Cryoablation of Septal Accessory Pathways: Learning While Freezing

Walter F. Kerwin, MD, Division of Cardiology, Section of Cardiac Electrophysiology, Cedars-Sinai Medical Center and the David Geffen School of Medicine at UCLA, Los Angeles, California

Septal accessory pathways provide the invasive electrophysiologist with serious challenges, particularly in the case of para-Hisian or mid-septal insertion sites.
Although radiofrequency energy has demonstrated efficacy in the elimination of accessory AV pathway conduction, it has also been associated with a non-trivial risk of heart block at septal and para-Hisian sites[1]. Because of these concerns, many EP labs, including our own, have concluded that cryoablation is the preferred modality for the mapping and elimination of septal accessory pathways. The advantages of cryoablation in this setting are well reported[2,3], and include the potential for reversing an induced AV block[4], the adherence of the catheter tip to the endocardium with freezing, and more discrete and controllable lesion formation[5]. The following two cases (concealed para-Hisian pathway and mid-septal WPW) illustrate techniques and observations from our laboratory that may be useful to others gaining experience with cryoablation.

Case 1

The patient is a 41 year-old woman with a lifelong history of supraventricular arrhythmias, first documented at the age of 8. She has been treated with various medications in the past, including inderal and atenolol, which proved ineffective in preventing the arrhythmia. As a child, she learned specific maneuvers that were effective in terminating the arrhythmia, such as laying supine and holding her breath. In the months prior to admission, she had several emergency room visits documenting the arrhythmia. In the first visit, a narrow-complex tachycardia was noted at a heart rate of 200 bpm and terminated with a single bolus of adenosine. She was discharged from the emergency department on atenolol 25 mg per day, only to re-present 3 days later, again with SVT. Adenosine was once again used to terminate the arrhythmia, however it was observed that several APCs following the termination re-triggered the arrhythmia and a second bolus of adenosine was required. In all instances, the arrhythmia was characterized as narrow complex with p-wave in the mid-ST segment and with a fixed RP interval.

A diagnostic EP study was performed using standard catheters (quad HRA, octapolar HIS, decapolar injectable-lumen CS, and quad RV). The baseline ECG was normal with no ventricular pre-excitation observed during the study. SVT was easily initiated with single atrial extra-stimulus or ventricular extra-stimulus and frequently during the study with simple catheter induced APCs. Figure 1 illustrates the effects of a single PVC given during His bundle refractoriness to advance atrial activation. A concealed septal accessory pathway participating in orthodromic AVRT was the presumptive diagnosis.

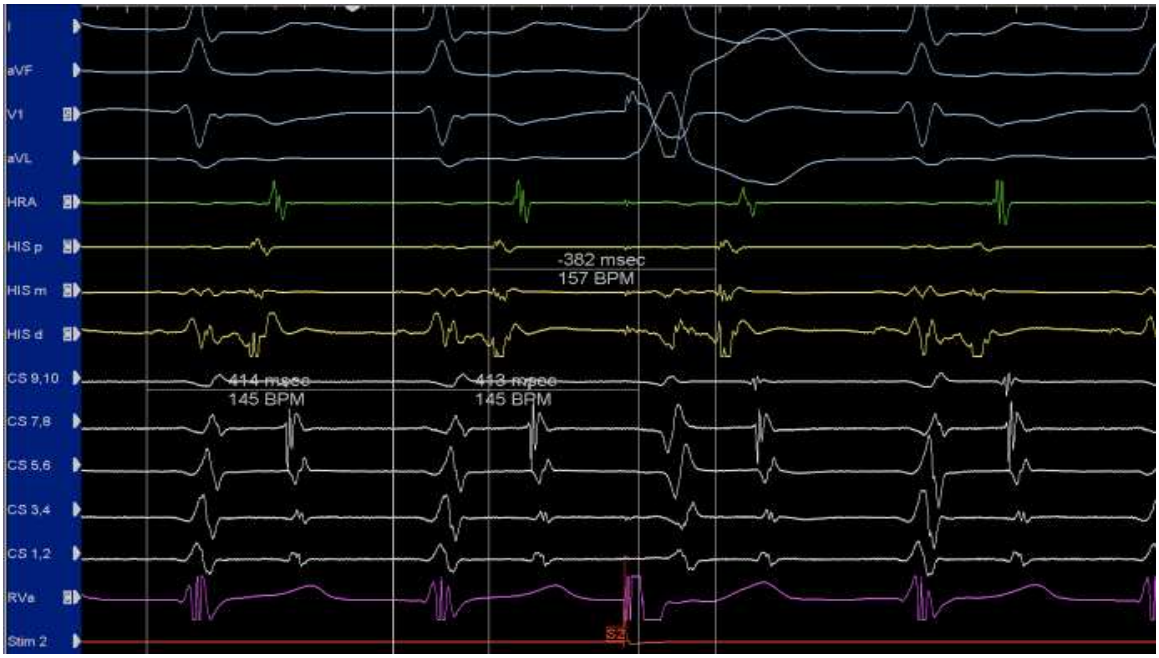
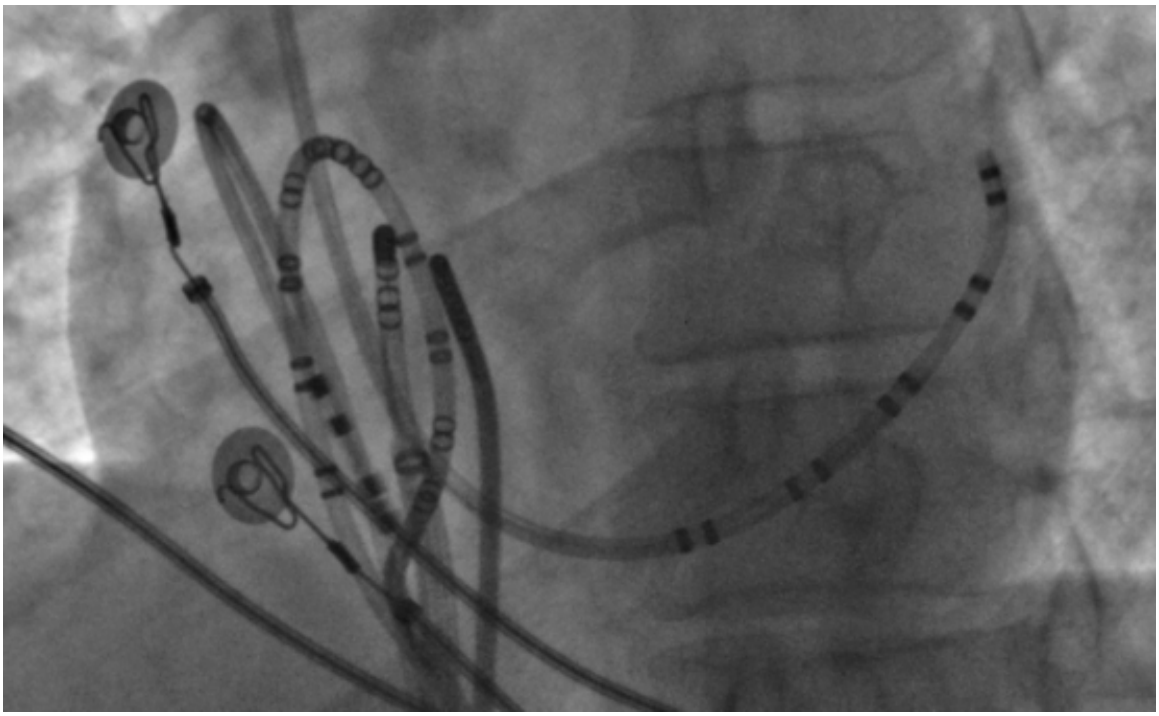
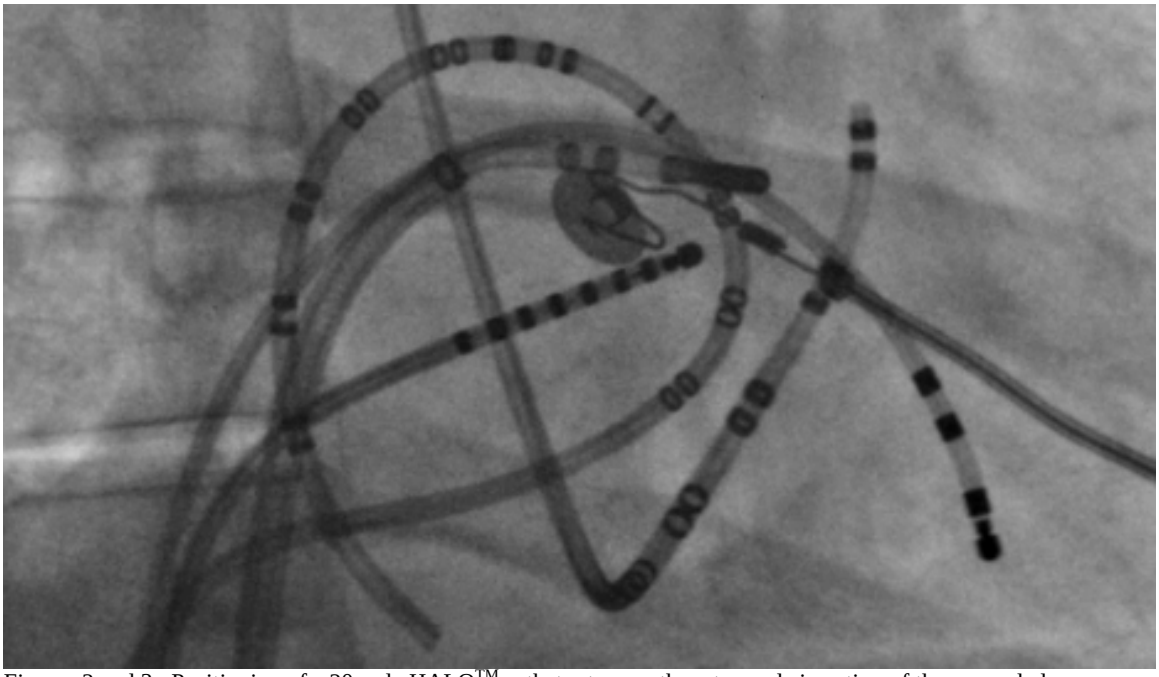


Figure 1: 41 year-old female with lifelong history of SVT. Short RP tachycardia, cycle length 414 ms. A late cycle (His refractory) PVC advances the subsequent atrial activation by 31 msec; the retrograde activation sequence remains unaltered. Findings during EP study consistent with orthodromic AV-reentrant tachycardia using a concealed para-Hisian accessory pathway. Antegrade AP conduction was not observed.

A 20-polo circular mapping catheter (HALO-XP™ Biosense-Webster, Diamond Bar, CA) was used to map the retrograde insertion of the accessory pathway during orthodromic tachycardia. Figures 2 and 3 illustrate the positioning of the HALO™ catheter, the His bundle catheter, and a 6-mm tip cryoablation catheter (FREEZOR EXTRA™, CryoCath, Inc., Kirkland, Quebec) along the septal aspect of the tricuspid annulus.





Figures 2 and 3: Positioning of a 20-pole HALO™ catheter to map the retrograde insertion of the concealed accessory pathway during AVRT. Figure 2 illustrates LAO 39 degree projection of the HALO catheter, with the His bundle catheter (octapolar) just inferior to the 6-mm tip FREEZOR EXTRA™ (CryoCath, INC, Kirkland, Quebec) cryo-ablation catheter. Figure 3 is the RAO 39 degree projection of the same catheters. The FREEZOR EXTRA™ catheter is positioned over the tightest coupled VA signal during AVRT, just millimeters superior to the His bundle.

Figure 4 shows corresponding intracardiac electrograms, with tightest VA coupling at poles 13,14 of the HALO catheter; the cryoablation catheter is positioned just anterior to poles 13,1and stabilized along the tricuspid annulus with an 8F guide sheath (Swartz-SRO™, St Jude Medical, Woodland Hills, CA).

Figure 4: Cryo-application during AVRT, with termination of arrhythmia within the first 15 seconds of injection (prior to ice ball formation). Upon termination of the arrhythmia, antegrade conduction is clearly observed down the His bundle, and the cryo-application is continued for 4-5 minutes. Early time to effect (AP annihilation, in this case) is a good sign, and pathway conduction did not return.

A single cryo-application was initiated with the FREEZOR EXTRA™ at this location, and as shown in Figure 4, termination of the tachycardia was achieved rapidly (less than 15 seconds), before complete ice-ball formation obscured the distal ablation electrocardiogram. Despite close proximity to the His bundle, antegrade conduction was observed to be stable along the His catheter throughout a single 4 minute consolidation freeze. Following delivery of the lesion and subsequent thawing, ventricular pacing was performed, documenting VA dissociation and arrhythmia non-inducibility. The patient has been symptom free for approximately one year since the ablation.

Several aspects of this case warrant discussion, particularly as to how cryoablation facilitated success in what might otherwise have been a very high-risk case for permanent AV block. To begin with, the close proximity of the accessory pathway to the His bundle would have rendered radiofrequency ablation during tachycardia unthinkable. Even if the RF catheter had been in the identical location, the first beat following termination of tachycardia might have revealed complete AV block that in all probability would be irreversible. The retrograde-only conducting properties of this accessory pathway would have mandated mapping during tachycardia or during adenosine infusion with ventricular pacing (probably impractical); ventricular extra-stimulation mapping would likely have resulted in retrograde fusion or induction of orthodromic tachycardia. In any event, ablation during sinus rhythm, particularly with RF, would multiply the risks to the patient, as serial lesion formation would likely be necessary with repeat testing to determine efficacy. The advantages of cryoablation, as illustrated in this case are several-fold. Because the biological effects on electrical conduction occur early during the cryo-thermal application (between 32 degrees C and 0 degrees C), an early *time to effect* to eliminate pathway conduction suggested that the lesion was accurately localized. The property of catheter tip to tissue adherence was capitalized upon to prevent the catheter tip from 'jumping' following termination of the tachycardia, and allowed for consolidation of the lesion at the accurate location with a 4 minute freeze at –85 degrees C. Importantly, it must be noted that given less favorable circumstances, the AV node or His bundle might have been the first structures eliminated during cryo-application. Because irreversible cryo lesions require that the target tissue achieve and maintain temperatures below 0 degrees centigrade, the operator must pay attention to antegrade conduction throughout lesion formation and be prepared to thaw immediately. Our experience with the 6-mm and 8-mm tip CryoCath ablation catheters for routine AV node reentry cases has given us confidence in the reversibility of transient heart block, and when observed, is usually preceded by a Wenkebach conduction pattern.

Case 2

The patient is a 19 year-old male with asymptomatic Wolff-Parkinson White syndrome. The abnormal ECG pattern was noted during monitoring for a recent dental procedure, and he was subsequently referred for further consultation and management recommendations. He has been active in cross country running and track during high school, and is currently pursuing a strength training program during his leisure time. He has no history of syncope, pre-syncope, chest pains or palpitations. He was advised of a small, nevertheless non-trivial risk of sudden arrhythmic death associated with the WPW syndrome, mostly in the setting of atrial fibrillation, and the findings from a recent clinical study of a relative risk reduction with catheter ablation of the accessory pathway in terms of preventing future arrhythmia or sudden cardiac death[6]. After discussion with the patient and his parents regarding relative risks and alternatives, the patient consented to undergo EP study and cryoablation of his accessory pathway. Figure 5 illustrates the 12 lead ECG pattern of ventricular pre-excitation, most notable for a brisk V1-V2 R-wave transition and a superior delta wave axis in the inferior leads, consistent with a mid-septal insertion.

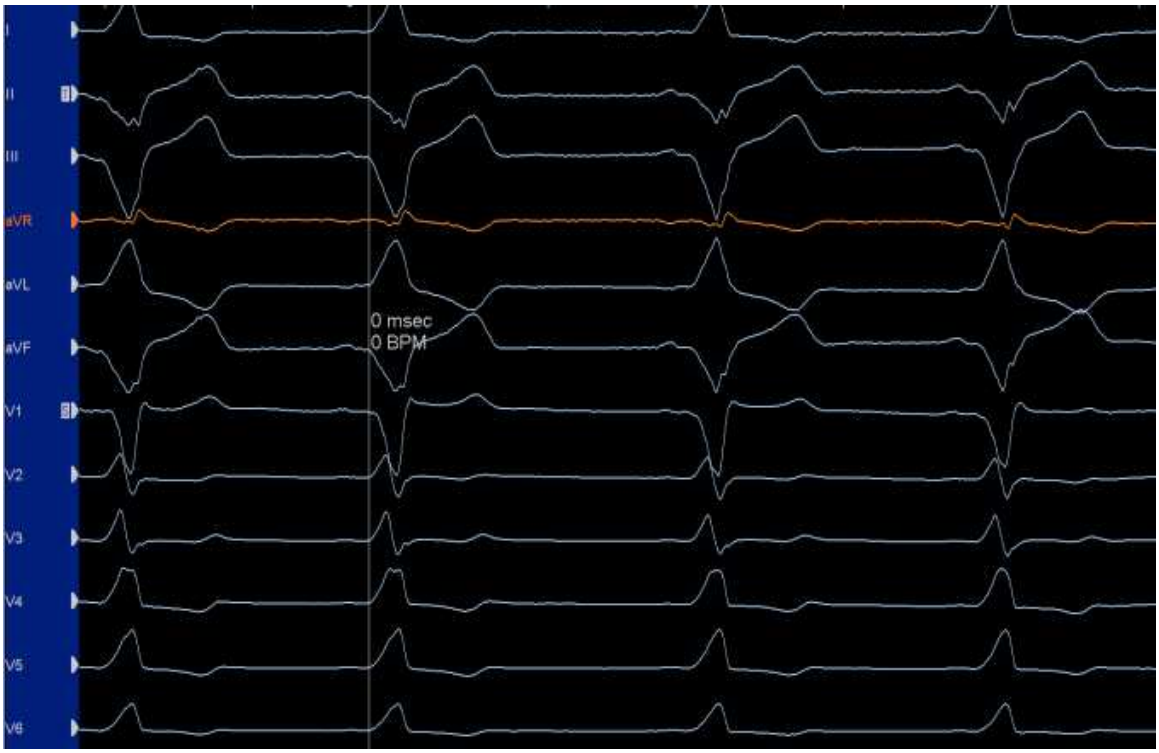


Figure 5: 19 year-old male with Wolff-Parkinson-White syndrome. Antegrade pre-excitation is manifest at baseline, with intrinsic negative delta waves in the inferior leads and V1-V2 transition in the precordial leads, consistent with a mid-septal accessory pathway.

Diagnostic EP study demonstrated the following: baseline HV interval 0 msec; AP antegrade block cycle length 300 msec, AP antegrade ERP 600/320 and 500/300; AP retrograde ERP 600/350. Orthodromic tachycardia, cycle length 290 msec, induced with atrial premature beats. Atrial fibrillation was induced with atrial pacing at 250 msec, was sustained and hemodynamically stable. The patient was cardioverted to sinus rhythm with a synchronized 100-joule biphasic shock.

A similar approach was incorporated for the mapping of this patient's accessory pathway as in Case 1, except that mapping of the antegrade insertion of the pathway was feasible in this case. Because of the negative delta wave in lead II, a coronary sinus venogram (not shown) was performed via the decapolar CS catheter (CSL™, St. Jude Medical, Woodland Hills, CA). There was no coronary sinus diverticulum, and mapping for earliest annular ventricular electrogram between the His bundle and coronary sinus ostium with a 6-mm tip FREEZOR EXTRA™ catheter suggested pathway insertion in the mid-septal region. A 20-pole HALO™ catheter was once again deployed to provide longitudinal discrimination of the pathway insertion along the tricuspid annulus. Figure 6 shows the intracardiac activation sequence during sinus rhythm; note that the octapolar His catheter was confirmed in the His bundle location during A1A2 pacing at AP ERP. The earliest antegrade ventricular electrocardiogram on the HALO™ catheter appears to lie between poles 8 and 9, and the ablation catheter records what appears to be a clearly definable pathway potential.

Serial cryo-applications were performed using the 6-mm tip FREEZOR EXTRA™ catheter at the site illustrated in figure 6, impressively without success. The technique of *fast mapping*, a term referring to the time to effect on pathway conduction of less than 30 seconds, is relevant to the 6-mm and 8-mm tip CryoCath ablation catheters as currently available in the US market (the 6-mm tip FREEZOR EXTRA™ available in Europe employs the proprietary CryoMapping mode, in which sub-maximal and reversible lesion applications are employed prior to a consolidating lesion at maximum negative temperatures).

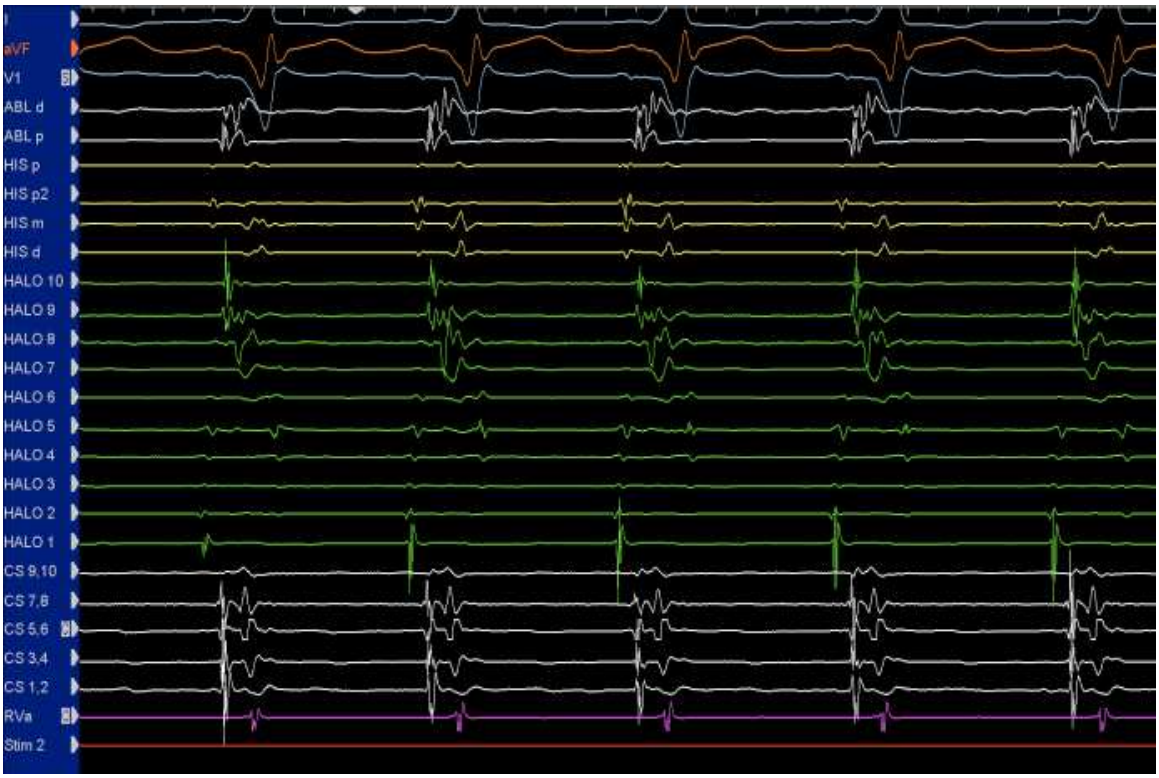


Figure 6: Intracardiac electrocardiograms recorded during sinus rhythm, with 20-pole Halo catheter positioned to map antegrade insertion of accessory pathway. Note that earliest ventricular electrogram was recorded between HALO^{TM} poles 8 and 9, and presence of accessory pathway potential on distal ablation catheter.

Fast mapping was utilized in this case, however despite the presence of the apparent AP potential, no effect was observed on the pathway conduction after 7 lesions, including several lesions of over 1 minute in duration. Parameters relevant to an early time to effect (< 30 seconds) include distance of the conducting tissue from the advancing arc of cooling (dynamic thermal gradient) and the relative dimensions of the conducting pathway; catheter tip to tissue non-adherence may lead to a failure to achieve maximum negative temperatures, however the console issues an alarm in such instances. High flow across the tricuspid annulus may also have contributed to failure to achieve pathway block with the 6-mm tip cryoablation catheter, due to the heat sink of the blood pool limiting tissue cooling. With mapped electrograms as good as were observed in this case, we hypothesized that the pathway was located deeper in the mid-septal fat, and elected to size up to the 8-mm tip FREEZOR MAX™ (CryoCath, Inc., Kirkland, Quebec).

Figure 7 illustrates the positioning of the 8-mm tip FREEZOR MAX™ at the site of successful accessory pathway elimination, with corresponding intracardiac electrocardiograms shown in figure 8. Re-assessment of our mapping technique was performed, including re-initiation of orthodromic tachycardia with confirmation of the antegrade and retrograde insertions of the accessory pathway using the 20-pole HALO™ catheter. The retrograde insertion of the pathway during orthodromic tachycardia appeared to be displaced more superiorly, toward the His bundle and nearest to pole 8 of the HALO^{TM} catheter. Initial cryo application to this site with the FREEZOR-MAX™ resulted in a time to effect (pathway elimination) of just under one minute, and the lesion was consolidated with a 5-minute freeze at –85 degrees C. Not surprisingly given the relatively lengthy time to effect (approximately 60 seconds), pathway conduction was noted to recover upon thawing.

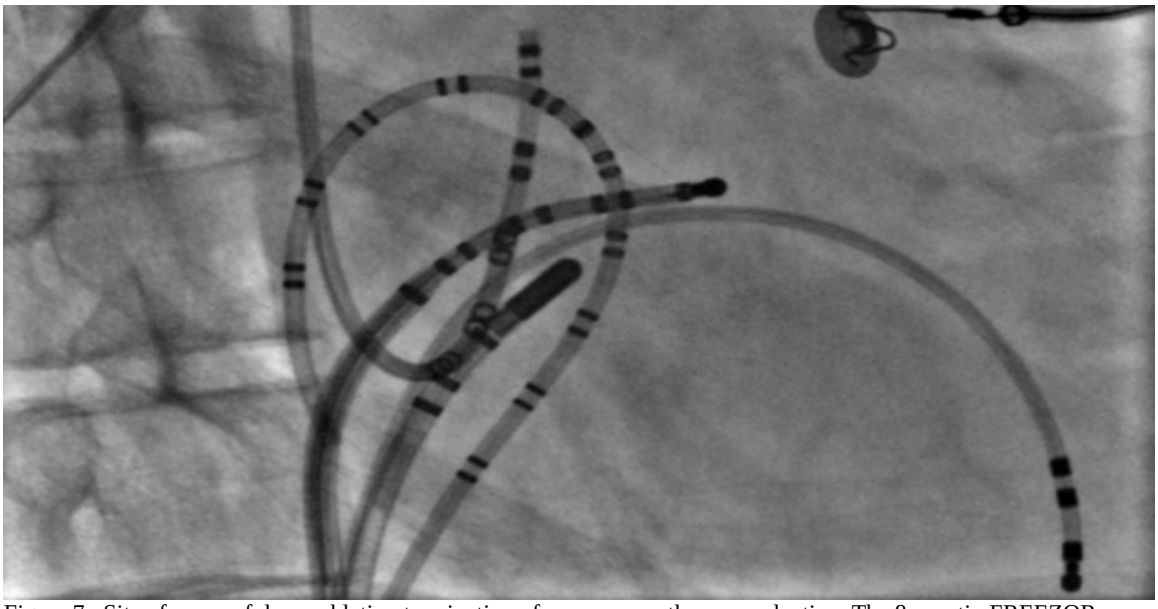


Figure 7: Site of successful cryoablation termination of accessory pathway conduction. The 8-mm tip FREEZOR-MAX™ catheter is positioned just nearest to HALO™ pole 8 along the tricuspid annulus, inferior to the octapolar His bundle catheter. Interestingly, this site mapped as the tightest coupled VA electrogram during orthodromic tachycardia.

A second cryo application was subsequently performed at the identical location, shown in Figure 8, with a time to effect of 7 seconds. The effects of the second cryo-lesion are observed in the first 4 beats to result in a progressive and definitive elimination of accessory pathway conduction, and a consolidating freeze was performed for 5 minutes at –85 degrees C; the pathway conduction never returned. Note that the interference on the distal ablation electrode is a consequence of ice-ball formation on the bipolar electrocardiogram, and is usual and expected; interference of a similar nature is often observed on targeted reference catheters. The extent of the lesion generated by the 8-mm FREEZOR MAX™ catheter is significant, as demonstrated by truncation of the atrial electrogram at HALO™ pole 8.

Figure 8: Elimination of accessory pathway conduction during cryoablation. Note the fuzzy interference on the distal ablation catheter, indicative of growing ice ball formation on the catheter tip as ablation temperature achieves a maximum –85 degrees C. A second lesion delivered at the same location (freeze-thaw-freeze cycle) resulted in a time-to-effect of less than 10 seconds, and following a 5-minute cryo-application, the pathway was permanently eliminated.

DISCUSSION

The two cases presented here are illustrative of some of the unique advantages of cryoablation technology, as well as some of the specific differences between cryoablation and radiofrequency ablation. Cryoablation represents a new paradigm for the interventional electrophysiologist, and there is a definite learning curve associated with applying cryobiology to achieve effective results. Unlike radiofrequency ablation, where large lesions are achieved almost immediately and permanently, lesion formation with cryoablation is progressive over time. The physical properties of the *dynamic thermal gradient*, in which a slowly expanding arc of tissue cooling results in transient effects on electrical conduction at regions less than 32 degrees C, and permanent electrical effects (ablation) at regions held below 0 degrees C, should always be kept in mind when applying cryo lesions. With the 6-mm and 8-mm tip cryoablation catheters available in the US market (CryoCath, Inc., Kirkland, Quebec), a technique of *fast mapping* is employed. This term simply refers to the fact that these catheters deliver the liquid nitrous oxide at a maximum flow rate from the onset of injection; there is a time dependent descent to maximum negative temperatures (usually –80 to –85 degrees C) that typically occurs in the first 20 to 30 seconds. Biological effects occurring in this time frame (elimination of pathway conduction, for example) are good signs of proximity to the structure being ablated, and continuing the injection for 4 minutes will generally lead to permanent ablation. Conversely, failure to achieve biological effects within the first 30 seconds suggests that the ablation site may be inaccurate, and that further mapping is warranted[2]. *Time to effect* is a more generic term, and is used as a measure of time to onset of the biologic effect following initiation of the nitrous injection.

In Case 1, for example, a nearly immediate *time to effect* was achieved to terminate orthodromic tachycardia (less than 15 seconds), suggesting close proximity of the cryoablation tip to the accessory pathway. Had AV block been observed in the first beats following termination, an immediate thaw cycle would likely have been effective in reversing the block, as it is necessary to maintain temperatures at sub-zero for a period of minutes to effectively ablate tissue. Because cryo-induced pathway interruption was presumed to be the mechanism for tachycardia termination, a consolidating lesion was performed for 4 minutes, resulting in permanent annihilation of pathway conduction.

By contrast, in Case 2 none of the sites mapped with the 6-mm catheter resulted in an early *time to effect*, despite what appeared to be outstanding target sites for ablation. In what amounts to be the cryoablation corollary to “learning while burning”, this case required “learning while freezing”. We hypothesized a deeper course of the pathway as it crossed the AV groove in the mid-septum, and that the inefficacy with the 6 mm tip cryoablation catheter was a function of inadequate lesion depth. Had this been a radiofrequency ablation case, the impulse might have been to increment up to a cool-tip or saline-perfused catheter for deeper penetration; probably not a good idea in such close proximity to the AV-node and His bundle. We elected to size-up to the 8-mm tip cryoablation catheter to achieve the goal of deeper lesion formation. With the first cryo application using the 8-mm tip catheter, the *time to effect* was just under 60 seconds, consistent with convergence of the *dynamic thermal gradient* with the accessory pathway. Despite a 5-minute cryo lesion, the pathway was observed to recover conduction over the first minute of thawing. Rather than move the catheter to a new location, a second lesion was performed at the same location, resulting in a nearly instantaneous *time to effect* of just under 7 seconds; a consolidating lesion applied at –85 degrees C over 5 minutes resulted in permanent annihilation of pathway conduction. This phenomenon, in which a repeat lesion is performed following a thaw cycle leading to an earlier time to effect and a more permanent interruption of electrical conduction, has been coined a *freeze-thaw-freeze cycle* by the cryoablation community. The implication of the *freeze-thaw-freeze cycle* is that deeper lesion formation is facilitated following the initial lesion and subsequent osmotic cellular lysis during thawing[7]. The biophysics of this phenomenon is a topic of ongoing investigation, however the cryo-ablationist may wish to capitalize on the *freeze-thaw-freeze cycle* to achieve better long-term outcomes.

CONCLUSIONS

For accessory pathways located in the septal location, the safety margin facilitated by croablation has raised the EP community standard of care. The unique aspects of cryo lesion formation, including potential for reversibility, tissue adherence, preservation of

underlying tissue architecture and diminished thrombus formation[7], will likely expand the role of cryoablation for this substrate and other regions of the heart where collateral tissue injury is a concern. Improvement in outcomes for individual operators will depend on increased experience and understanding of cryo lesion formation.

REFERENCES

1. Calkins H, Yong P, Miller J, 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.
2. Gaita F, Riccardi R, Hocini M, et al. Safety and efficacy of accessory pathways adjacent to the normal conduction system. *J Cardiovasc Electrophysiol* 2003;14:825-829.
3. Miyazaki A, Blaufox AD, Fairbrother JPS. Cryo-Ablation for septal substrates in pediatric patients. *J Am Coll Cardiol* 2005:45:581-588.
4. Rodriguez L, Leunissen J, Hoekstra A, et al. Transvenous cold mapping and cryo-ablation of the AV node in dogs: observations of chronic lesions and comparison to those obtained using radiofrequency ablation. *J Cardiovasc Electrophysiol* 1998;9:1055-61.
5. Skanes AC, Dubuc M, Klein GJ, et al. Cryothermal ablation of the slow pathway for the elimination of atrioventricular nodal reentrant tachycardia. *Circulation* 2000;102:2856-60.
6. Pappone C, Santinelli V, Manguso F, et al. A randomized study of prophylactic catheter ablation in asymptomatic patients with the Wolff-Parkinson-White syndrome. *N Engl J Med* 2003 Nov 6;349(19):1803-11.
7. Lustgarten DL, Keane D, Ruskin J. Cryothermal abltion: Mechanism of tissue injury and current experience in the treatment of tachyarrhythmias. *Progress in Cardiovascular Diseases,* Vol. 41, No. 6 (May/June), 1999: pp 481-498