Much like other fields, cardiac electrophysiology is at the receiving end of a rapidly accumulating knowledge base of genomics that could potentially help our patients. While the promise clearly exists, there are several developments that need to occur before this new information will find clinical utilization. These can be discussed in the context of two broad categories of arrhythmias: a) established familial primary arrhythmia disorders, and b) more common, complex forms of heart disease leading to arrhythmias.

**Primary arrhythmia disorders**
The last two decades have witnessed a significant increase in the number of culprit genes identified for primary arrhythmia disorders such as the long QT and Brugada syndromes. Genetic testing for the identification of mutations in these genes is commercially available, but the diagnostic approaches are still cumbersome and expensive. In the very near future, rapid advancements in technology will facilitate high-throughput platforms that will enhance performance and decrease the expense associated with these tests. At present, the main utility of genetic testing lies in excluding a particular condition or establishing the diagnosis with certainty. We still do not utilize results of genetic testing to determine which specific drug or other treatment could be used to benefit the patient. However, there are early findings of modifier genes that may have additional effects on a gene mutation and adversely affect prognosis. For example, recently published specific variants in the NOS1AP gene were found to increase risk of events in the long QT syndrome. In order to fully utilize information from genetic testing to either stratify risk or provide tailored therapy, significantly more effort must be made to harness the vast array of genomic information rapidly being made available.

**Common, complex arrhythmias**
Heart rhythm disorders are more likely to manifest together with other cardiac or extra-cardiac abnormalities. For instance, atrial fibrillation will most commonly keep company with hypertension, and ventricular fibrillation is most commonly associated with coronary artery disease. While several studies have identified a genetic contribution for both of these arrhythmias, there are important differences from the primary arrhythmia disorders. There are clear indications that instead of one main culprit gene, there is likely a network of genes that contribute to the genesis of complex arrhythmias. In addition, it is important to separate the effects of these specific genes from others that may contribute to associated conditions such as coronary artery disease. In the past decade, the ability to perform genome-wide association studies to pinpoint such gene networks has been a notable advance. Several novel loci have been identified for both atrial and ventricular fibrillation, and more discoveries are following in rapid succession. Following closely on the heels of genome-wide association studies are novel technologies that will allow sequencing of the entire genome, as well as the ability to collate and analyze the large amounts of genomic information that will be available. How will this information be utilized for clinical benefit?

**Personalized medicine: realizing the promise of genomics**
The identification of novel single nucleotide polymorphisms (SNPs) by performing genome-wide association studies in patients with a specific arrhythmia is a sentinel event that initiates an investigative cascade. Is the SNP causally involved or merely marking the presence of another important gene or variant located close to it? Could these SNPs influence genesis of arrhythmias by “remotely con-

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Emerging Technologies for Atrial Fibrillation Ablation

Michael Shehata, MD, FACC

Atrial fibrillation (AF) remains the most common type of sustained cardiac arrhythmia in the United States, affecting an estimated three million people. Therapeutic options for the treatment of AF have traditionally focused on rate or rhythm control strategies. Over the last decade, catheter ablation for AF has emerged as an important treatment modality aimed at rhythm control. Leading to the development of this technique was the work of Michel Haïssaguerre, MD, and colleagues demonstrating that often, the focal electrical triggers of AF are located within the pulmonary veins. This ultimately brought about ablative strategies aimed at electrical isolation of the pulmonary veins from the left atrium.

The superiority of catheter ablation over anti-arrhythmic drug therapy has been demonstrated in patients with paroxysmal and persistent atrial fibrillation. There have been at least five prospective, randomized trials that compared the outcomes of AF ablation versus anti-arrhythmic drug therapy. A recent meta-analysis of these studies revealed that 77 percent of patients treated with catheter ablation were free from AF at a 12-month follow-up period as compared with 29 percent of patients assigned to receive drug therapy.1 The overall complication rate from this complex interventional procedure has also decreased with experience, with major complication estimates ranging between 2 and 6 percent based on randomized control trials and international survey data.

In the past 10 years, catheter ablation has undergone an evolution with the development of multiple techniques aimed at both pulmonary vein isolation as well as ablation of other non-pulmonary vein triggers. It currently is the most widely performed ablation procedure for cardiac arrhythmias in the U.S. The cornerstone of the procedure currently relies on creating point-by-point radiofrequency burns around the pulmonary vein ostia with a 4-8 mm catheter tip to achieve electrical isolation. The use of three-dimensional electro-anatomic mapping systems during these procedures allows for the creation of a chamber geometry that can be overlaid on a previously acquired CT or MRI image of the left atrium. This in turn has dramatically reduced fluoroscopy times and radiation exposure.

Newer tools have been recently developed to improve the efficiency, safety and efficacy of pulmonary vein isolation procedures. These include the development of balloon catheters that can be placed into the pulmonary vein ostium and allow the delivery of a circumferential ablation lesion using various energy sources, such as a recently FDA-approved modality of cryothermal energy that freezes the tissue. Circular multipolar electrode catheters are in development that allow the delivery of radiofrequency energy around the pulmonary vein ostia with few applications, thereby improving efficiency.

Additionally, the development of remote robotic and magnetic guidance systems has improved the efficacy of these procedures. These systems allow the operator to perform the mapping and ablation portions of the procedure remotely from a separate control room with the use of a robotic sheath or a magnetically guided catheter.

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Over the past two decades, catheter ablation for atrial fibrillation (AF) has been established as an effective treatment modality for patients with failed anti-arrhythmic drug therapy. There has been a substantial increase in the number of catheter ablation procedures for AF performed in the U.S., annually. Atrial tachycardias (ATs) following catheter ablation for AF are also increasingly encountered in the clinical practice of electrophysiology. An increasing number of AF procedures have resulted in a substantial increase in these post-ablation arrhythmias, ranging from 10 to 40 percent in the published literature. These ATs often occur following circumferential pulmonary vein ablation (CPVA) for paroxysmal AF or stepwise ablation for long-lasting persistent AF due to extensive atrial scarring, which can result in localized reentrant AT or some forms of macroreentrant ATs through slow conduction channels adjacent to scar areas. Mapping and ablation of scar-related ATs following AF catheter ablation can be performed with good clinical outcomes.

Technologies that aid in the mapping and ablation of these arrhythmias have improved substantially over the last few years. These systems enable the creation of three-dimensional anatomic models of cardiac chambers. They also provide detailed activation maps of critical reentry circuits that drive ATs, as well as scar distribution within the atria. The combination of activation and scar mapping is crucial to a successful procedure. In the majority of cases, a single radiofrequency application usually terminates tachycardia at the site of the critical region involving the reentry circuit.

Figure 1: A 50-year-old man was referred for catheter ablation of atrial tachycardia after two previous procedures for ablation of atrial fibrillation with pulmonary vein isolation. Activation mapping of the left atrium showing earliest site of activation located at the left atrial anterior roof (A). Voltage map of the left atrium reveals dense scar less than 0.2 mV adjacent to the area of earliest activation (B). Intracardiac electrogram at the site of successful ablation shows prolonged duration fractioned signal (C). Ablation at this site with one radiofrequency application resulted in successful termination of the tachycardia (D).

Figure 2: A 60-year-old man with atrial tachycardia following multiple previous procedures for atrial fibrillation. Intracardiac electrograms show an organized atypical atrial flutter with a macroreentry involving the mitral annulus (A). An ablation line was created with radiofrequency energy from the lateral mitral valve annulus to the left inferior pulmonary vein (B). Additional ablation within the coronary sinus resulted in termination of the tachycardia.

Figure 3: A 76-year-old man presenting with atrial tachycardia following previous pulmonary vein isolation procedure for atrial fibrillation. Three-dimensional activation mapping shows a macroreentrant circuit involving the roof of the left atrium. A single radiofrequency application near the right posterior atrium resulted in termination of the tachycardia. Inset panel shows fractionated signal at the successful ablation site (A). Voltage mapping of the chamber reveals dense scar throughout the posterior left atrium less than 0.2 mV (B).

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Advancements in catheter ablation have demonstrated both safety and efficacy with patient and operator. Previous studies have resulted in less radiation exposure to the patient. The advancement in the field of catheter ablation procedures for AF has been remarkable, but much remains to be done. Ongoing and future research is being directed at understanding the underlying mechanisms of this complex disorder. Future trials should also be aimed at studying the benefit of catheter ablation in 1) elderly patients, 2) patients with significant left ventricular dysfunction and heart failure, and 3) those with permanent or longstanding persistent atrial fibrillation. Additionally, as more long-term outcome data emerges, we may be able to better assess the durability of AF ablation procedures and provide improved prognostic information to patients with this complex arrhythmia disorder. The Cedars-Sinai Heart Institute will be participating in the CABANA trial, the largest randomized clinical trial for AF ablation. This study is currently enrolling patients and will compare ablative strategies versus medical therapy in patients with atrial fibrillation.

Reference