Catheter Ablation as Treatment for Atrial Fibrillation

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Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for transcatheter catheter ablation of the pulmonary veins as treatment for atrial fibrillation when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered
Transcatheter radiofrequency ablation of arrhythmogenic foci may be considered medically necessary as a treatment for either of the following indications which have failed to respond to adequate trials of antiarrhythmic medications:
- Symptomatic paroxysmal or symptomatic persistent atrial fibrillation; or
- As an alternative to atrioventricular nodal ablation and pacemaker insertion in patients with class II or III congestive heart failure and symptomatic atrial fibrillation.

Repeat radiofrequency ablations may be considered medically necessary in patients with recurrence of atrial fibrillation and/or development of atrial flutter following the initial procedure. (See Considerations)

When Policy Topic is not covered
Transcatheter ablation of arrhythmogenic foci is considered investigational as a treatment for all indications except for specific cases of atrial fibrillation as noted above.

Transcatheter cryoablation of arrhythmogenic foci as a treatment for atrial fibrillation is considered investigational.

Considerations
There is not one single procedure for catheter ablation, but several variations. Electrical isolation of the pulmonary vein musculature (pulmonary vein isolation) is the cornerstone of most atrial fibrillation ablation procedures, but additional ablation sites may also be included during the initial ablation. Potential additional ablation procedures include: creation of linear lesions within the left atrium; ablation of focal triggers outside the pulmonary veins; ablation of areas with complex fractionated atrial electrograms; and ablation of left atrial ganglionated plexi. The specific ablation sites may be determined by electroanatomical mapping to identify additional sites of excitation. As a result, sites may vary from patient to patient, even if they are treated by the same physician. Patients with long-standing persistent atrial fibrillation may need more extensive ablation. Similarly, repeat ablation procedures for recurrent atrial fibrillation generally involve more extensive ablation than do initial procedures.

As many as 30% of patients will require a follow-up (repeat) procedure because of recurrence of atrial fibrillation or developing atrial flutter. In most of the published studies, success rates were based on having as many as 3 separate procedures, although these repeat procedures may be more limited than the initial procedure.

Description of Procedure or Service
Radiofrequency ablation using a percutaneous catheter-based approach is widely used to treat supraventricular arrhythmias. Atrial fibrillation frequently arises from an abnormal focus at or near the junction of the pulmonary veins and the left atrium, thus leading to the feasibility of more focused ablation techniques directed at these structures. Catheter-based ablation, using both radiofrequency ablation and cryoablation, is being studied in the treatment of various types of atrial fibrillation.

Background
Atrial fibrillation is the most common cardiac arrhythmia, with a prevalence estimated at 0.4% of the population, increasing with age. The underlying mechanism of atrial fibrillation involves an interplay between electrical triggering events and the myocardial substrate that permits propagation and maintenance of the aberrant electrical circuit. The most common focal trigger of atrial fibrillation appears to be located within the cardiac muscle that extends into the pulmonary veins.

Atrial fibrillation accounts for approximately one-third of hospitalizations for cardiac rhythm disturbances. Symptoms of atrial fibrillation, e.g., palpitations; decreased exercise tolerance; and dyspnea, are primarily related to poorly controlled or irregular heart rate. The loss of atrioventricular (AV) synchrony results in a decreased cardiac output, which can be significant in patients with compromised cardiac function. In addition, patients with atrial fibrillation are at higher risk for stroke, and anticoagulation is typically recommended. Atrial fibrillation is also associated with other cardiac conditions, such as valvular heart disease, heart failure, hypertension, and diabetes. Although episodes of atrial fibrillation can be converted to normal sinus rhythm using either pharmacologic or electroshock conversion, the natural history of atrial fibrillation is one of recurrence, thought to be related to fibrillation-induced anatomic and electrical remodeling of the atria.

Atrial fibrillation can be subdivided into 3 types:
- paroxysmal (episodes that last fewer than 7 days and are self-terminating),
- persistent (episodes that last for more than 7 days and can be terminated pharmacologically or by electrical cardioversion), or
- permanent.

Treatment strategies can be broadly subdivided into rate control, in which only the ventricular rate is controlled and the atria are allowed to fibrillate, or rhythm control, in which there is an attempt to re-establish and maintain normal sinus rhythm. Rhythm control has long been considered an important treatment goal for management of atrial fibrillation, although its primacy has recently been challenged by the results of several randomized trials that reported that pharmacologically maintained rhythm control offered no improvement in mortality or cardiovascular morbidity compared to rate control.

Currently, the main indications for a rhythm control are for patients with paroxysmal or persistent atrial fibrillation who have hemodynamic compromise associated with episodes of atrial fibrillation or who have bothersome symptoms despite adequate rate control. A rhythm-control strategy involves initial pharmacologic or electronic cardioversion, followed by pharmacologic treatment to maintain normal sinus rhythm. However, antiarrhythmic medications are often not effective in maintaining sinus rhythm. As a result, episodes of recurrent atrial fibrillation are typical, and patients with persistent atrial fibrillation may require multiple episodes of cardioversion. Implantable atrial defibrillators, which are designed to detect and terminate an episode of atrial fibrillation, are an alternative in patients otherwise requiring serial cardioversions, but these have not yet achieved widespread use. Patients with paroxysmal atrial fibrillation, by definition, do not require cardioversion but may be treated pharmacologically to prevent further arrhythmic episodes.

Treatment of permanent atrial fibrillation focuses on rate control, using either pharmacologic therapy or ablation of the AV node, followed by ventricular pacing. Although AV nodal ablation produces symptomatic improvement, it does entail lifelong anticoagulation (due to the ongoing fibrillation of the atria), loss of AV synchrony, and lifelong pacemaker dependency. Implantable defibrillators are contraindicated in patients with permanent atrial fibrillation.
The cited treatment options are not considered curative. A variety of ablative procedures have been investigated as potentially curative approaches, or perhaps modifying the arrhythmia such that drug therapy becomes more effective. Ablative approaches focus on interruption of the electrical pathways that contribute to atrial fibrillation through modifying the arrhythmia triggers and/or the myocardial substrate that maintains the aberrant rhythm. The Maze procedure, an open surgical procedure often combined with other cardiac surgeries (e.g., valve repair), is an ablative procedure that involves sequential atriotomy incisions designed to create electrical barriers that prevent the maintenance of atrial fibrillation. Because of the highly invasive nature of this procedure, it is currently mainly reserved for patients who are undergoing open heart surgery for other reasons, such as valve repair or coronary artery bypass grafting.

Radiofrequency ablation using a percutaneous catheter-based approach is a widely used technique for a variety of supraventricular arrhythmias, in which intracardiac mapping identifies a discrete arrhythmogenic focus that is the target of ablation. The situation is more complex for atrial fibrillation, since there is not a single arrhythmogenic focus. Since the inception of ablation techniques in the early 1990s, there has been a progressive understanding of the underlying electrical pathways in the heart that are associated with atrial fibrillation. In the late 1990s, it was recognized that atrial fibrillation most frequently arose from an abnormal focus at or near the junction of the pulmonary veins and the left atrium, thus leading to the feasibility of more focused, percutaneous ablation techniques. The basic strategies that have emerged for focal ablation within the pulmonary veins, as identified by electrophysiologic mapping, are segmental ostial ablation guided by pulmonary vein potential (electrical approach), or circumferential pulmonary vein ablation (anatomic approach). Circumferential pulmonary vein ablation using radiofrequency energy is the most commonly used approach at the present time. The procedure also can be done using cryoablation technology. Use of currently-available catheters for atrial fibrillation ablation has a steep learning curve because they require extensive guiding to multiple ablation points. One of the potential advantages to cryoablation techniques is that cryoablation catheters have a circular or shaped endpoint, allowing a “one-shot” ablation. Other types of radiofrequency catheters, such as Medtronic’s radiofrequency-based Pulmonary Vein Ablation Catheter®, that incorporate circular or otherwise shaped endpoints are under investigation.

Repeat procedures following an initial radiofrequency ablation are commonly performed if atrial fibrillation recurs or if atrial flutter develops post-procedure. The need for repeat procedures may, in part, depend on clinical characteristics of the patient (age, persistent vs. paroxysmal atrial fibrillation, atrial dilatation, etc.), and the type of initial ablation performed. Repeat procedures are generally more limited than the initial procedure. For example, in cases where electrical reconnections occur as a result of incomplete ablation lines, a "touch up" procedure is done to correct gaps in the original ablation. In other cases where atrial flutter develops following ablation, a "flutter ablation" is performed, which is more limited than the original atrial fibrillation ablation procedure. A number of clinical and demographic factors have been associated with the need for a second procedure, including age, length of atrial fibrillation, permanent atrial fibrillation, left atrial size, and left-ventricular ejection fraction.

Regulatory Status
In February 2009, the NAVISTAR® THERMOCOOL® Irrigated Deflectable Diagnostic/Ablation Catheter and EZ Steer ThermoCool NAV Catheter (Biosense Webster Inc.) were approved by the U.S. Food and Drug Administration (FDA) through the pre-market approval (PMA) process for “catheter-based cardiac electrophysiological mapping (stimulating and recording), and when used with the Stockert 70 generator, for the treatment of a) Type I atrial flutter in patients age 18 or older; b) recurrent drug/device refractory sustained monomorphic ventricular tachycardia (VT) due to prior myocardial infarction (MI) in adults; c) drug refractory recurrent symptomatic paroxysmal atrial fibrillation, when used with compatible three-dimensional electroanatomic mapping systems.” (For radiofrequency ablation)

In December 2010, Medtronic’s Arctic Front® Cardiac CryoAblation Catheter and CryoConsole were approved by the FDA for the “treatment of drug refractory recurrent symptomatic paroxysmal atrial fibrillation.” In addition, Medtronic’s Freezor® MAX Cardiac CryoAblation Catheter was approved as an
adjunctive device to be used in conjunction with the Arctic Front system for “gap cryoablation to complete electrical isolation of the pulmonary veins, cryoablation of focal trigger sites, and creation of ablation line between the inferior vena cava and the tricuspid valve.” (For cryoablation)

In addition, the FDA has also granted PMA approval to numerous catheter ablation systems for other ablation therapy for arrhythmias such as supraventricular tachycardia, atrial flutter, and ventricular tachycardia.

Rationale
This policy was originally created in 2004 and updated periodically with literature review since that time. The most recent literature search was performed through February 4, 2014. Following is a summary of the key literature to date.

In patients with paroxysmal or persistent atrial fibrillation, catheter ablation may be considered an alternative to drug therapy. (1) In patients with permanent atrial fibrillation, catheter ablation may be considered an alternative to drug therapy or to atroventricular (AV) nodal ablation and pacing. (2) For all types of atrial fibrillation, it is possible that catheter ablation may not be curative as a sole treatment but might alter the underlying myocardial triggers or substrate in such a way that subsequent pharmacologic therapy may become more effective.

There is ongoing controversy regarding the relative benefits of rhythm versus rate control in atrial fibrillation, which underlies the evaluation of evidence on catheter ablation. Randomized trials of pharmacologic therapies have not demonstrated the superiority of rhythm versus rate control. (3-5) However, the apparent equivalency of these two strategies with pharmacologic therapy cannot be extrapolated to the rhythm control achieved with ablation. Antiarrhythmic medications used for rhythm control are only partially effective and have serious complications, including proarrhythmic properties, which can be lethal. Therefore, nonpharmacologic strategies for rhythm control have the potential to achieve superior outcomes than have been seen with pharmacologic strategies.

Outcome assessment in atrial fibrillation

A variety of outcomes for treatment of atrial fibrillation may be considered. (6) The mortality and morbidity related to atrial fibrillation, such as cardiovascular mortality, stroke, and heart failure, are the most important clinical outcomes. However, these are uncommon events, and currently available trials are not powered to detect differences in these outcomes. Quality of life (QOL) is also an important outcome, as these measures reflect important manifestations of atrial fibrillation, such as symptoms and reduced exercise tolerance. Atrial fibrillation has been shown to be associated with lower QOL scores, and maintenance of sinus rhythm has been associated with higher QOL scores for patients with paroxysmal atrial fibrillation.

Recurrence of atrial fibrillation is a more problematic outcome measure, since the intermittent and often transient nature of recurrences makes accurate measurement difficult. (6) This outcome measure has been reported in different ways. For example, the proportion of patients in sinus rhythm at the end of the study, the time to first recurrence, and the number of recurrences within a time period have been reported. A recent publication highlights the difficulties in measuring atrial fibrillation recurrence and recommends a measure of atrial fibrillation “burden,” defined as the percentage of time an individual is in atrial fibrillation, as the optimal measure of treatment efficacy. (6) However, this parameter requires continuous monitoring over a relatively long period of time, which is inconvenient for patients, resource intensive, and usually not pragmatic in patients who do not already have an implanted pacemaker.

Recommendations for outcome assessment in trials of atrial fibrillation treatment were included in the 2006 American College of Cardiology/American Heart Association practice guidelines for the treatment of atrial fibrillation. (7) These guidelines pointed out that the appropriate endpoints for evaluation of treatment efficacy in patients with paroxysmal or persistent atrial fibrillation have little in common. For example, in studies of persistent atrial fibrillation, the proportion of patients in sinus rhythm at the end of
follow-up is a useful endpoint, but this is a less useful measure in studies of paroxysmal atrial fibrillation. Given all these variables, ideally, controlled clinical trials would report a range of outcomes (including QOL) and complications in homogeneous patient groups and compare to the most relevant treatment alternatives, such as pharmacologic therapy; defibrillator therapy; and AV nodal ablation, depending on the classification of atrial fibrillation (paroxysmal, persistent, or permanent).

Radiofrequency Ablation for Atrial Fibrillation

Systematic Reviews

The literature review for this policy was originally based on a 2008 TEC Assessment. (8) Six randomized, controlled trials (RCTs) met the inclusion criteria for this TEC Assessment. (9-14) The trials differed in their patient populations, the specific catheter ablation techniques used, and the comparisons made. The trials addressed 3 distinct indications for catheter ablation: 1) patients with paroxysmal atrial fibrillation, as a first-line treatment option (n=1 trial (14)); 2) patients with symptomatic paroxysmal or persistent atrial fibrillation who have failed treatment with antiarrhythmic drugs (n=4 trials (9, 11-13)); and 3) patients with symptomatic atrial fibrillation and heart failure who have failed treatment with standard medications for rate control and who would otherwise be considered for AV nodal ablation and pacemaker insertion (n=1 trial (10)).

All 6 trials reported that maintenance of sinus rhythm was improved for the catheter ablation group. Recurrence rates of atrial fibrillation at 1 year ranged from 11–44% for the catheter ablation groups in these trials, compared with 63–96% for the medication groups. Four of the 6 trials reported QOL outcomes. One of these (11) only reported within-group comparisons, as opposed to between-group comparisons. The other 3 trials (9, 10, 14) reported improvements in QOL associated with catheter ablation. These QOL measures were self-reported, and since both trials were unblinded, there is the possibility of reporting bias due to placebo effect.

None of the available trials reported meaningful data on cardiovascular morbidity and mortality associated with atrial fibrillation. The Assessment concluded that radiofrequency catheter ablation is more effective than medications in maintaining sinus rhythm across a wide spectrum of patients with atrial fibrillation and across different variations of catheter ablation. The evidence on QOL is suggestive, but not definitive, of a benefit for patients undergoing catheter ablation. For other outcomes, the evidence did not permit conclusions. It was not possible to estimate the rate of serious complications, such as pulmonary vein stenosis, cardiac tamponade, or atrio-esophageal fistula with precision given the limited number of patients in the trials and the continued evolution of the technique. However, the rate of serious complications is expected to be low, likely in the 1–5% range.

Based on these findings, TEC criteria were met for 2 indications: patients with symptomatic paroxysmal or persistent atrial fibrillation who have failed treatment with antiarrhythmic drugs and patients with symptomatic atrial fibrillation and heart failure who have failed treatment with standard medications for rate control and who would otherwise be considered for AV nodal ablation and pacemaker insertion. For the first indication, the conclusion followed from the premise that reducing episodes of recurrent atrial fibrillation for this population will reduce or eliminate the symptoms associated with episodes of atrial fibrillation. For the other indication, the single multicenter RCT available was judged sufficient to conclude that catheter ablation improved outcomes compared to the alternative, AV nodal ablation and pacemaker insertion. While this trial was relatively small, it was judged to be otherwise of high quality and reported improvements of a relatively large magnitude across a range of clinically important outcome measures, including QOL, exercise tolerance, left-ventricular ejection fraction, and maintenance of sinus rhythm.

Since the publication of the 2008 TEC Assessment, several additional systematic reviews and meta-analyses of catheter ablation for atrial fibrillation have been published. A Cochrane Review on catheter ablation for paroxysmal and persistent atrial fibrillation was published in 2012. (15) This review included 7 (RCTs) of catheter ablation versus medical therapy. Main conclusions were that catheter ablation was
superior at reducing the recurrence of atrial fibrillation (risk ratio [RR]: 0.27, 95% confidence interval [CI]: 0.18-0.41) but that there were no differences in mortality (RR: 0.50, 95% CI: 0.04-5.65), embolic complications (RR: 1.01, 95% CI: 0.18-5.68), or death from thromboembolism (RR: 3.04, 95% CI: 0.13-73.4).

In 2013, Ganesan et al. published results from a systematic review and meta-analysis of studies reporting long-term outcomes after percutaneous catheter ablation for paroxysmal and nonparoxysmal atrial fibrillation.(16) The authors included 19 studies (RCTs, case-control and cohort studies, and case series) that reported catheter ablation outcomes at greater than or equal to 3 years after the index ablation procedures. Sample sizes in these studies ranged from 39 to 1404, with a total of 6167 patients included overall. For a single procedure, the pooled overall success rate at 12 months post-procedure was 64.2% (95% CI 57.5% to 70.3%). At late follow-up, the overall single-procedure success, defined as freedom from atrial arrhythmia at latest follow-up, was 53.1% (95% CI 46.2% to 60.0%). The pooled overall multiple-procedure long-term success rate was 79.8% (95% CI 75.0% to 83.8%). The analysis was unable to identify any predictors of short- or long-term recurrence. Reporting of periprocedural complications was heterogeneous across the studies, but complication rates were generally low.

Three systematic reviews and meta-analyses comparing radiofrequency ablation to antiarrhythmic drug therapy for atrial fibrillation were published from 2008-2009.(17-19) Nair et al.(17) included 6 RCTs comparing radiofrequency ablation to antiarrhythmic drug therapy for atrial fibrillation, 5 of which were included in the TEC Assessment.(9, 11-14) Two systematic reviews published in 2008 (18, 19) summarized and synthesized the RCT evidence on catheter ablation versus alternate therapy. These reviews included 4 of the 6 trials reviewed for the TEC Assessment. (11-14) Noheria et al. (18) included 3 of these 4 RCTs, (12-14) as well as an additional small RCT of 30 patients not included in the TEC Assessment. (20) Gjesdal et al. (19) included 5 RCTs in their analysis, including the 4 trials in the Noheria et al. systematic review, and 1 additional trial (included in the TEC Assessment) that compared catheter ablation plus antiarrhythmic drugs with antiarrhythmic drugs alone. (11) All three systematic reviews concluded that catheter ablation was more effective than pharmacologic treatment in maintaining normal sinus rhythm. Nair et al. demonstrated a pooled relative risk for atrial fibrillation at 1 year post-procedure of 0.35 compared with antiarrhythmic drug therapy. (17) In combined analysis, Noheria et al. (18) reported atrial-fibrillation-free survival at 1 year to be 75.7% in the catheter ablation group compared to 18.8% in the comparison group. The relative risk for maintaining sinus rhythm was 3.73 (95% confidence interval [CI]: 2.47–5.63) for the catheter-ablation group compared to alternative treatment. Gjesdal et al. (19) concluded that the available evidence was of moderate quality and consistent in reporting that atrial-fibrillation-free survival was superior for the catheter ablation group. However, due to unexplained heterogeneity, these authors did not perform a combined analysis.

Additional RCTs
Since the TEC Assessment, six additional RCTs comparing radiofrequency ablation (RFA) versus pharmacologic treatment have been identified. Wilber et al. (21) enrolled 167 patients who had failed at least one antiarrhythmic medication and had at least 3 atrial fibrillation episodes in the prior 6 months. Patients were randomly assigned to either catheter ablation or continued drug therapy and followed for 9 months. At the end of follow-up, 66% of patients in the ablation group were free of recurrent atrial fibrillation compared to 16% of patients in the medication group. Adverse events related to treatment occurred in 4.9% (5/103) of patients treated with ablation and in 8.8% (5/57) of patients treated with medications.

Forleo et al. (22) randomly assigned 70 patients with type 2 diabetes and atrial fibrillation to either radiofrequency ablation or an antiarrhythmic medication. Follow-up was for 1 year, with the primary outcome being recurrence of atrial fibrillation. At the end of the trial, 42.9% of patients in the medication group were free of atrial fibrillation compared to 80% of patients in the ablation group. There was also a significant improvement in QOL for patients in the ablation group. Adverse events from medications occurred in 17.2% (6/35) patients, whereas complications from ablation occurred in 2.9% (1/35).
An RCT of RFA ablation as the initial therapy for paroxysmal atrial fibrillation was published in 2012. (23) A total of 294 patients were randomized to initial treatment with catheter ablation or pharmacologic therapy. Patients were followed for up to 24 months for the primary outcomes of burden of atrial fibrillation (percent of time in atrial fibrillation on Holter monitor) at each time point and cumulative burden of atrial fibrillation over all time points. For the individual time points, the burden of atrial fibrillation was lower in the catheter ablation group at 24 months (9% versus 18%, p=0.007), but not at other time points. The cumulative burden did not differ significantly for the catheter ablation group compared to pharmacologic therapy (90th percentile of cumulative burden, 13% versus 19%, p=0.10). The secondary outcome of percent of patients free from atrial fibrillation at 24 months was greater for the catheter ablation group (85% vs. 71%, p=0.004), as was the secondary outcome of freedom from symptomatic atrial fibrillation (93% vs. 84%, p=0.01). There was one death in the ablation group due to a procedural-related stroke, and there were 3 patients in the ablation group who developed cardiac tamponade following the procedure.

Mont et al. conducted an RCT comparing radiofrequency catheter ablation to antiarrhythmic drug therapy among 146 patients with symptomatic persistent atrial fibrillation.(24) Patients were randomized in a 2:1 fashion to catheter ablation (n=98) or antiarrhythmic drug therapy (N=48). Although the study was terminated before the planned sample size of 208 was met due to lower than expected enrollment, at 12 months of follow up, the proportion of patients who were free of sustained episodes of atrial fibrillation was higher in the catheter ablation group than the antiarrhythmic drug therapy group (70.4% vs. 43.7%, P=0.002). Quality of life scores did not significantly differ between the groups. Longer term outcomes were not reported.

Several studies have compared catheter ablation to medical therapy for atrial fibrillation in the setting of heart failure. Hunter et al. conducted an RCT comparing catheter ablation to medical rate control for patients with persistent atrial fibrillation and symptomatic heart failure, with adequate rate control at the time of enrollment.(25) The study’s primary end point was difference between groups in left ventricular ejection fraction (LVEF) at 6 months post-procedure. Fifty patients were randomized, 26 to catheter ablation and 24 to medical management. At 6 months, 81% of the catheter ablation group was free from recurrent atrial fibrillation off antiarrhythmic drugs. LVEF at 6 months post-procedure was 40% (±12%) in the catheter ablation group, compared to 31% (±13%, P=0.015). Catheter ablation was also associated with improvements in health-related quality of life. Jones et al. reported result from an RCT comparing catheter ablation to medical rate control for patients with symptomatic heart failure, left ventricular ejection fraction less than or equal to 35%, and persistent atrial fibrillation.(26) Fifty-two patients were randomized, 26 each to catheter ablation or medical rate control. At 12 months post-procedure, sinus rhythm was maintained in 88% of the catheter ablation group, with a single-procedure success rate of 68%. For the study’s primary outcome, peak oxygen consumption at 12 months post-procedure, there was a significant increase in the catheter ablation group compared with the medical management group (+3.07 mL/kg/min, 95% CI 0.56 to 5.59, P=0.018).

Longer-term outcomes.

The available RCTs mainly report on short-term outcomes up to 1 year and, therefore, do not evaluate the rate of late recurrences after 1 year. Longer-term outcomes have been reported by several authors. These studies generally report rates of early recurrence in the range of 20-30%, requiring repeat ablations. Rates of longer-term recurrence are lower if early recurrence does not occur, in the range of 1-2% per year.

Hussein et al. (27) reported on 831 patients who were treated in 2005, with a median follow-up of 55 months. During the first year following ablation, 23.8% had a recurrence of atrial fibrillation. During the remaining follow-up, recurrences occurred in 8.9% additional patients. The overall rate of arrhythmia-free and off drugs was 79.4% at 55 months. An additional 10.5% of patients were arrhythmia-free on drugs, for a total rate of 89.9% clinical improvement.
In 2013, Bunch et al. reported results from a prospective cohort study comparing risk of stroke between patients with atrial fibrillation who had undergone catheter ablation, patients with atrial fibrillation who did not undergo ablation, and patients without a history of atrial fibrillation. A total of 4212 patients with atrial fibrillation who had undergone catheter ablation were age/sex matched in a 1:4 ratio to 16,848 subjects in each of the other groups. The mean follow up time was 3.9 years. At 1 year post-procedure, significantly more patients with atrial fibrillation who did not undergo ablation had a stroke (3.5%) than those with atrial fibrillation who underwent ablation (1.4%) or had no history of atrial fibrillation (1.4%; P for trend <0.001). During the follow up period, for all ages and CHADS2 profiles, patients with atrial fibrillation who had ablation had a lower stroke risk than those with atrial fibrillation without ablation.

Several smaller studies have also reported longer-term follow-up after radiofrequency catheter ablation. Weerasooriya et al. (29) reported 5-year follow-up in 100 patients treated with catheter ablation. Recurrences were most common within the first 6 months, with repeat procedures being common during that period. At 1, 2, and 5 years post-ablation, arrhythmia-free survival was 87%, 81%, and 63%, respectively. Tzou et al. (30) reported long-term follow-up for 123 patients who had a previous successful ablation, defined as free of atrial fibrillation at 1 year. At 3 years of follow-up, 85% of patients were still free of atrial fibrillation and off of all medications, and at 5 years, 71% remained free of atrial fibrillation. The authors estimated a late recurrence rate of approximately 7% per year for patients with an initial successful procedure. In a similar study, Bertaglia et al. (31) reported outcomes after 6 years of follow-up for 229 patients who had a single, successful ablation. At 1-year follow-up, 77% of patients (177/229) were free of atrial fibrillation and off of all medications. After a mean additional follow-up of 49.7 +/- 13.3 months for these 177 patients, 58% remained free of atrial fibrillation. Sawhney et al. (32) reported 5-year success rates in 71 patients who underwent ablation in 2002 or 2003. Freedom from symptomatic atrial fibrillation off medications was achieved in 86% of patients at 1 year, 79% at 2 years, and 56% at 5 years. A substantial minority of patients (22.5%) had recurrence at times greater than 2 years post-ablation. A 2013 study by Anselmino et al. followed 196 patients who underwent radiofrequency catheter ablation for paroxysmal or persistent atrial fibrillation and had left ventricular ejection fraction less than or equal to 50% for a mean of 46.2 months. (33) During follow up, 29.6% of patients required repeat ablation procedures. At the end of follow up, 37.8% had at least one episode of atrial fibrillation, atrial flutter, or ectopic atrial tachycardia.

Section Summary: Numerous RCTs of radiofrequency ablation (RFA) of the pulmonary veins versus medical management report that freedom from atrial fibrillation at 1 year is higher with RFA compared to medical management. The trials mainly include patients who have failed anti-arrhythmic medications, although 2 trials treat patients with paroxysmal atrial fibrillation as initial treatment. These studies report that a majority of patients undergoing RFA are free of atrial fibrillation at 1 year. Quality of life is also improved in these trials for patients undergoing catheter ablation. A smaller number of studies evaluate outcomes longer than 1 year and report that late recurrences occur up to 5 years but are uncommon after the first year. Complications from RFA are reported at low rates in the RCTs, but the numbers of patients in these trials are too low to accurately estimate rates of uncommon events. There is a lack of data on clinical outcomes other than freedom from atrial fibrillation. Larger RCTs are underway to evaluate long-term clinical outcomes such as stroke and mortality.

Cryoablation of the pulmonary veins
A number of studies reported outcomes of ablation using cryoablation. These were mainly case series (34, 35) reporting success rates in the range of that reported for radiofrequency ablation. One small matched analysis compared 20 patients undergoing cryoablation with 20 patients undergoing radiofrequency ablation, matched for age, gender, left ventricular ejection fraction, and atrial fibrillation history. (36) Freedom from atrial fibrillation at 6 months was 55% for the cryoablation group, compared to 45% for the radiofrequency ablation group, a difference that was not significantly different.

In 2013, Packer et al. reported results of the STOP-AF trial, an RCT of cryoablation versus antiarrhythmic medications. (37) This study enrolled 245 patients with paroxysmal atrial fibrillation who had failed at least 1 (median 1.2) membrane-active antiarrhythmic medications. Patients were
randomized in 2:1 fashion to either cryoballon ablation (n=163) or drug therapy (n=82). At 1-year follow-up, 69.9% of patients in the ablation group were free of atrial fibrillation versus 7.3% in the medication group. The single-procedure success rate was 57.7%. There was also a significantly greater reduction in symptoms for the ablation group. Seventy-nine percent of the drug treatment group crossed over to cryoablation during 12 months of study follow up because of recurrent, persistent atrial fibrillation. Cryoablation procedure-related adverse events occurred in 5 patients (3.1%); major atrial fibrillation events occurred in 3.1% of the cryoablation group compared to 8.5% of the drug-treatment group (noninferiority P<0.001). Phrenic nerve injury occurred at a rate of 13.5%, with 86% resolved at 12 months.

The Mesh Ablator versus Cryoballoon Pulmonary Vein Ablation of Symptomatic Paroxysmal Atrial Fibrillation (MACPAF) study was a single-center RCT comparing cryoablation to radiofrequency ablation with the HD Mesh Ablator Catheter (Bard®, purchased by Boston Scientific in 2013) for atrial fibrillation. The HD Mesh Ablator Catheter, which is not cleared for use in the U.S., is a multielectrode radiofrequency catheter that involves a mesh electrode that is designed to deliver radiofrequency energy to multiple points of contact. Primary short-term results for MACPAF were reported by Koch et al. in 2013.(39) The study randomized symptomatic paroxysmal atrial fibrillation to catheter ablation with the Arctic Front® cryoablation catheter or the HD Mesh Ablator. The study’s primary endpoint was complete isolation of the pulmonary veins at the end of the procedure. Enrollment was initially planned for 108 with symptomatic paroxysmal atrial fibrillation that was inadequately controlled with antiarrhythmic drug treatment. However, at interim analysis, the HD Mesh Ablator demonstrated a lack of efficacy for the primary endpoint and the study’s data safety monitoring board prematurely terminated the subject. Forty-four patients with drug resistant paroxysmal atrial fibrillation were randomized at the time the study was terminated and comprise the intention-to-treat analysis cohort. The per-protocol analysis cohort included 32 patients. Three patients withdrew before the catheter procedure; 9 additional patents were excluded from analysis due to use of a study non-compliant catheter (n=2), identification of a trigger arrhythmia which was subsequently ablated (n=1), failure of transseptal puncture (n=1), or ablation occurring after the interim analysis (n=5). For the primary endpoint, by intention-to-treat analysis, complete pulmonary vein isolation was achieved in 13/23 (56.5%) of patients in the cryoablation group, compared with 2/21 (9.5%) of patients in the mesh ablator group (P=0.001). In the per-protocol cryoablation group, 76.5% of subjects had complete pulmonary vein isolation. Major complications included 1 case of retroperitoneal hematoma in the cryoablation group and 1 case of pericardial tamponade requiring drainage in the mesh ablator group.

Malmborg et al. reported results from an RCT comparing cryoablation with the Arctic Front® cryoballoon catheter to radiofrequency ablation with the Pulmonary Vein Ablation Catheter®.(40) One hundred ten patients with paroxysmal or persistent atrial fibrillation were randomized, 54 to the cryoablation group and 56 to the radiofrequency ablation group. Complete pulmonary vein isolation was achieved in 98% of the cryoablation group, compared with 93% of the radiofrequency ablation group (P=0.37). At 6 month follow up, freedom from atrial fibrillation (absence of symptoms and no atrial fibrillation episodes on 7-day Holter monitoring or 12-lead ECG) without antiarrhythmic drug treatment was achieved in 52% of the cryoablation group and 38% of the radiofrequency ablation group (P=0.13).

Schmidt et al. used data from a prospective German registry of catheter ablation procedures to compare radiofrequency to cryoablation for paroxysmal atrial fibrillation.(41) The cohort included 905 patients who underwent cryoablation and 2870 patients who underwent radiofrequency ablation who were enrolled from January 2007 to August 2011. The two groups were generally similar, with the exception that patients who underwent radiofrequency ablation were significantly more likely to have valve disease (8.1% vs. 3.0%, P<0.0001) and an ejection fraction less than or equal to 40% (2.4% vs. 1.2%, P<0.05). Rates of acute success were similar for the two groups (97.5% for cryoablation vs. 97.6% for radiofrequency ablation, P=0.92), as were rates of major procedure-related adverse cardiac and cerebrovascular events (0.4% for cryoablation vs. 0.2% for radiofrequency ablation, P=0.15). The overall procedural complication rates were similar for the two groups (4.6% for each group, P=1.0); the rate of post-procedural phrenic nerve palsy was significantly higher for the cryoablation group (2.1% for cryoablation vs. 0% for radiofrequency ablation, P=0.15). Long term follow rates are not reported.
A meta-analysis of studies of cryoablation was published in 2011. (42) This analysis included the STOP-AF results in abstract form and a total of 22 other non-randomized studies, primarily case series. Procedural success was reported in over 98% of cases. At 1 year, the rates of success, as defined by no recurrent atrial fibrillation, were 73% (95% CI: 69-77%) for paroxysmal atrial fibrillation and 60% (95% CI: 54-66%) for persistent atrial fibrillation. Complications were inconsistently reported among the available studies. The most common complication reported was phrenic nerve palsy, which occurred in 6.4% of patients. Other rates of reported complications were pericardial effusion or tamponade (1.5%), groin complications at insertion site (1.8%), stroke (0.3%), and pulmonic stenosis (0.9%).

Vogt et al. reported longer-term follow up for 605 patients who underwent cryoablation for symptomatic, paroxysmal or persistent atrial fibrillation.(43) Follow up data beyond 12 months were available for 451 patients (median follow up 30 months). Of those with follow up available, 278 (61.6%) were free of atrial fibrillation recurrence with no need for repeat procedures after a 3 month blanking period. After 1, 2, and 3 repeat procedures, rates of freedom from atrial fibrillation were 74.9%, 76.2%, and 76.9%, respectively. Phrenic nerve palsy was the most common adverse event, occurring in 2% of patients, all of which resolved within 3-9 months. There were two periprocedural strokes, and one case each of periprocedural pericardial tamponade and pericardial effusion.

Neumann et al. reported 5 year outcomes after a single cryoablation procedure among 163 patients with symptomatic, drug-refractory paroxysmal atrial fibrillation.(44) Fifty-three percent of subjects were free from recurrent atrial fibrillation, atrial tachycardia, or atrial flutter at 5 years of follow up with no additional procedures (after a 3 month blanking period).

There are ongoing trials of cryoablation versus RFA for atrial fibrillation. The FreezeAF trial (42, 45) is a randomized controlled noninferiority trial comparing cryoablation to RFA for patients with paroxysmal atrial fibrillation. Enrollment of 244 patients is planned, and patients will be followed for at least 1 year. The primary outcome is freedom from atrial fibrillation off all drugs. Secondary outcomes include longer-term success rates, procedural data, and cost-effectiveness.

**Section Summary:** The evidence related to cryoablation for atrial fibrillation includes three RCTs and numerous uncontrolled case series. The STOP AF trial, which compared cryoablation to antiarrhythmic medication therapy, reported that cryoablation is superior to medical management, and that rates of freedom from arrhythmia at 1 year in the cryoablation group are in the range reported with radiofrequency ablation. Nonrandomized studies also report that cryoablation has efficacy in the same range as radiofrequency ablation. However, data from randomized trials directly comparing cryoablation to radiofrequency ablation are limited. Interpretation of the MACPAF study is limited by early termination due to unexpectedly low efficacy of the radiofrequency ablation method used. While the Malmborg et al. study is suggestive that cryoablation is comparable to radiofrequency ablation, success in the RFA group was also unusually low. This study is also limited by relatively short-term follow up (6 months) and use of a catheter that is not cleared for use in the U.S.

Therefore, the evidence is not sufficient to determine the comparative efficacy of cryoablation compared to RFA. Ongoing RCTs, particularly the FreezeAF trial, are currently addressing this question.

**Repeat procedures**

Repeated procedures for recurrent atrial fibrillation or atrial flutter were commonly performed in most of the clinical trials included in this policy statement. Of the 10 RCTs reviewed that compared radiofrequency ablation to medical management, only 2 (14, 22) did not include repeated procedures. In the other 5 studies, one or more repeated procedures were allowed, and success rates reported generally incorporated the results of up to 3 procedures. In 4 studies that reported these data, repeated procedures were performed in 8.2%,(24) 9%,(12) 20%,,(10) and 32%,(11) of patients randomized to ablation. In their RCT of catheter ablation of atrial fibrillation in patients with heart failure, Hunter et al. report that repeat procedures were required in 65.4% of the catheter ablation group.(25) Stabile et al.
did not report specifics on how many patients actually underwent repeated procedures, but limited data in the publication indicated that up to 30% of treated patients were eligible for repeated procedures. In the Jais et al. study, (9) patients underwent a mean of 1.8 procedures per patient and a median of 2 procedures per patient, indicating that approximately 50% of patients in the ablation group underwent at least one repeated procedure.

Because of this high rate of repeated procedures, the results reported in these studies do not reflect the success of a single procedure. Rather, they more accurately estimate the success of an ablation strategy that includes repeated procedures for recurrences that occur within the first year of treatment. Nonrandomized evidence suggests that early reablation increases the success of the procedure, when defined as maintenance of sinus rhythm at 1 year. (47) There is variability in the protocol for when repeated procedures should be performed. There is also uncertainty concerning other details on repeated procedures, such as how soon after the initial procedure it should be done, the threshold of atrial fibrillation recurrence that should prompt a repeat, and whether medications should be tried prior to a repeated procedure. (47)

Pokushalov et al. reported results of an RCT comparing repeat catheter ablation to antiarrhythmic drug therapy for patients with paroxysmal atrial fibrillation who had failed an initial pulmonary vein isolation procedure. (48) After an initial post-ablation blanking period, 154 patients with symptomatic atrial fibrillation recurrence were randomized to drug therapy (n=77) or repeat ablation (n=77). Patients were followed for 3 years with an implanted cardiac monitor. At the 3-year follow up, 58% (45/77) of the repeat ablation group were free from atrial fibrillation or atrial tachycardia on no antiarrhythmic drugs, compared to 12% (9/77) of the antiarrhythmic therapy group (P<0.01). In the antiarrhythmic drug group, 43 patients (56%) crossed over to receive repeat ablation; in the repeat ablation group, 21 patients (27%) required antiarrhythmic drug therapy. By intention to treat analysis, 65% (50/77) of the repeat ablation group and 45% (35/77) of the drug therapy group were free from atrial fibrillation or atrial tachycardia (P=0.02).

Complications

Individual clinical trials and case series report relatively low rates of complications, but may be limited in their ability to detect uncommon outcomes due to their small size. In 2013, Gupta et al. reported results from a systematic review and meta-analysis of periprocedural complications following catheter ablation for atrial fibrillation. (49) The authors included 192 studies that included at least 100 participants undergoing catheter ablation for symptomatic atrial fibrillation, and that reported complications. The total sample size was 83,236 patients. The overall acute complication rate was 2.9% (95% CI 2.6 to 3.2), with significant heterogeneity across studies. The most common complications were vascular complications (1.4%), cardiac tamponade (1.0%), pericardial effusion (0.7%), stroke/transient ischemic attack (TIA) (0.6%), and pulmonary vein stenosis (0.5%).

In addition to the complication rates reported in available clinical trials and case series, there have been a number of database studies and post-marketing surveillance that report complications in larger numbers of patients than are in the clinical trials. A representative sample of these studies is discussed below, some of which were included in the Gupta et al. review (Shah et al.(50), Dagres et al.(51)).

Waldo et al. reported the results of an FDA-directed post-marketing safety study involving 1,275 patients from 6 prospective, multicenter studies of RFA ablation using an open-irrigated catheter. (52) A total of 4.9% (63/1,275) of patients experienced any acute serious complication within 7 days of the procedure. Vascular access complications were most common, ranging from 0.5% to 4.7% across the 6 studies. Exacerbations of heart failure occurred in 1.5% of patients, and 2 patients experienced cardiac tamponade. There were no strokes or TIAs reported post-procedure.

Shah et al. (50) used data from a California hospital database to evaluate complications in 4,156 patients who underwent catheter ablation for atrial fibrillation. Major complications occurred in 5.1% (211/4,156) of patients, with approximately half of these (2.6%, 110/4,156) consisting of hemorrhage or
hematoma at the vascular entry site. The most common cardiac complication was cardiac perforation and/or tamponade, which occurred in 2.5% (104/4,156) of patients. Less common rates of serious adverse events included death (0.02%), stroke/TIA (0.31%), and pneumothorax/hemothorax (0.1%). Factors that were predictive of complications were female gender, older age, prior hospitalizations for atrial fibrillation, and less hospital experience with ablation.

In a study of Medicare beneficiaries, Ellis et al. (53) identified 6,065 admissions from 168 hospitals in which RFA for atrial fibrillation was performed. The total rate of in-hospital complications was 9.1%, with vascular complications accounting for over half of the total complications at a rate of 5.7%. The mortality rate was 0.4%, and 0.6% of patients suffered a stroke or transient ischemic attack (TIA). Perforation or tamponade occurred in 3.1% of patients and pneumothorax occurred in 0.4% of patients. The presence of chronic obstructive pulmonary disease (COPD) or unstable angina was associated with a higher risk of complications, while obesity and hyperlipidemia were associated with a lower risk. Age and hospital volume were not significant predictors of risk, but low hospital volume was a significant predictor of in-hospital death.

Complications of catheter ablation were reported in a large cohort of 1,000 patients undergoing ablation at a high-volume center in Europe. (51) There were no deaths definitely attributable to the procedure, but there were 2 deaths of uncertain cause within the first 30 days following ablation. Overall, 3.9% of patients had a major complication resulting from the procedure. Tamponade was the most serious life-threatening complication, occurring in 1.3% of patients. Major vascular complications occurred in 1.1%. Thromboembolism, cerebrovascular accident/transient ischemic attack, atrio-esophageal fistula, and endocarditis were all reported complications that occurred at a rate of less than 1%.

Cappato et al. (54) performed a multicenter, retrospective case series to estimate the overall mortality rate following ablation. Data were collected on 32,569 patients from 162 clinical centers worldwide. There were 32 deaths reported, for a mortality rate of 0.98 per 1,000 patients. The most common causes of death were tamponade (n=8), stroke (n=5), atrio-esophageal fistula (n=5), and pneumonia (n=2).

In the MACPAF study, one goal was to identify adverse events, particularly cerebral thromboembolism through the use of serial magnetic resonance imaging (MRIs) and neuropsychological testing. While there is some evidence that radiofrequency ablation for patients with atrial fibrillation improves stroke risk, a clinically significant stroke or TIA attack occurs in 0.1-0.8% of patients undergoing catheter ablation, and several case series have demonstrated peridural brain lesions on diffusion weighted MRI imaging in up to 18% of patients undergoing catheter ablation of the left atrium. Thus, the MACPAF investigators evaluated patients pre- and post-catheter ablation with brain MRI at 3 Tesla and neurologic and neuropsychological testing. Short term outcomes from these evaluations were reported by Haeusler et al. in 2013 and demonstrated that new ischemic lesions occurred in 41% of all patients. (55) However, these brain lesions were not associated with cognitive dysfunction immediately post-procedure. Longer-term follow up was reported by Herm et al. in 2013. (56) At follow-up MRI at 6 months post-procedure, 31.3% of the acute brain lesions had formed a persistent glial scar. Similar to the short-term findings, there was no significant effect of either the ablation procedure or the presence of persistent brain lesions on attention or executive functions, short-term memory, or learning after 6 months.

Section Summary: Several large, database studies estimate the rate of adverse events from catheter ablation in the clinical care setting. The range of major adverse events in these studies is from 4-9%. Deaths have been reported and occur at rates less than 1%. Vascular complications at the groin site are the most common adverse events, occurring at rates of up to 5%. Serious cardiovascular adverse events such as tamponade and stroke occur uncommonly, at rates of approximately 1% or lower. There is some evidence that new ischemic lesions are commonly found on MRI post-procedure, but the clinical significance of these defects is unclear.

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers
In response to requests, input was received from 2 physician specialty societies (3 reviewers) and 2 academic medical centers while this policy was under review in 2011. While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted. While the input was mixed, there was general agreement with the policy statements. One reviewer commented that use of cryoablation may have a specific role when ablation targets are close to the AV node.

**Ongoing Clinical Trials**

A search of the website ClinicalTrials.gov on February 20, 2014, using the keyword “catheter ablation” and “atrial fibrillation” identified a large number of randomized comparative studies evaluating catheter ablation for atrial fibrillation that are currently enrolling patients. A sample of some of the representative studies are as follows:

- **Rhythm Control - Catheter Ablation With or Without Anti-arrhythmic Drug Control of Maintaining Sinus Rhythm Versus Rate Control With Medical Therapy and/or Atrioventricular Junction Ablation and Pacemaker Treatment for Atrial Fibrillation** (NCT01420393) – This study randomizes patients with heart failure with NYHA class II or II symptoms and paroxysmal or persistent atrial fibrillation to one of two groups: (1) rhythm control via catheter ablation with or without antiarrhythmic drug control to maintain sinus rhythm; or (2) medical therapy and/or atrioventricular junction ablation and pacemaker placement. Enrollment is planned for 1000 subjects; the planned study completion date is September 2016.

- **Catheter Ablation vs Anti-arrhythmic Drug Therapy for Atrial Fibrillation Trial (CABANA)** (NCT00911508) – This study randomizes patients with paroxysmal atrial fibrillation to left atrial ablation using a circular mapping catheter-guided ablation, antral isolation using a circular guided approach, or wide area circumferential ablation OR to drug-therapy based rate or rhythm control. Enrollment is planned for 2200 subjects; the planned study completion date is September 2017.

- **Clinical Evaluation of the Blazer Open-Irrigated Ablation Catheter for the Treatment of Paroxysmal Atrial Fibrillation (ZERO-AF)** (NCT01687166) – This study randomizes patients with symptomatic paroxysmal atrial fibrillation to the Blazer Open-Irrigated radiofrequency ablation catheter or and FDA-approved open-irrigated ablation catheter. Enrollment is planned for 472 subjects; the planned study completion date is December 2015.

- **CatHeter Ablation of perSistEnd Atrial Fibrillation: Pulmonary Vein Isolation Versus Defragmentation. The CHASE-AF Study** (NCT01580124) – This study randomizes patients with persistent atrial fibrillation to one of two pulmonary vein isolation strategies: (1) pulmonary vein isolation via catheter ablation alone; or (2) pulmonary vein isolation followed by atrial defragmentation and eventual linear ablation in case of atrial tachycardia aiming for acute restoration of sinus rhythm. Enrollment is planned for 150 subjects; the planned study completion date was November 2013. No results have been reported.

- **Multi-electrode PulmonarY Vein Isolation Versus Single Tip Wide Area Catheter Ablation for Paroxysmal Atrial Fibrillation (PAF) (MYSTIC-PAF)** (NCT01696136) – This study randomizes patients with paroxysmal atrial fibrillation to atrial fibrillation with a multi-electrode catheter to atrial fibrillation with a single-tip ablation catheter. Enrollment is planned for 120 subjects; the planned study completion date is December 2015.

- **Catheter Ablation for Recently Diagnosed Paroxysmal Atrial Fibrillation (CABAL)** (NCT01505296) – This study randomizes patients with recently diagnosed paroxysmal atrial fibrillation to catheter ablation or antiarrhythmic drug therapy. Enrollment is planned for 200 subjects; the planned study completion date was January 2014. No results have been reported.
TOCCASTAR - TactiCath Contact Force Ablation Catheter Study for Atrial Fibrillation (NCT01278953) – This study randomizes patients with paroxysmal atrial fibrillation to a catheter ablation with a contact force-sensing catheter or a standard ablation catheter. Enrollment is planned for 400 subjects; the planned study completion date was July 2013. No results have been reported.

Catheter Ablation vs. Standard Conventional Treatment in Patients With LV Dysfunction and AF (CASTLE-AF) (NCT00643188) – This study randomizes patients with paroxysmal or persistent atrial fibrillation, failure or intolerance of antiarrhythmic drug therapy, and left ventricular ejection fraction less than or equal to 35% to treatment with radiofrequency catheter ablation or conventional therapy. Enrollment is planned for 420 subjects; the planned study completion date is November 2019.

Ablation as First Line Treatment in Paroxysmal Atrial Fibrillation (AFLIT-PAF) (NCT01466842) – This study randomizes patients with paroxysmal atrial fibrillation who have no history of antiarrhythmic drug use to catheter ablation using cryothermic energy or antiarrhythmic drug therapy. Enrollment is planned for 160 subjects; the planned study completion date is January 2016.

Prospective Randomized Study on Clinical Effectiveness of Cavo-Tricuspid Isthmus Block in Patients With Paroxysmal Atrial Fibrillation (NCT02019407) – This study randomizes patients with paroxysmal atrial fibrillation to catheter-based pulmonary vein isolation or pulmonary vein isolation with cavo-tricuspid isthmus block. Enrollment is planned for 50 subjects; the planned study completion date is November 2015.

Summary

Results of randomized, controlled trials that compare radiofrequency ablation with antiarrhythmic medications report that freedom from atrial fibrillation is more likely following ablation compared with medications. Results of long-term follow-up of 5 to 6 years following ablation demonstrate that late recurrences continue to occur in patients who are free of atrial fibrillation at 1 year. However, the majority of patients who are atrial-fibrillation-free at 1 year remain atrial-fibrillation-free at 5 to 6 years. Rates of complications following ablation remain somewhat uncertain. Death is rare, and a 2013 systematic review including over 83,000 patients reported a major complication rate of 2.9%. Based on this evidence, radiofrequency ablation of the pulmonary veins is considered medically necessary for symptomatic paroxysmal or persistent atrial fibrillation, when antiarrhythmic medications have failed to adequately control symptoms.

Nonrandomized studies of cryoablation report success rates in the range seen for radiofrequency ablation, and the one randomized, controlled trial (RCT) suggests that cryoablation is more effective than medications. Two additional small RCTs compare cryoablation to radiofrequency ablation, but are limited by their short term follow up and by the comparison device used. In both of these studies, RFA had an unusually low success rate. As a result, it is not yet possible to determine whether outcomes of cryoablation are similar to that for radiofrequency ablation. Further randomized, controlled trials comparing the two techniques are currently underway. Thus, cryoablation of the pulmonary veins is considered investigational.

Repeat procedures are commonly within the first year after initial ablation and are associated with an incremental improvement in maintenance of sinus rhythm. These repeat procedures are of a more limited nature compared to the initial ablation, targeting specific areas where ablation may not be complete, and/or a focused ablation for treatment of post-ablation atrial flutter. These repeat procedures, generally up to 2 repeat ablations, may therefore be considered medically necessary.

Practice Guidelines and Position Statements
An expert consensus document on catheter and surgical catheter ablation for atrial fibrillation was developed jointly by 7 cardiac specialty societies (HRS, EHRA, ECAS, ACC, AHA, APHRS, STS) in 2012. (57) The following recommendations were made concerning indications for catheter ablation:

- Symptomatic AF [atrial fibrillation] refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication
  - Paroxysmal: Catheter ablation is recommended (Class I recommendation, Level of evidence A)
  - Persistent: Catheter ablation is reasonable (Class IIa recommendation, Level of evidence B)
  - Longstanding Persistent: Catheter ablation may be considered (Class IIb recommendation, Level of evidence B)

- Symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent
  - Paroxysmal: Catheter ablation is reasonable (Class IIa recommendation, Level of evidence B)
  - Persistent: Catheter ablation may be considered (Class IIb recommendation, Level of evidence C)
  - Longstanding Persistent: Catheter ablation may be considered (Class IIb recommendation, Level of evidence C)

In 2006, the American College of Cardiology published an update to their practice guidelines for the treatment of atrial fibrillation. These guidelines reflect the results of the rate versus rhythm controlled randomized studies. (7) Explicit recommendations are classed as I, IIa, IIb, or III. Class IIa is defined as: “the weight of evidence or opinion is in favor of the procedure or treatment.” The recommendations are further classified according to the type of data available. Class C data are defined as “expert consensus.”

The guidelines describe the use of ablation of the pulmonary vein (PV) and note that the “…technique of ablation has continued to evolve from early attempts to target individual ectopic foci within the PV to circumferential electrical isolation of the entire PV musculature.” Two specific recommendations regarding the use of catheter ablation were judged class IIa. These are 1) “It is reasonable to use ablation of the AV node or accessory pathway to control heart rate when pharmacological therapy is insufficient or associated with side effects. (Level of Evidence: B); and 2) “Catheter ablation is a reasonable alternative to pharmacological therapy to prevent recurrent [atrial fibrillation] in symptomatic patients with little or no [left atrial] enlargement. (Level of Evidence: C).”

The guidelines also encourage further research in this area given uncertainties in patient populations, technique, and outcome assessment. The authors state that “despite these advances, the long-term efficacy of catheter ablation to prevent recurrent [atrial fibrillation] requires further study.”

The American College of Physicians and American Academy of Family Physicians issued clinical practice guidelines in 2003 for patients with new-onset atrial fibrillation. (58) These guidelines state the majority of patients with new-onset atrial fibrillation should be treated with a pharmacologic rate control strategy and long-term anticoagulation. Similar to the American College of Cardiology/American Heart Association guidelines, this document does not include specific recommendations for catheter-based ablation techniques in their treatment algorithms.

**Medicare National Coverage**
None

**References**


8. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Catheter ablation of the pulmonary veins as a treatment for atrial fibrillation. TEC Assessments 2008; Volume 23 Tab 11.


45. Luik A, Merkel M, Hoeren D et al. Rationale and design of the FreezeAF trial: a randomized controlled noninferiority trial comparing isolation of the pulmonary veins with the cryoballoon catheter versus open irrigated radiofrequency ablation in patients with paroxysmal atrial fibrillation. Am Heart J 2010; 159(4):555-60 e1.
57. Calkins H, Kuck KH, Cappato R et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Developed in partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC) and the European Cardiac Arrhythmia Society (ECAS); and in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS), and the Society of Thoracic Surgeons (STS). Endorsed by the governing bodies of the American College of Cardiology Foundation, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, the Asia Pacific Heart Rhythm Society, and the Heart Rhythm Society. Heart Rhythm 2012; 9(4):632-96 e21.

Billing Coding/Physician Documentation Information
93656 Comprehensive electrophysiologic evaluation including transseptal catheterizations, insertion and repositioning of multiple electrode catheters with induction or attempted
induction of an arrhythmia with atrial recording and pacing, when possible, right ventricular pacing and recording, His bundle recording with intracardiac catheter ablation of arrhythmogenic focus, with treatment of atrial fibrillation by ablation by pulmonary vein isolation

93657 Additional linear or focal intracardiac catheter ablation of the left or right atrium for treatment of atrial fibrillation remaining after completion of pulmonary vein isolation (List separately in addition to code for primary procedure)

93799 Unlisted cardiovascular service or procedure

This new combination code is not to be used with any of the following CPT codes: 93279-93284, 93286-93289, 93462, 93600, 93602, 93603, 93610, 93612, 93618, 93619, 93620, 93621, 93653, or 93654.

Additional Policy Key Words
Pulmonary Vein Isolation

Policy Implementation/Update Information

<table>
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<tr>
<th>Date</th>
<th>Description</th>
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<tr>
<td>5/1/08</td>
<td>New policy; considered investigational.</td>
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<tr>
<td>1/8/2009</td>
<td>Interim update. Policy revised to include medically necessary statements effective 1/8/2009. Title changed from Pulmonary Vein Isolation as a Treatment of Atrial Fibrillation to Catheter Ablation of the Pulmonary Veins as Treatment for Atrial Fibrillation.</td>
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<tr>
<td>5/1/09</td>
<td>Policy statement revised to include medically necessary and investigational indications for a CTA related to catheter ablation of the pulmonary veins. The “and” between the 2 bullets in the policy statement will be changed “or.”</td>
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<tr>
<td>5/1/10</td>
<td>Specific information added to Considerations section regarding repeat procedures. Policy statement added that repeat procedures may be considered medically necessary in specific situations.</td>
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<tr>
<td>5/1/11</td>
<td>Policy statement regarding radiofrequency ablation unchanged; new statement regarding cryoablation as investigational added. The term “radiofrequency” is removed from the policy title; policy renamed.</td>
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<td>5/1/12</td>
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<td>5/1/14</td>
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