Over the past 12 years, catheter ablation of atrial fibrillation (AF) has emerged from being a novel, largely unproven procedure to its role today as a very commonly performed procedure for treatment of patients with symptomatic AF. In fact, catheter ablation of AF has become one of the most commonly performed catheter ablation procedures at most large medical centers throughout the world. The objective of the present report is to provide a state-of-the-art review of the techniques, outcomes, and complications of catheter ablation of AF. Three main topic areas will be discussed. First, I will review the current approaches for and outcomes of AF ablation. Second, I will identify and briefly review areas in the field of AF ablation about which less is known and that remain active areas for research. Third, I will briefly review the current status of a number of emerging technologies, approaches, and tools that are being developed with the aim of improving the outcomes of AF ablation. Finally, I will conclude by sharing with you my perspective on the indications for AF ablation.

Current Techniques and Success Rates of AF Ablation

It is now widely recognized that circumferential ablation of the pulmonary veins (PVs) with the goal of obtaining electric isolation of the PVs is the cornerstone for most AF ablation procedures. This ablation technique involves delivering a series of point-by-point radiofrequency lesions that encircle the 2 left and 2 right PVs either by creating a single circumferential lesion around the 2 right PVs and another around the 2 left PVs or by including lesions between the ipsilateral PVs, resulting in a figure 8 lesion set (Figures 1A and 1B). Electric isolation of the PVs is most commonly confirmed by use of a circular multipolar electrode catheter (Figure 2). Irrigated radiofrequency ablation catheters, used in conjunction with an electroanatomic mapping system, are the most commonly used tools. A balloon-based cryoablation system was approved for clinical use in the United States in 2011. Information concerning this ablation system will be discussed below under “New Techniques and Tools.” AF ablation procedures are performed either with conscious sedation or with anesthesia. A computed tomography or magnetic resonance imaging scan is commonly performed before the procedure to define the precise PV anatomy. The majority of patients who present for ablation in atrial fibrillation also undergo a transesophageal echocardiogram before the procedure to exclude an atrial thrombus. Patients are typically admitted for 1 night after the procedure on a short-stay basis. It is increasingly common to perform AF ablation in patients fully anticoagulated with warfarin.

Success rates for catheter ablation of AF depend on a large number of variables. Of particular importance are the type of AF (paroxysmal, persistent, or long-standing persistent AF), the presence or absence of comorbid conditions such as obesity and sleep apnea, the definition of success, and the duration of follow-up. The Heart Rhythm Society’s consensus document on AF ablation recommends that success be defined as freedom from symptomatic or asymptomatic AF, atrial tachycardia, or atrial flutter lasting ≥30 seconds 12 months after AF ablation. It is recognized that this is a very strict definition of success that is best used for clinical trials. A 3-month blanking period is recommended. This is because it is common for patients to develop AF shortly after an ablation procedure, in part because of transient pericardial inflammation. From a clinical perspective, a marked reduction of AF burden associated with a reduction of symptomatic AF is commonly considered a clinical success from a patient and physician perspective.

The results of catheter ablation of AF can be derived from a number of different sources. A recent study reported the outcomes of 2 meta-analyses of the safety and efficacy of catheter ablation of AF and antiarrhythmic drug therapy. The results of 63 radiofrequency ablation studies were included in these analyses. The single-procedure success rate of ablation with no antiarrhythmic drug therapy was 57% (95% confidence interval [CI], 50%–64%), the multiple-procedure success rate with no antiarrhythmic drugs was 71% (95% CI, 65%–77%), and the multiple-procedure success rate with antiarrhythmic drugs or with unknown antiarrhythmic drug usage was 77% (95% CI, 73%–81%). In comparison, the success rate for antiarrhythmic therapy was 52% (95% CI, 47%–57%). There have been at least 7 prospective randomized clinical trials that compared the outcomes of AF ablation with antiarrhythmic drug therapy. A meta-analysis of 4 of these studies reported that 162 (76%) of 214 patients treated with catheter ablation were free of AF compared with 41 (19%) of 218 patients randomized to antiarrhythmic drug therapy. The study concluded that there was a more than 3.7-fold higher probability of remaining in sinus rhythm with catheter ablation than with antiarrhythmic medications. A fifth small, multicenter randomized trial also reported

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that catheter ablation was superior to antiarrhythmic drug therapy. Catheter ablation was successful in 89% of patients compared with a 23% success rate for antiarrhythmic drug therapy. Of note, the median number of AF ablation procedures performed in the catheter ablation arm of that study was 2.

Another recent clinical trial of radiofrequency catheter ablation was a relatively large multicenter clinical trial involving 167 patients with paroxysmal AF performed as part of the approval process for the Impella PC catheter in 2011. This study compared catheter ablation with antiarrhythmic drug therapy and found that catheter ablation was superior to antiarrhythmic drug therapy. Catheter ablation was successful in 89% of patients compared with a 23% success rate for antiarrhythmic drug therapy. Of note, the median number of AF ablation procedures performed in the catheter ablation arm of that study was 2.

Figure 1. Electroanatomic map with an integrated computed tomographic image of the left atrium and pulmonary veins (viewed from the back) showing the lesion set created for ablation of paroxysmal atrial fibrillation. Circumferential lesions are created around the 2 right (R) and 2 left (l) pulmonary veins, either without (A) or with (B) an additional lesion created between the pulmonary veins, resulting in a figure 8 pattern.

Figure 2. Shown are recordings from a circular multielectrode ablation catheter placed in the right superior pulmonary vein (PV 1, 2 through PV 13, 14). These recordings from the circumferential multielectrode mapping catheter are labeled as LS 1, 2 through LS 13, 14. Left, Baseline recordings with a small atrial electrogram and large pulmonary vein potentials. Right, After ablation, the pulmonary vein potentials are no longer present, which demonstrates pulmonary vein isolation.
process for an irrigated radiofrequency ablation system. At 12 months of follow-up, catheter ablation resulted in 66% efficacy compared with 16% efficacy for antiarrhythmic drug therapy. This study also revealed that catheter ablation reduced symptoms and improved quality of life. The most recent study was a prospective randomized trial of cryoballoon ablation. Although not published in final form, the results of that study revealed consistent findings, with catheter ablation of AF being superior to antiarrhythmic drug therapy. In considering the results of these clinical trials, it is important to recognize that each of these trials enrolled predominantly middle-aged white men with paroxysmal AF and few comorbidities.

The quality and quantity of data concerning the outcomes of AF ablation in patients with nonparoxysmal AF, including both persistent and long-standing persistent AF (>12 months of continuous AF), are considerably less than for patients with paroxysmal AF described above. In fact, there have been no prospective multicenter randomized clinical trials of ablation versus antiarrhythmic drug therapy that have precisely defined the outcomes of AF ablation in this patient population. The notable absence of a consistent body of evidence reflects the heterogeneity of the patient population and ablation strategies that are encompassed under the umbrella “nonparoxysmal AF.” It is now increasingly well recognized that the duration of continuous AF is an important predictor of the efficacy of AF ablation. Patients with continuous AF of ≤12 months duration are very different from patients who have been in continuous AF for 4 years. Whereas the primary goal of the vast majority of electrophysiologists performing AF ablation in a patient with paroxysmal AF will be to achieve PV isolation using a circumferential approach, the approaches used for ablation of patients with nonparoxysmal AF are far more varied. This is currently an area of debate at most AF meeting and conferences. Whereas many electrophysiologists prefer to perform circumferential AF isolation as the initial procedure in all AF patients, there are other electrophysiologists who feel strongly about creating linear ablation lesions and about using targeted ablation of areas of the atrium that demonstrate a high degree of fractionated electrogans during AF (referred to as CAFEs). A final group of electrophysiologists advocate for a stepwise approach to AF ablation, whereby the procedure is continued until AF terminates. Critics of the more extensive ablation procedures argue that these approaches are, in essence, atrial debulking. Proponents of this approach argue that it results in substrate modification, which is critical for the success of the procedure. A recent meta-analysis of studies that reported the outcomes of catheter ablation of persistent and long-standing persistent AF concluded that the single-procedure success rate of each of these strategies is similar, provided that circumferential PV ablation is performed with an end point of electric isolation of the PVs. It is clear that this is an area in which more research is needed to better define the optimal ablation approach and the anticipated success rate in particular patient populations.

In our experience and based on our review of the literature, we would estimate the single-procedure efficacy of AF ablation in an optimal candidate for AF ablation, similar to those enrolled in randomized clinical trials with paroxysmal AF, to be between 60% and 80%. The efficacy of a single procedure in a less optimal patient, such as a patient with persistent AF, lies between 50% and 70%. The single-procedure efficacy of the procedure in a suboptimal patient, such as a patient with continuous AF for 4 years, is 40% or less. It is important to recognize that performing a second or third ablation procedure results in an increase in the cumulative success rate.

There have been a large number of studies that have published data recently concerning the long-term efficacy of AF ablation. The first of these studies was published 5 years ago and described the long-term outcomes of a series of 264 patients who were free of AF and not taking antiarrhythmic drugs at the 12-month point after an initial ablation procedure. During a mean follow-up of 28±12 months, AF recurred in 23 patients (8.7%). The actuarial recurrence rate of AF at 5 years was 25.5%. AF recurrence was more likely in patients with hypertension and hyperlipidemia, with a recurrence rate of 75% if both of these risk factors were present. Similar findings have been reported in each of the subsequent trials. Of particular note is a recent report from a highly experienced electrophysiology laboratory that reported that only 29% of patients who underwent AF ablation at their center were free of AF 5 years after a single ablation procedure. Importantly, in this trial, AF ablation procedures were performed in 2001 and 2002 by a segmental approach to achieve PV isolation. A more recent series that used a circumferential approach to achieve PV isolation reported better long-term outcomes, with 47% of patients free of AF after 4.8 years of follow-up. It is now recognized that when a patient is brought back to the electrophysiology laboratory with recurrent AF, recurrence of PV conduction in 1 or more veins is almost universally observed. This finding highlights the difficulty in achieving permanent PV isolation with current ablation technologies and approaches. Taken as a whole, this now large body of data provides compelling evidence that catheter ablation of AF should not be considered a curative procedure, but is best considered as a tool to control AF and the associated symptoms of AF, similar to the goals of antiarrhythmic drug therapy.

Complications of AF Ablation

Catheter ablation of AF is a demanding and complex interventional electrophysiological procedure that is associated with an important risk of major complications. An international survey of AF ablation procedures in 2005 reported a 6% incidence of major complications. The incidence of complications was 1.2% for cardiac tamponade, 0.94% for stroke or transient ischemic attack, 1.3% for PV stenosis, and 0.05% for death. A recent update of this survey reported a 4.5% complication rate. The complication rate reported in the large recent meta-analysis of AF ablation cited previously was 4.9%. Of particular note is a report from an international survey of AF ablation of 162 centers, which reported details on 32 deaths that occurred during or after AF ablation procedures in 32,569 patients (0.1%). Causes of death included tamponade in 8 patients (25% of deaths), stroke in 5 (16%), atrial-esophageal fistula in 5 (16%), and pneumonia in 2 (6%). There is more recent evidence suggesting that the complication rate of AF ablation is falling. A recent consecutive series of patients undergoing AF ablation reported a major complication rate of 0.8%, with no instances of death, stroke/transient ischemic attack, atrial-esophageal fistula, or PV stenosis. A review of the complication rate at our institution reveals that it has decreased from
approximately 11% in 2002 to 1.6% in 2010 (H.C., unpublished data, 2011).

On the basis of our review and knowledge of the literature, as well as our clinical experience with AF ablation, we would estimate that the current incidence of major complications lies between 1% and 5%. The incidence is 0.5% to 2% for cardiac tamponade, 0.3% to 1% for stroke/transient ischemic attack, 0.5% to 2% for vascular injury, and <1% for PV stenosis, and the risk for development of an atrial-esophageal fistula and/or death is <0.1%.

Some Unanswered Questions Concerning the Outcomes of AF Ablation

Although great progress has been made in improving the techniques and outcomes of catheter ablation of AF, there are a number of important unanswered questions. First, the optimal approach for ablation and the long-term outcomes of AF ablation in patients with long-standing persistent AF need to be better defined. Second, the safety and efficacy of catheter ablation of AF in patient populations poorly represented in the clinical trials to date need to be defined. This is especially true in the elderly, as well as in patients with heart failure. Finally, more information is needed on the impact of AF ablation on mortality and stroke risk. Although patients with AF have an increased risk of stroke and an increased mortality, it is unclear whether AF ablation reduces the risk of stroke and increases survival. There are several large case series that have reported a low risk of stroke after AF ablation.32-33 Although the stroke rate is low in these series, few patients at high risk of stroke were monitored after anticoagulation was stopped for a significant period of time. It is for this reason that the Heart Rhythm Society’s consensus document concluded that a desire to discontinue anticoagulation therapy is not an appropriate indication for AF ablation and that a patient’s CHADS2 score, rather than the presence or absence of AF, should be used to determine the appropriate anticoagulation approach after an AF ablation procedure.3

Another retrospective study reported that AF ablation patients were at significantly lower risk of death, stroke, and dementia than AF patients who did not undergo ablation.34 Because of the design and limitations of that trial, it should be considered largely as hypothesis generating rather than as providing definitive answers to these important questions. The impact of AF ablation on both stroke and survival is currently being evaluated in the CABANA (Catheter Ablation versus Antiarrhythmic Drug Therapy for Atrial Fibrillation) trial.13 Another important issue that needs to be resolved is the clinical significance of new apparently clinically silent defects detected by diffusion-weighted magnetic resonance imaging of the brain in a small subset of patients after AF ablation procedures.35,36

It is notable that most AF ablation procedures have been performed in white male patients <70 years of age.37 It therefore remains uncertain what the safety and efficacy of AF ablation are in other populations of patients, including elderly patients. One recent study compared the safety and efficacy of catheter ablation in 3 groups of patients (patients <65 years of age, patients between the ages of 65 and 74 years, and patients older than 75 years) over a 27-month follow-up period.20 No difference in the success and cancellation rates were observed between the 3 groups. However, patients >75 years old were less likely to undergo repeated procedures and preferred to continue antiarrhythmic drug therapy. Another large case series reported a 73% success rate and a 1% complication rate among 174 patients >75 years of age who underwent AF ablation.38 Although the results of these studies are encouraging, it is clear that more research is needed. The CABANA trial is expected to be very valuable in this regard.28 A number of clinical trials have examined the role of catheter ablation of AF in patients with congestive heart failure. The initial major study to address this important topic was published in 2004.39 That study examined the role of catheter ablation in 58 patients with heart failure with an ejection fraction <45% and in 58 control subjects. During a mean follow-up of 12±7 months, 78% of patients with heart failure and 84% of control subjects remained in sinus rhythm. Of particular note is that the ejection fraction improved by 21±13%. Improvements were also seen in exercise capacity and quality of life. Another study, the Pulmonary Vein Antrum Isolation versus AV Node Ablation with Bi-Ventricular Pacing for Treatment of Atrial Fibrillation in Patients with Congestive Heart Failure (PABA-CHF) study, compared the efficacy of AF ablation with atioventricular node ablation and pacemaker implantation.40 The primary end point of this prospective, multicenter clinical trial was a composite of ejection fraction, distance on a 6-minute walk, and Minnesota Living with Heart Failure questionnaire score after a 6-month follow-up. This study demonstrated an overall superiority of PV antrum isolation to atioventricular node ablation, as evidenced by a lower score on the PABA-CHF questionnaire (60 versus 82), longer walking distance (340 versus 297 m), and higher ejection fraction (35% versus 28%). A third case-control series reported that the efficacy of AF ablation was similar in patients with and without left ventricular systolic dysfunction and also reported an improvement in ejection fraction at 6-month follow-up.41 A recent meta-analysis42 reported that the single-procedure efficacy of AF ablation was lower in patients with systolic dysfunction, but with repeat procedures, a similar success rate could be achieved among patients with and without systolic dysfunction. Taken as a whole, the results of these studies suggest that catheter ablation of AF is reasonable in highly selected patients with heart failure.

New Techniques and Tools

There is currently great interest in the development of new ablation tools that will improve the safety and efficacy of AF ablation. There is also interest in developing ablation tools that will shorten procedure time and allow the procedure to be performed by less skilled operators. In this section, we will review some of the new tools and approaches that either have just become clinically available or are being evaluated in clinical trials.

Several months ago, a cryoballoon ablation system was released for clinical use for treatment of patients with paroxysmal AF. This balloon-based ablation system isolated PVs by freezing the tissue that lies in contact with a balloon that is cooled to −80°C.43,44 This ablation system has been approved for clinical use for many years in Europe and has recently been released for clinical use in the United States. The results of the clinical trial have been published in abstract form.13 The study randomized 245 patients to antiarrhythmic drug therapy or
catheter ablation. Catheter ablation was successful in 70% of patients (including repeat ablation procedures) compared with a 7% success rate for antiarrhythmic drug therapy. A large number of trials have been performed to evaluate the safety and efficacy of the cryoballoon ablation system in Europe. One of the largest and most recent of these studies was published in 2008.45 That study reported the outcomes of 346 patients with drug-refractory predominantly paroxysmal AF. During a median follow-up of 12 months, after 1 or more procedures, sinus rhythm was maintained without the need for antiarrhythmic drug therapy in 74% of patients with paroxysmal AF and in 42% of patients with persistent AF. Although the results of these initial studies suggest promise for the cryoballoon ablation system, the ultimate clinical value of this system will be better defined once electrophysiologists in the United States have gained more experience with it. At the present time, it appears to be best suited for patients with paroxysmal AF.

Another balloon-based ablation system uses laser energy for lesion formation. This ablation system involves balloon catheters that use a diode laser to burn the myocardial tissue.45 Relatively few data are available concerning the outcomes of AF ablation with this ablation system, which is currently being evaluated in clinical trials.45

Another PV-based ablation system is a circumferential decapolar PV ablation catheter that uses phased radiofrequency energy as an energy source.46-47 A prospective randomized clinical trial comparing this ablation system and antiarrhythmic drug therapy for treatment of patients with persistent and long-standing persistent AF has completed enrollment in the United States, but this system is currently not available for clinical use in the United States.

Over the past several years, it has become recognized that contact force is a major determinant of the size of ablation lesions. Because of this, a number of radiofrequency ablation catheters have been developed that provide feedback to the operator on the degree of force with which the ablation catheter is contacting the wall of the atrium.48-50 These systems were initially evaluated in Europe and have been released in Europe on a limited clinical basis. The initial clinical results are encouraging, although definitive data proving that these ablation catheter systems improve outcomes are not currently available. The electrophysiology community is very hopeful that clinical research will demonstrate that these systems allow creation of more permanent lesions and therefore allow the problem of PV reconnection to diminish and reduce the need for repeat ablation procedures. Another area of intense research focus concerns the relationship between AF and the autonomic nervous system.51 Several small clinical trials have assessed the efficacy and safety of procedures that target and ablate ganglonated plexi in both humans and dogs and have compared these procedures to circumferential PV isolation.51-54 The results of these studies have been somewhat conflicting, and more research is under way.

There currently are 2 ablation tools available that fall under the broad umbrella of remote/automatic/robotic ablation systems. The first is a robotic magnetic navigation system that consists of 2 computer-controlled focused-field permanent magnets placed on either side of the patient, and the second is a remote navigation system that uses a robotically controlled steerable sheath.55,56 Both of these systems are currently being used clinically for AF ablation. The ultimate clinical role of these systems will depend in large part on demonstrations that they improve efficacy, lower complication rates, or shorten procedure times. It is hoped that data will soon be available to address these important issues. The use of real-time magnetic resonance imaging to guide AF ablation procedures is another approach being taken to improve the safety and efficacy of catheter ablation of AF. In the past 5 years, a number of studies have demonstrated the value of using magnetic resonance imaging to image myocardial scar, both before ablation as a predictor of success and after ablation.57-59 Substantial progress has also been made on developing the tools to allow electrophysiology studies and catheter ablation procedures to be performed in a magnetic resonance scanner.59 This is likely to be an active area for research over the next 5 years.

Clinical Role of AF Ablation
Catheter ablation of AF is now an important therapeutic modality for patients with AF. There is considerable evidence available demonstrating that catheter ablation of AF is more effective than antiarrhythmic drug therapy in controlling AF and that AF ablation improves quality of life. This is especially true for patients with paroxysmal AF without other severe comorbidities, because it is in these patients that most of the evidence of the effectiveness of AF ablation has been generated. Catheter ablation is indicated for treatment of patients with symptomatic AF in whom 1 or more attempts at antiarrhythmic drug therapy have failed.1-4 Although current guidelines state that it is appropriate to perform catheter ablation as first-line therapy in selected patients, in my clinical practice this is rare. This reflects a number of important realities concerning the field of AF ablation. First, catheter ablation of AF is a complex procedure that is not free of the risk of potentially life-threatening complications, such as an atrial-esophageal fistula, stroke, and cardiac tamponade. Although these complications are rare and their incidence is falling, they must be considered by both patients and physicians. Second, the techniques and tools of AF ablation continue to improve. If a patient can have their AF controlled for 2 to 3 years with use of a well-tolerated antiarrhythmic medication, the ablation procedure they are likely to receive several years later is likely to be associated with greater safety and higher efficacy. In my mind, this approach is only relevant for patients with paroxysmal AF who can be maintained predominantly in sinus rhythm on an antiarrhythmic medication. For patients with symptomatic AF who cannot be maintained in sinus rhythm, earlier ablation is likely preferable to a delayed ablation procedure that results in further atrial remodeling.

At the end of the day, it is truly remarkable to consider that catheter ablation of AF is now an effective, safe, and commonly performed ablation procedure. When the field of radiofrequency catheter ablation emerged in the late 1980s, few would have predicted that catheter ablation would emerge as an important treatment alternative for patients with AF.

Disclosures
Dr Calkins has received honoraria from Biosense Webster and has served as a consultant/advisory board member for Biosense Webster, Medtronic, Atricure, VytronUS, Sanofi-Aventis, and iRhythm.
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Catheter Ablation to Maintain Sinus Rhythm
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