Catheter cryoablation of cardiac arrhythmias

Peter L. Friedman

Purpose of review
The purpose of the review is to provide an update on the safety and efficacy of catheter cryoablation.

Recent findings
Catheter cryoablation is a safe and clinically effective method for ablation of atrioventricular nodal reentrant supraventricular tachycardia. Although the acute procedural success rate of catheter cryoablation for this arrhythmia may be slightly lower than that reported for radiofrequency ablation, it has an excellent safety profile, with no reported instances of inadvertent atrioventricular block requiring implantation of a permanent pacemaker. Using this technology, one can perform reversible cryomapping, which helps to identify suitable ablation targets while identifying sites where cryoablation should be avoided. For patients with midseptal and parahissian accessory pathways, in whom the risk of producing inadvertent atrioventricular block is substantial, catheter cryoablation is a safe and effective alternative to radiofrequency ablation. Catheter cryoablation of common atrial flutter causes much less patient discomfort than radiofrequency ablation, with excellent acute and long-term efficacy. Catheter cryoablation also can be used to isolate the pulmonary veins during ablation of atrial fibrillation. As compared with radiofrequency ablation, the risk of acute thromboembolic complications and of pulmonary vein stenosis appears to be lower with cryoablation.

Summary
For many cardiac arrhythmias, catheter cryoablation is a safe and effective alternative to radiofrequency ablation. The ability to identify suitable ablation targets by reversible cryomapping is a particularly useful feature of this technology. Although the acute procedural success rate of cryoablation may not equal that of radiofrequency ablation in all circumstances, as catheter technology evolves it is likely that the efficacy of cryoablation will improve and the list of arrhythmias that can be treated with this method will expand.

Keywords
supraventricular tachycardia, atrial flutter, atrial fibrillation, accessory pathway, cryomapping, cryoablation, atrioventricular node

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Abbreviations

AV	atrioventricular
AVNRT	atrioventricular nodal reentry
RF	radiofrequency
SVT	supraventricular tachycardia

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Introduction

Radiofrequency (RF) catheter ablation is a safe, highly effective treatment for a wide array of cardiac arrhythmias and has become the standard against which all other ablation technologies are judged. Nonetheless, RF ablation does have important limitations that have spurred the search for alternative methods. RF energy causes disruption of the endothelium and of the underlying tissue architecture, which predisposes to thrombus formation and thromboembolism [1]. Excessive heating during RF application can lead to a sudden, unexpected impedance rise resulting in barotrauma and cardiac perforation. When RF energy is applied in or near pulmonary veins, dense fibrosis and contraction of the scar can lead to pulmonary vein stenosis [2]. Application of RF energy at some sites, such as the cavotricuspid isthmus, is quite painful. Finally, successful and safe ablation using RF energy requires accurate localization of the correct site of origin of the arrhythmia using conventional mapping techniques and anatomic landmarks. If the ablation target is near the compact atrioventricular (AV) node or His bundle, inaccurate localization of the target can lead to inadvertent AV block, necessitating the implantation of a permanent pacemaker [3].

Catheter cryoablation is a promising new technology that avoids some of the limitations inherent to RF ablation. Epicardial or endocardial application of cryoenergy using hand-held probes has long been used as an ablation method during cardiac surgery, yielding lesions that are transmural, sharply demarcated, noninflammatory, and minimally thrombogenic [4]. Now there are several commercially available percutaneous cryoablation catheters that enable one to deliver cryoenergy to the tip or the distal shaft of the catheter, thereby avoiding the need for cardiac surgery [5,6]. These devices all rely on the Joule-Thompson effect, whereby a refrigerant at high pressure, for example, liquid N_2O, flows down the central lumen of an injection tube and then evaporates at the tip of the catheter into the outer shaft at lower pressure, causing cooling of the catheter tip. The tip temperature can be precisely controlled by altering the rate of flow of refrigerant. Catheter tip temperatures of −30°C or slightly higher cause reversible suppression of local electrical activity useful for cryomapping, whereas tip temperatures of −60°C or less result in irreversible damage of the target tissue, the desired effect during cryoablation [7,8].

Cryomapping

Suppression of local cardiac electrical activity by cooling a site briefly to approximately −30°C can be used to predict whether cryoablation at that site will be effective at eliminating the ablation target. This type of cryomapping can be termed efficacy cryomapping. An example of efficacy cryomapping during catheter ablation of supraventricular tachycardia (SVT) due to AV nodal reentry (AVNRT) is illustrated in Figures 1 through 4. In this example, a patient with marked first-degree AV block (Fig. 1) and AVNRT was referred for ablation. Tachycardia was inducible only during infusion of isoproterenol (Fig. 2). Cryomapping at the target site caused temporary anterograde block in the slow pathway, rendering SVT noninducible (Fig. 3). As predicted by cryomapping, cryoablation at the same site permanently abolished SVT (Fig. 4). Similarly, efficacy cryomapping can be used to identify successful cryoablation sites during ablation of accessory pathways or ectopic foci [9•,10,11••]. Another type of mapping, termed safety cryomapping, can actually be performed either in cryomapping or cryoablation mode. With this approach, the effects of cryoapplication at a given site are closely monitored for the appearance of unintended consequences, such as the production of AV block (Fig. 5). When undesirable effects occur during cryomapping or cryoablation, the tissue is allowed to rewarm and the catheter is then moved to another mapping site. The utility of this approach is based on the observation that effects seen during cryomapping are typically reversible, as long as catheter tip temperatures are maintained at or above −30°C and the time of application is limited to less than 80 seconds. In a recent multicenter study, the electrophysiologic effects of cryomapping performed in this manner were completely reversible within seconds more than 80% of the time [12••]. Similarly, adverse effects that occur during cryoablation are also usually reversible if cryoapplication is halted promptly (Fig. 6). In contrast, the effects of RF are rarely reversible, which is why application of RF cannot be used as a catheter mapping technique.

Cryoablation of supraventricular tachycardia

Catheter cryoablation has been used successfully to treat patients with SVT caused by AVNRT, AV reentrant SVT caused by the presence of an accessory pathway (AVRT), atrial tachycardia, and to ablate the AV node in patients with atrial fibrillation and uncontrolled ventricular rates [6,8,11••,12••]. The most extensive experience has been in patients with AVNRT. In a recent large, multicenter prospective trial, the acute procedural success rate in this group was 93% in patients who had at least one qualifying cryoablation, with a very low rate of SVT recurrence for those patients in whom acute procedural success was achieved [12••]. Although this acute

Figure 1. Surface electrocardiogram leads II and V1 along with bipolar electrograms from the high right atrium (HRA), coronary sinus (CS), distal His bundle recording site (HISd), ablation catheter (ABL), and RV apex during sinus rhythm in a patient with marked first-degree atrioventricular (AV) block referred for ablation of AV nodal reentry.

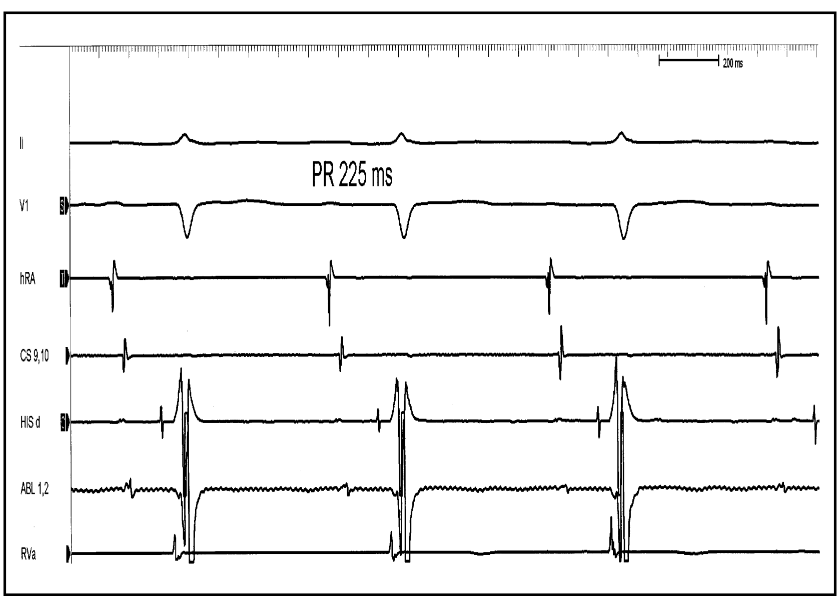
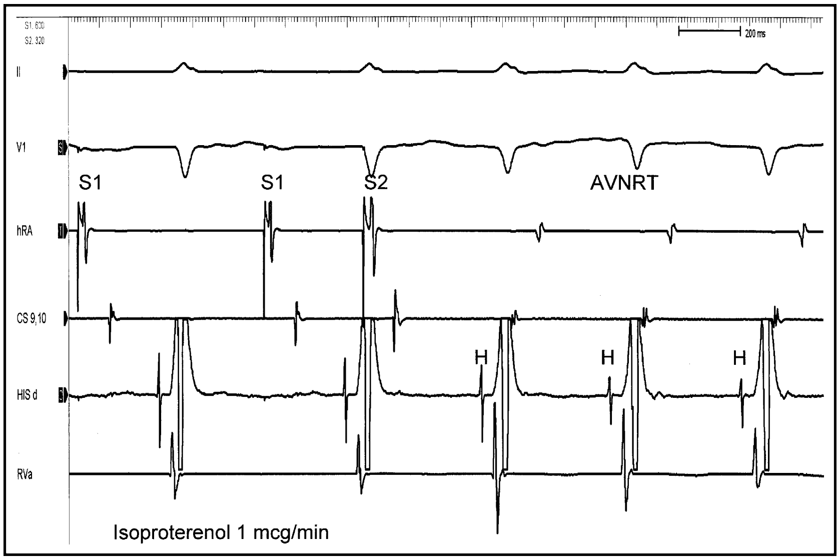


Figure 2. Programmed atrial stimulation during infusion of isoproterenol. During atrial pacing (S1), a single atrial premature stimulus (S2) induces sustained atrioventricular nodal reentry. H, His bundle deflections.



procedural success rate is somewhat lower than has been reported for RF ablation, it is worthwhile to remember that catheter cryoablation is still an emerging technology and that the handling characteristics of the presently available catheters are somewhat different than those of standard RF ablation catheters. As experience grows, it is likely that the acute procedural success rate of catheter cryoablation for AVNRT will approach if not equal that customarily seen with RF ablation. One point that has become clear is that, largely because of the ease and rapid reversibility of cryomapping, catheter cryoablation of AVNRT is an exceptionally safe procedure. World-wide experience in AVNRT has now exceeded several thousand patients without a single instance of inadvertent AV block necessitating the implantation of a permanent pacemaker having been reported.

Catheter cryoablation of accessory pathways, although successful in some patients, has been associated with a lower acute procedural success rate than cryoablation of AVNRT and a much lower acute procedural success rate than one would expect from RF ablation. In the multicenter "Frosty" trial, acute procedural success in patients who had accessory pathways and who had at least one qualifying cryoablation was only 77%, although the risk of recurrent SVT was gratifyingly low in patients who

Figure 3. Same patient as Figures 1 and 2, during cryomapping at the site of the slow atrioventricular (AV) nodal pathway. The atrial premature stimulus now blocks anterogradely in the slow pathway, preventing initiation of atrioventricular nodal reentry. An example of efficacy cryomapping. Note that the first-degree AV block of the first sinus beat after S2 has not worsened compared with the first-degree AV block present before cryomapping shown in Figure 1.

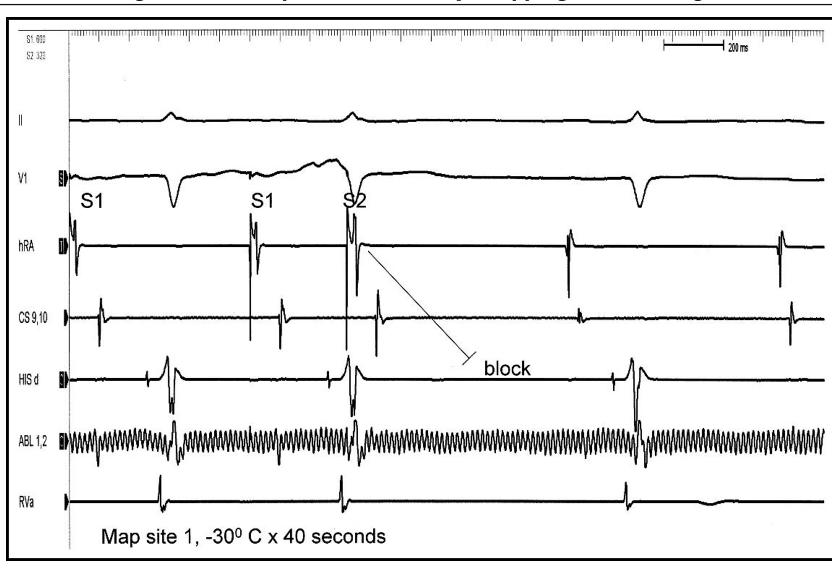
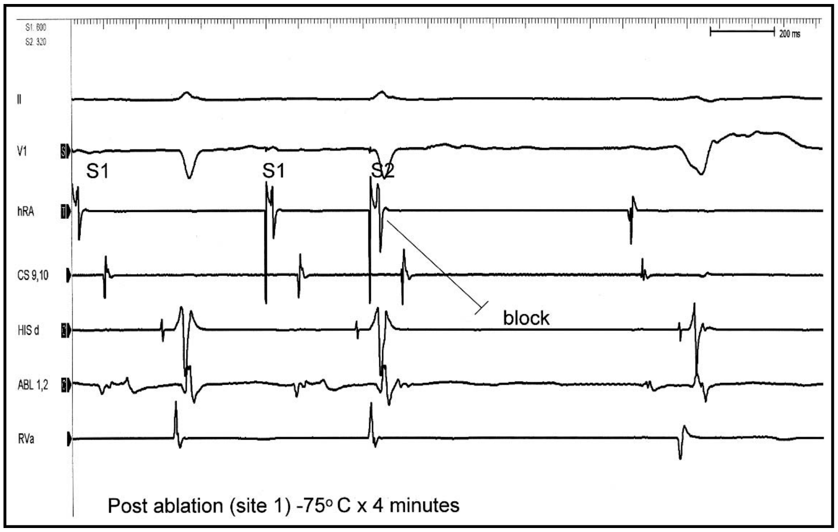


Figure 4. After cryoablation at map site 1 shown in Figure 3 and rewarming, programmed atrial stimulation now fails to induce atrioventricular nodal reentry because the atrial premature beat blocks anterogradely in the slow pathway.



had an acutely successful procedure [12••]. The explanation for the relatively low acute procedural success rate in patients with accessory pathways is not known, but may relate to the fact that cryoablation lesions affect a smaller volume of tissue than lesions made with an RF catheter of comparable tip size [13]. Because cryoablation lesions are more focused, they may need to be delivered extremely close to a small discrete target such as an accessory pathway to achieve success, whereas RF lesions may be effective even when delivered at some distance from the pathway.

Although catheter cryoablation may not be the ablation method of choice for accessory pathways in many locations, it is an effective and very safe alternative to RF ablation for septal accessory pathways located near the compact AV or His bundle. Three recent studies reported a total of 45 patients who had midseptal or parahissian accessory pathways and who underwent catheter cryoablation [9•,11••,14••]. Eighteen of these patients had failed a prior RF ablation attempt, either because of recurrent SVT after an apparently successful procedure or because the RF ablation procedure was halted before

Figure 5. Same organization of tracings as Figure 1, but in a different patient with atrioventricular nodal reentry, during cryoablation at the presumed site of the slow pathway. This site was too close to the compact atrioventricular (AV) node, and AV nodal block appeared during ablation.

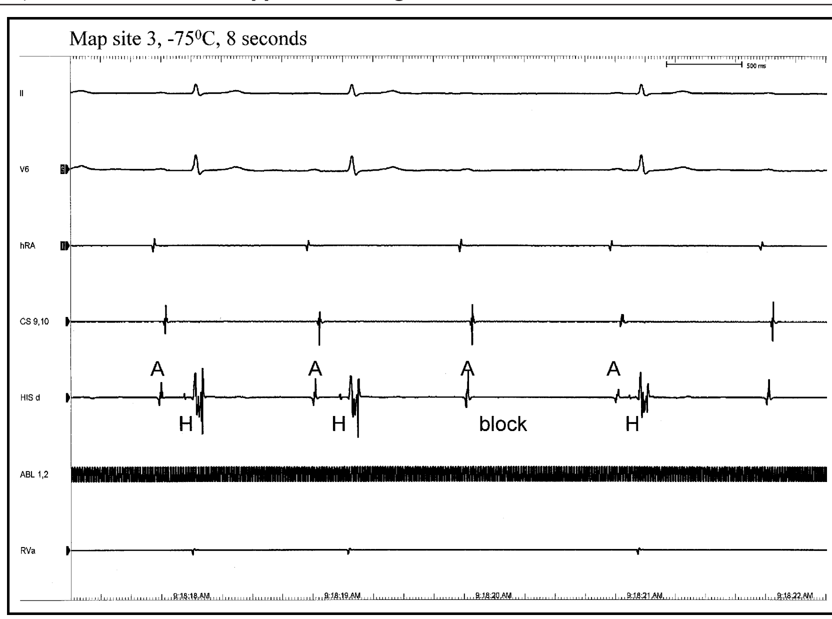
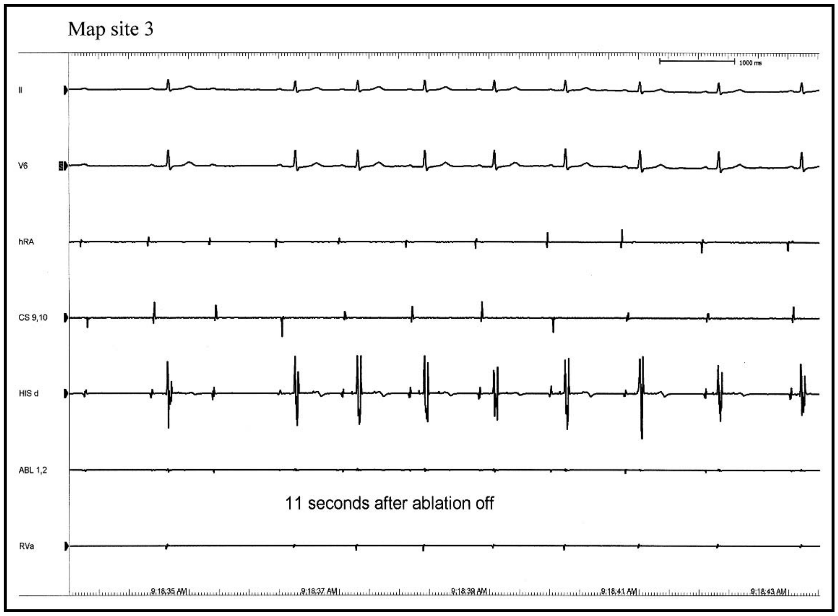


Figure 6. Same patient as shown in Figure 5. Atrioventricular nodal conduction resumes 11 seconds after stopping cryoablation, an example of safety cryomapping during cryoablation.



successful ablation as a result of threat to the normal conduction system during RF application. Cryoablation sites were chosen based on block in the accessory pathway during cryomapping without evidence of impaired AV nodal conduction, even though a His potential was frequently recorded at such sites. Cryoablation was acutely successful in 43 of 45 or 96% of these patients [9•,11••,14••]. SVT recurred in seven individuals, or 16% of the patients who had an acutely successful cryoablation procedure. Six of these patients underwent a second successful cryoablation [9•,11••,14••]. None of the 45 patients had permanent damage to the AV node or His bundle and none required implantation of a permanent pacemaker. Transient prolongation of the A-H interval or transient AV block observed during cryomapping or cryoablation always resolved quickly after interruption of the cryoapplication.

Permanent junctional reciprocating tachycardia, an orthodromic AV reentrant SVT in which a decrementally conducting concealed accessory pathway typically functions as the retrograde limb of the circuit, is another arrhythmia for which catheter cryoablation has been shown to be an effective and safe alternative to RF ablation [15••]. The accessory pathways in patients with permanent junctional reciprocating tachycardia often are located in the midseptal or posteroseptal regions, sometimes within the coronary sinus or middle cardiac vein. These last two locations are not ideal for RF ablation, because of proximity to the right or circumflex coronary arteries, which can be damaged by RF application, and because reduction of blood flow around the ablation catheter, particularly in the middle cardiac vein, increases impedance and limits RF delivery. Cryoablation may be a better alternative in such circumstances; the risk of coronary artery damage appears to be lower and reduction of blood flow around the catheter actually augments rather than hinders cryoablation.

Cryoablation of atrial flutter and atrial fibrillation

In patients with cavotricuspid isthmus–dependent right atrial flutter, RF catheter ablation has become the treatment of choice, offering a greater chance of freedom from recurrent arrhythmia and a better quality of life as compared with antiarrhythmic drug therapy [16]. However, RF application in the cavotricuspid isthmus frequently causes severe pain and, rarely, can damage the right or circumflex coronary artery, which courses beneath the isthmus in the AV groove [17,18]. Catheter cryoablation of the cavotricuspid isthmus is an alternative to RF ablation [6]. When the two methods were applied in a randomized fashion in a small group of patients, bidirectional isthmus block was achieved in 100% of patients with cryoablation and 97% of patients with RF ablation, a difference that was not statistically significant [19•]. Acute complications were not seen with either approach. Procedure duration and fluoroscopy times were also similar in the two groups, but patients undergoing cryoablation had a much lower perception of pain during the procedure as compared with RF ablation [19•]. During long-term follow-up, the recurrence rate of atrial flutter after an acutely successful cryoablation procedure was approximately 10% [20•]. This also compares favorably to the reported recurrence rate after successful RF ablation [16]. The safety and efficacy of catheter cryoablation of non-isthmus-dependent right or left atrial flutters or incisional atrial tachycardia have not yet been studied.

Catheter cryoablation can also be used to isolate the pulmonary veins during ablation of atrial fibrillation, and may help to avoid some of the complications seen after RF ablation in these patients, such as the development of pulmonary vein stenosis [21•]. Two approaches have been reported in clinical studies. One method is to use a cryoablation catheter that freezes only at its tip. Using such a catheter along with a circumferential mapping catheter deployed within the target vein, one creates point-by-point cryolesions aimed at the venoatrial connections until complete isolation of the vein has been achieved. This method achieves complete pulmonary vein isolation in a high proportion of patients [22••]. However, the method is laborious and is characterized by long fluoroscopy time and procedure duration [22••]. An alternative approach has been to use a deflectable circular-tipped self-expanding cryoablation catheter that freezes along a 64-mm distal segment of the shaft. The catheter is deployed in the target vein, expanded to ensure close apposition of the freezing segment with the vein wall, and then cryoablation is performed. A circumferential mapping catheter also deployed in the vein is used to determine when isolation has been achieved. Isolation of the vein using such a catheter can frequently be achieved with only a single cryoapplication [23•]. Accordingly, procedure duration and fluoroscopy times appear to be shorter using this approach [23•]. Clinical trials are presently under way to characterize better the safety and efficacy of pulmonary vein isolation using catheter cryoablation. However, it is noteworthy that thromboembolic complications and pulmonary vein stenosis have not been reported in any of the patients who have undergone this procedure thus far [22••,23•].

Conclusion

Cryoablation has come a long way in the past several decades since it was first applied to arrhythmia management during cardiac surgery. As cryoablation catheter technology evolves, it is likely we will see an ever-increasing array of devices with various tip sizes and configurations, capable of making lesions that are deeper, larger, and of different shapes. These changes in catheter design are likely to translate into greater safety and efficacy, as well as an expanded list of cryoablation targets. At present, most catheter cryoablation procedures have been directed at supraventricular arrhythmias, but it is likely that this approach will also have merit for ventricular arrhythmias. Idiopathic ventricular tachycardia (VT) arising from the right ventricular outflow tract, for example, can be effectively treated by RF ablation, but not without risk of barotrauma and perforation which, in rare cases, has proven fatal. Cryoablation may prove to be a safer alternative. Similarly, some idiopathic ventricular tachycardias arise from the coronary cusps, where RF application can damage nearby coronary arteries. This is another circumstance in which cryoablation may have an advantage. Cryomapping of scar-related ventricular tachycardia could be used to complement our present reliance on activation sequence and entrainment mapping when trying to localize ventricular tachycardia circuits. Cryoablation of arrhythmias arising from the epicardial surfaces of the atria or ventricles is another potentially fruitful avenue of exploration. Because the pericardial space is confined and devoid of circulating blood, cryoablation should be particularly effective in this environment. Indeed, epicardial cryoablation probes that can be placed percutaneously or with minimally invasive surgical techniques are presently being developed [24]. As recent studies clearly demonstrate, catheter cryoablation has become an important arrow in the interventional electrophysiologist's ablation quiver.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • Of special interest
- •• Of outstanding interest

1 Zhou L, Keane D, Reed G, et al.: Thromboembolic complications of cardiac radiofrequency catheter ablation: a review of the reported incidence, pathogenesis and current research directions. J Cardiovasc Electrophysiol 1999, 10:611–620.

2 Saad EB, Marrouche NF, Saad CP, et al.: Pulmonary vein stenosis after catheter ablation of atrial fibrillation: emergence of a new clinical syndrome. Ann Intern Med 2003, 138:634–638.

3 Calkins H, Yong P, Miller JM, et al.: Catheter ablation of accessory pathways, atrioventricular nodal reentrant tachycardia and the atrioventricular junction. Final results of a prospective multicenter clinical trial. Circulation 1999, 99:262–270.

4 Lustgarten DL, Keane D, Ruskin J: Cryothermal ablation: mechanism of tissue injury and current experience in the treatment of tachyarrhythmias. Prog Cardiovasc Dis 1999, 41:481–498.

5 Dubuc M, Talajic M, Roy D, et al.: Feasibility of cardiac cryoablation using a transvenous steerable electrode catheter. J Interv Card Electrophysiol 1998, 2:285–292.

6 Rodriguez LM, Geller JC, Tse HF, et al.: Acute results of transvenous cryoablation of the supraventricular tachycardia (atrial fibrillation, atrial flutter, Wolff-Parkinson-White syndrome, atrioventricular nodal reentry tachycardia). J Cardiovasc Electrophysiol 2002, 13:1082–1089.

7 Dubuc M, Roy D, Thibault B, et al.: Transvenous catheter ice mapping and cryoablation of the atrioventricular node in dogs. Pacing Clin Electrophysiol 1999, 22:1488–1498.

8 Skanes A, Dubuc M, Klein G, et al.: Cryothermal ablation of the slow pathway for the elimination of atrioventricular nodal reentrant tachycardia. Circulation 2000, 102:2856–2860.

9 • Gaita F, Riccardi R, Hocini M, et al.: Safety and efficacy of cryoablation of accessory pathways adjacent to the normal conduction system. J Cardiovasc Electrophysiol 2003, 14:825–829.

First reported series of patients with midseptal and parahissian accessory pathways to undergo successful catheter cryoablation, without damage to normal conduction system.

10 Theuns DAMJ, Kimman GP, Szili-Torok T, et al.: Ice mapping during cryothermal ablation of accessory pathways in WPW: the role of the temperature time constant. Europace 2004, 6:116–122.

11 •• Wong T, Markides V, Peters NS, et al.: Clinical usefulness of cryomapping for ablation of tachycardias involving perinodal tissue. J Interv Card Electrophysiol 2004, 10:153–158.

A small but well-described series of patients undergoing cryoablation near the compact AV node. Included patients with atrial tachycardia as well as accessory pathways.

12 Friedman PL, Dubuc M, Green M, et al.: Catheter cryoablation of supraventricular tachycardia: results of the multicenter prospective “Frosty” trial. Heart Rhythm 2004, 1–2:129–138.
•• The largest multicenter experience of catheter cryoablation for SVT, with emphasis on utility and reversibility of cryomapping.

13 Khairy P, Chauvet P, Lehmann J, et al.: Lower incidence of thrombus formation with cryoenergy lesions versus radiofrequency catheter ablation. Circulation 2003, 107:2045–2050.

14 Atienza F, Arenal A, Torrecilla EG, et al.: Acute and long-term outcome of transvenous cryoablation of midseptal and parahissian accessory pathways in patients at high risk of atrioventricular block during radiofrequency ablation. Am J Cardiol 2004, 93:1302–1305.
•• The largest single center experience reporting safety and efficacy of catheter cryoablation of midseptal and parahissian accessory pathways in a consecutive series of patients.

15 Gaita F, Montefusco A, Riccardi R, et al.: Cryoenergy catheter ablation: a new technique for treatment of permanent junctional reciprocating tachycardia in children. J Cardiovasc Electrophysiol 2004, 15:263–268.
•• First report of catheter cryoablation of this unusual form of SVT in a pediatric population. Demonstrated safety of cryoablation in the coronary sinus or middle cardiac vein.

16 Natale A, Newby KH, Pisano E, et al.: Prospective randomized comparison of antiarrhythmic therapy versus first-line radiofrequency ablation in patients with atrial flutter. J Am Coll Cardiol 2000, 35:1898–1904.

17 Hindricks G: Complications of radiofrequency catheter ablation of cardiac arrhythmias. Eur Heart J 1993, 14:1644–1653.

18 Ouali S, Anselme F, Savoure A, et al.: Acute coronary occlusion during radiofrequency catheter ablation of typical atrial flutter. J Cardiovasc Electrophysiol 2002, 13:1047–1049.

19 Timmermans C, Ayers GM, Crijns HJGM, et al.: Randomized study comparing radiofrequency ablation with cryoablation for the treatment of atrial flutter with emphasis on pain perception. Circulation 2003, 107:1250–1252.
• Only randomized study published directly comparing efficacy of RF ablation and cryoablation. This study clearly demonstrated greater patient comfort with cryoablation.

20 Manusama R, Timmermans C, Limon F, et al.: Catheter-based cryoablation permanently cures patients with atrial flutter. Circulation 2004, 109:1636–1639.
• Study showing that long-term rate of recurrence of atrial flutter after acutely successful catheter cryoablation was equivalent to RF ablation.

21 Avitall B, Lafontaine D, Rozmus G, et al.: The safety and efficacy of multiple consecutive cryo lesions in canine pulmonary veins-left atrial junction. Heart Rhythm 2004, 1:203–209.
• Report of experiments in dogs with cryoablation balloon inflated in pulmonary veins that demonstrated feasibility of electrical isolation of the veins and absence of any acute evidence for pulmonary vein stenosis.

22 Tse HF, Reek S, Timmermans C, et al.: Pulmonary vein isolation using transvenous catheter cryoablation for treatment of atrial fibrillation without risk of pulmonary vein stenosis. J Am Coll Cardiol 2003, 42:752–758.
•• First report in a large series of patients undergoing pulmonary vein isolation with a percutaneous 10-F catheter. This study demonstrated that pulmonary vein isolation was possible by applying spot cryolesions, using pulmonary vein potentials as the cryoablation target. There were no reported instances of pulmonary vein stenosis during long-term follow-up with this approach.

23 Wong T, Markides V, Peters NS, et al.: Percutaneous isolation of multiple pulmonary veins using an expandable circular cryoablation catheter. Pace 2004, 27:551–554.
• Single case report using new 7-F deflectable circular cryoablation catheter to isolate pulmonary veins, suggesting greater ease of producing electrical isolation and shorter procedure duration with this approach.

24 Doll N, Meyer R, Walther T, et al.: A new cryoprobe for intraoperative ablation of atrial fibrillation. Ann Thorac Surg 2004, 77:1460–1462.