature now prevent injury to veins, and improvements in mapping techniques are further reducing the incidence of ablation deep within the vein.

Basket Catheter Now Used as Diagnostic Tool in Pulmonary Vein Mapping

One of the most promising advances in mapping techniques involves a new application for the basket catheter, which was originally designed for mapping the body of the right atrium for atrial tachycardia. Having achieved highly successful results in applying the basket catheter in smaller structures, Weill Cornell's electrophysiology lab now routinely uses the new technique as a diagnostic tool to guide pulmonary vein ablation.

The basket catheter consists of a shell with eight struts, each of which contains electrodes. This array records the complex electrical geometry of veins, yielding important information not available via conventional catheters. According to Dr. Steven Markowitz, "The basket catheter improves the efficiency of the procedure and reduces the procedure time."

Moreover, it more accurately identifies the ostia of the pulmonary veins and therefore minimizes pulmonary vein stenosis.

Non-contact Electroanatomical Mapping

It is often important to localize AF triggers outside the pulmonary veins from a single heartbeat, say the NYP teams. Non-contact electroanatomical mapping uses a balloon electrode that fits into the right or left atrial cavity. There it obtains data from 3000 points on the heart's inner

surface. Mathematical techniques and sophisticated computer graphics then manipulate the electrical data to identify where abnormal activity originates and propagates. Unlike current techniques that obtain data on a single point-by-point basis, non-contact electroanatomical mapping provides a complete map of the chamber's electrical activity from a single beat.

While diagnosis of arrhythmias with a contact electrode may be sufficient in cases of persistent rhythms, paroxysmal AF triggers are extremely difficult to map. As a result, many centers have great difficulty locating foci outside the pulmonary vein. The unique ability of non-contact electroanatomical mapping to precisely locate paroxysmal foci offers an unprecedented solution to this problem. ■

Clinical Trials

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mended indefinitely because patients appear to often have episodes that they don't feel, and the risk of emboli continues."

AFFIRM (the Atrial Fibrillation Follow-up Investigation of Rhythm Management) was conducted by the NHLBI in North America and represents the largest study on AF ever conducted, with over 4000 patients participating. In both AFFIRM and RACE (Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation), most patients were older and had persistent, recurrent atrial fibrillation with few or no symptoms after rate control, accurately representing a significant portion of the actual AF patient population.

While the studies question the wisdom of pursuing sinus rhythm among asymptomatic patients, rhythm control should still be pursued among the substantial proportion of patients who continue to suffer symptoms despite rate

control. As such, the quest for better antiarrhythmic medications and cardioversion techniques continues.

At Columbia, a team led by Michael Argenziano, MD and Mehmet C. Oz, MD is working to improve surgical

investigational agents are being tested in patients aged 18 – 80 with persistent atrial fibrillation of more than 3 days but less than 6 months duration, who require cardioversion and maintenance of sinus rhythm for clinical improvement, and who



The Electrocardiogram in Atrial Fibrillation

treatments of AF through a minimal access, thoracoscopic approach. Cardiologists in the electrophysiology laboratory continue to improve catheter-based approaches to AF ablation, particularly in patients with frequent episodes unassociated with significant structural heart disease.

Under the direction of Dr. Reiffel, protocols are now testing new antiarrhythmic drugs such as azimilide and piboserod against older agents. These two

have no contraindication to the specific drug being tested (which varies by drug). Each trial is placebo-controlled and blinded in order to determine the actual efficacy and tolerance profile of the drug, as is the norm for FDA-approved protocols evaluating new agents in preparation for their anticipated release in the U.S., providing efficacy and safety are confirmed. Physicians are encouraged to contact Dr. Reiffel to discuss eligibility of any potential patient candidate. ■

VALVE PROCEDURES	ADVANTAGES	DISADVANTAGES
Aortic and mitral tissue valve replacements (xenografts), bovine pericardial or porcine	Highly reliable solution for valves that cannot be repaired No need to administer anticoagulants (coumadin) Minimal access options available	Durability between 10 and 20 years. Necessity for repeat surgery
Aortic homograft valve replacement	Ideal for complex aortic valve infection and certain other specific circumstances	Durability not significantly greater than xenografts
Ross procedure for aortic valve replacement: a combination of autograft and homograft in which the patient's own pulmonic valve is used to replace the native aortic valve, and a homograft valve is used to replace the native pulmonic valve	Ideal for infants and children when prosthetic options do not exist Anticoagulation not needed May offer best durability of all tissue valve options for the aortic valve, and for valves that escape early failure	More complex operation with slightly increased risk 10% incidence of early failure of the pulmonary valve in the aortic position The pulmonary homograft will require reoperation in 10 – 20 years
Aortic and mitral mechanical valves made of steel and carbon alloys	Highly reliable solution for valves that cannot be repaired Excellent durability – in stress tests, over 100 years Minimal access options available	Morbidity associated with prolonged anticoagulation – bruising, longer bleeding times, and restriction from contact sports Potential for embolism if clot forms
Mitral valve repair	No need for anticoagulation Preservation of native valve also preserves ventricular function Durability, potentially for life of the patient Applicable to most regurgitant valves, less often to stenotic valves Minimal access and robotic operations well established	Not all valves can be repaired Very complex repairs have longer operating time and less predictable results
Aortic valve repair	No long-term anticoagulation Minimal access options available	Techniques are evolving Currently applicable to a small minority of leaking valves Long-term durability undetermined

Biventricular Pacing for Congestive Heart Failure CONTINUED FROM P.4

often improved with pacing. These observations led Dr. Stein and his colleagues at Weill Cornell to explore the role of pacing for heart failure.

Since the idea's inception, the electrophysiology laboratory has participated in the CONTAK CD, Companion, and PAVE clinical trials of pacing for heart failure. In addition to conducting clinical research, Dr. Stein also trains physicians in implanting and programming the devices.

These trials have consistently demonstrated that biventricular pacing improves symptoms, exercise capacity (as measured by the six-minute walk

“ Biventricular pacing represents a totally new application for pacing devices. This essentially treats a plumbing problem with electrical therapy. ”

test), and quality of life (32% in one trial). Now, data from the Companion trial (to be published in 2003) are the

first to show that biventricular pacing not only improves functional status, but prolongs life compared to medical therapy. This study randomized about 1500 patients to receive best medical therapy, biventricular pacing, or pacing with defibrillation. Biventricular pacing plus defibrillation yielded a 40% improvement in symptoms, compared to a 20% improvement with pacing alone, over medical management. Although follow-up of these patients will continue, this study stopped enrolling patients in November 2002 due to the clear survival advantage of pacing in the patient population. ■

Surgical Options

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developed the most minimally invasive approach of all – a totally closed chest procedure. For his presentation, “A totally endoscopic, beating heart approach to pulmonary vein isolation for the treatment of atrial fibrillation,” Dr. Argenziano received the “Best Presentation” award at the 2002 scientific sessions of the International Society for Minimally Invasive Cardiac Surgery (ISMICS). In over 150 cases performed thus far at Columbia, the success rate of the modified Maze procedure exceeds 70%. And because the minimal access approach is less traumatic, many patients with lone AF are now choosing to undergo the procedure in lieu of medical management. ■

NewYork-Presbyterian Heart Institute is a service line management model designed to provide financial, operational, and clinical direction to promote the growth and development of cardiology and cardiovascular surgical activities. The Heart Institute is comprised of physicians of Columbia University College of Physicians & Surgeons and Weill Medical College of Cornell University representing medical and surgical disciplines working together with other health professionals in a collaborative process.

Faculty Highlights



Geoffrey W. Abbott, PhD Assistant Professor of Medicine, Division of Cardiology, Department of Medicine and Department of Pharmacology at Weill Medical College of Cornell University

One of the leading researchers on the physiology of potassium channels, Geoffrey W. Abbott, PhD has been instrumental in numerous discoveries that will affect pharmacologic interventions in cardiology. After discovering the KCNE superfamily of ion channel regulatory subunits and linking one, MiRP1, to inherited arrhythmia in man, Dr. Abbott and colleagues showed that a common polymorphism in MiRP1 can cause long Q-T syndrome in affected individuals who take the antibiotic Bactrim.

Dr. Abbott took his Bachelors degree in Zoology, Masters degree in Molecular Pathology, and Doctorate degree in Biochemistry, in the United Kingdom. Pursuing the study of the structure and function of potassium channels that he had begun in the U.K., he then completed a post-doctorate fellowship at Yale University School of Medicine.

Dr. Abbott's recent publications include “MiRP2 forms potassium channels in skeletal muscle with Kv3.4 and is associated with periodic paralysis.” *Cell*, 2001; 104 217-231.

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Steven O. Marx, MD Silverberg Assistant Professor of Medicine, Columbia University College of Physicians & Surgeons

In less than a decade of molecular cardiology research, Steven O. Marx, MD has already helped to deliver a major new therapeutic application. His work on the effects of rapamycin, in conjunction with Andrew Marks, MD and other colleagues, directly led to the development of a rapamycin-coated stent for use after balloon angioplasty. By inhibiting smooth muscle cell growth, this stent (CYPHER, produced by Cordis) dramatically inhibits restenosis and is expected to receive FDA approval this year. Other current research by Dr. Marx includes the regulation of ion channels in arrhythmogenesis and heart failure.

Dr. Marx completed his medical education at Albany Medical College, residency at the University of Rochester's Strong Memorial Hospital, and fellowship in cardiology at Mt. Sinai Medical School. His recent publications include “Requirement of a macromolecular signaling complex for beta adrenergic receptor modulation of the KCNQ1-KCNE1 potassium channel.” *Science* 2002; 295:496-9.

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