How to perform cryoablation for atrioventricular nodal reentrant tachycardia

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Introduction

Atrioventricular nodal reentrant tachycardia (AVNRT) is the most common narrow complex tachycardia encountered in clinical practice [1]. AVNRT is more common in women (70–78%) than in men. It is also not infrequently encountered in pediatric population [2–4]. Mechanisms of this tachycardia are well understood and effective ablative techniques have been developed. The selective elimination of one of the dual AV nodal conducting pathways with preservation of AV nodal conduction was first reported by Pritchett et al. [5] in the surgical AVNRT era. Pioneered in the early 1990’s by Jackman et al. [5], radiofrequency (RF) ablation currently offers high success rates but is not free of complications. In a multicenter trial of RF catheter ablation (RFCA), the success rate for AVNRT ablation was 97% with a 5% recurrence rate [2]. In this series, ablation was associated with 1% risk of complete heart block plus a 2% chance for developing a conduction problem not requiring pacemaker implantation [2]. Older age of patients as well as presence of structural heart disease increased the risk for developing complete heart block [2]. Additional inherent limitations of RF energy-based ablation include sudden excessive heating associated with an increase in impedance and subsequent “steam pop” and tissue barotrauma. Furthermore, RFCA ablation results in endothelial destruction, which can increase the risk for thrombus formation on the endocardial surface of the ablation lesion [6].

Catheter cryoablation (CCA), conversely, offers several unique advantages over RFCA, including an ability to map without formation of permanent lesions (or at least large permanent ones), and catheter stability during the ablation. During a cryoablation lesion an ice ball forms and the catheter is frozen and fixed to the tissue preventing dislodgement or movement. The corollary of this fact is that manipulation of the catheter can be only done when temperature returns to physiologic temperature, otherwise it may theoretically result in perforation or other tissue injury. Lesions created with CCA are well demarcated and endothelial injury is minimal resulting in a lower thrombotic potential [6–8]. Cryoablation was initially used in a surgical approach to AVNRT ablation and provided a high success rate [9–13]. Subsequently, percutaneous catheter based techniques were developed for the same purpose. These catheters depend on the Joule-Thompson effect for chilling the tip [14]. The cryoablation catheter has 2 lumens, one used to deliver compressed nitrogen oxide refrigerant that expands in the catheter tip and another one for evacuation of the decompressed refrigerant. Nitrogen oxide delivery and thus tip temperature is controlled during the ablation by the console. For the mapping modality the temperature is maintained at no colder than –30°C. For the purpose of ablation the temperature is lowered to –70°C to –80°C for 2 to 4 min. Catheter-based cryoablation has been shown to be effective in ablation of atrial flutter, atrial fibrillation, AVNRT and accessory pathways located near the His bundle [6, 15–19]. This technology can be safely used also in unusual locations when application of RFCA may not be feasible or safe including the coronary sinus and middle cardiac vein [20, 21].
In our lab we use CCA frequently for ablation of AVNRT, especially in children, and essentially exclusively for ablation of anteroseptal and midseptal, accessory pathways. One advantage of CCA of AVNRT over RFCA lies in the ability to continue an isoproterenol infusion during ablation. In this paper we will provide a detailed description of our technique for CCA of AVNRT.

**Mechanisms of cryoablation lesion formation**

CCA works by several effects. The first effect is an extracellular one with freezing application of cryotherapy. There is development of extracellular ice, also called the solute effect injury, which occurs at –20°C. This leads to escape of water from the intracellular space to the extracellular space since extracellular water is tied up in ice. The second effect occurs at temperatures of about –40°C at which point intracellular ice begins to develop resulting in injury to the intracellular organelles. The third effect is a vascular injury with cessation of blood flow due to freezing and with thawing further injury with return of some blood flow [14]. As with other energy sources such as RF energy, there is a gradient of injury due to a gradient of temperature. Cryoablation’s effects can vary from reversible (especially if only slight, brief cooling occurs), to permanent (with longer and/or lower temperature applications), or in some cases even progressive due to vascular and other injuries after the conclusion of the low temperature application.

**Patient preparation and procedure**

In our EP laboratory we routinely use a three to four catheter setup for supraventricular tachycardia ablation. We place a 5 F nondeflectable decapolar coronary sinus (CS) catheter from right internal jugular vein or a 6–7 F deflectable, octapolar or decapolar from the right femoral vein approach (operator dependent). Other catheters placed include His and right ventricular (RV) catheters and sometimes a separate RA catheter. The RV catheter is repositioned to the right atrium for right atrial pacing at some point as well if a separate RA catheter was not placed. Once the arrhythmia is induced and mapped we exchange the RV (or RA) catheter for the ablation catheter. To improve catheter stability and maneuverability we routinely use a long sheath (such as SR-0, St. Jude Medical, California). We prefer using the medium curve 6-mm cryoablation catheter (CryoCath, Kirkland, QE) in adult population. Although the ability to cryomap is currently lost with a larger tip catheter as opposed to the 4-mm one, the 6-mm one creates bigger lesions and allows for fewer applications possibly shortening the procedure. Outside the U.S., cryomapping with the 6-mm catheter is possible due to regulatory and approval differences. If patients are only inducible during the isoproterenol infusion we continue it during the CCA since we can achieve superb catheter stability during the freeze. Maintaining isoproterenol infusion during CCA also allows for rapid testing of ablation effectiveness without the need for isoproterenol washout should there be need for additional lesions. With radiofrequency we typically stop isoproterenol prior to ablation to maximize catheter stability and minimize catheter movement, which may cause permanent atrioventricular (AV) block; after a potentially successful lesion characterized by accelerated junctional rhythm, we reevaluate inducibility after restarting isoproterenol; oftentimes the sequence of washout and re-initiation must be repeated two or more times.

The following case illustrates our typical approach. The patient is a 74-year-old male with history of pause-dependent polymorphic ventricular tachycardia, treated with an implanted defibrillator. He had experienced an episode of narrow complex tachycardia that was associated with near syncope and hypotension. Device interrogation did not disclose any additional information since his tachycardia fell below the detection rate of the device. The patient was brought to the electrophysiology lab for an EP study with possible ablation. Dual AV nodal physiology was present at baseline. After infusion of 0.5 mcg/kg/min of isoproterenol AV nodal echo beats were present and finally tachycardia was induced with single premature extrastimuli delivered from the CS catheter (Fig. 1A, B). Concentric retrograde activation was present on the coronary sinus catheter and the shortest VA time noted was 33 ms, consistent with AVNRT (Fig. 1C). The tachycardia was entrained with right ventricular pacing and a VAV response was present, again consistent with AVNRT (not shown) [22, 23]. The RV catheter was then exchanged for a 6-mm Freezor CCA catheter (CryoCor, Kirkland, Quebec, Canada). The ablation catheter was positioned with fluoroscopy guidance in 4:30 o’clock position on the tricuspid annulus to maintain an approximately 2:1 ratio of ventricular to atrial signal. Pacing of the proximal pole of the CS catheter was started with drive CL of 550 ms and premature beats at 270 ms, which consistently resulted in fast pathway block with conduction over slow pathway. With fluoroscopy control the
cryotherapy application started and when the temperature dropped to −70°C fluoroscopy was no longer used to monitor position of the catheter since it became adherent to the tissue. This lesion was ineffective since the premature beat was still conducted despite application of cryothermy. The application then was terminated and catheter repositioned slightly higher on the TA at approximately the 4:00 position. Typically cryoablation is delivered for a 4-minute lesion if an effect is noted in terms of loss of the jump, echo beats or inducibility; if no desired effect is observed the lesion is typically terminated prematurely after about 60 s. The pacing continued and another lesion was applied. Again, slow pathway block did not occur. The lesion was terminated and catheter repositioned to a 3:30 position. Since no block in slow pathway was observed the lesion was terminated. It is our usual strategy to give lesion located progressively superior on TA if no effect was seen. We very rarely place lesions above the 3:00 position with RFCA and usually not with CCA either. Another technique has been described before, however, in which lesions and placed even higher on TA until PR prolongation or Wenckebach block is seen. At this time decision was made to reposition catheter to 3:30 position, but this time with more clockwise rotation to facilitate better contact (Fig. 2A). We continued pacing with slow pathway conduction evident (Fig. 2B) and this time 20–30 s after cryothermy application block in slow pathway became apparent, an indication of effectiveness of the lesion (Fig. 2C). One needs to be skeptical of an effect of the lesion later (more than 30–60 s) into the ablation since it is more likely to reverse with re-warming. Subsequently, another four (consolidation) lesions were applied around successful lesion, each lasting 4 min. Please note that the extrastimulus testing of slow pathway and fast pathway function continued throughout the entire time as well as isoproterenol infusion. After these lesions were delivered multiple attempts were made at tachycardia induction without success, and only single echo beats were present. After 30 min of waiting time the procedure ended. This case illustrates well that when CCA is used no junctional beats are seen during the ablation. The operator needs to be alert for AV block or non-physiological PR prolongation during sinus rhythm or pacing during the cryoablation and terminate the lesion immediately; block can occur during cryoablation even when it does not happen during cryomapping because the ice ball and freezing temperature gradients extend further with the lower catheter temperatures achieved. If retrograde block during termination of AVNRT (as opposed to antegrade, slow pathway termination), or at any time in sinus or paced rhythm if antegrade block or an increase in the PR interval is observed the cryoablation should be immediately discontinued. We perform atrial pacing at an increased rate but at a rate exhibiting stable fast pathway conduction (e.g., 100–120 bpm) during CCA to allow earlier recognition of undesirable compact node or fast pathway effect (Fig. 3).
Special considerations for AVNRT cryoablation in the pediatric population

The mechanism of SVT in children appears to have an age-dependent distribution. AV nodal re-entrant tachycardia accounts for 5% of SVT in children less than 1 year of age, approximately 25% of SVT in children who are between 1 and 5 years, and 31% of SVT in children more than 10 years of age [24]. Radiofrequency catheter ablation is a well-established therapy for most supraventricular tachycardias in children [25, 26]. Because of the smaller heart size relative to the ablation lesion size, however, the theoretical risk of injuring cardiac structures is higher in small children [27]. RFCA for AVNRT carries a risk for ablation-induced AV block [28]. A body weight of less than 15 kg was reported as an independent risk factor for AV block during RFCA [29]. Transvenous CCA of AVNRT has recently become available as an alternative with ability to deliver smaller, well-defined lesions [30] and to “cryomap” and reverse potential loss of AV nodal conductivity [16]. The property whereby the catheter becomes adherent to the myocardial tissue surface during cryoablation (cryoadherence) allows reassessment of tachycardia inducibility without discontinuation of isoproterenol infusion.

Figure 2. A. Left anterior oblique fluoroscopic image of cryocatheter position for successful cryolesion, as well as coronary sinus catheter and His bundle catheter; B. Conduction down the slow pathway during initiation of cryoenergy; C. Block in the slow pathway during delivery of cryoenergy.

Figure 3. A. High grade AV block during cryoablation; cryoablation was halted; B. Normal conduction (which had resumed in about 15–30 s). No further conduction block was observed clinically in this patient. Note that if cryoablation had not been promptly terminated permanent AV block would have been very possible.
The initial pediatric experience [31] reported equivalent safety of cryoablation, but lower acute success rate (83% for AVNRT) and higher recurrence rates (9–14% at three months of follow up) when compared to RFCA performed in large multicenter trials. Explanations suggested for the lower success rate and higher recurrence rate included a stiffer cryoablation catheter, learning curve in proficiency of cryoablation and smaller lesion size using the 4-mm cryocatheter tip. Collins et al. [32] retrospectively compared acute success rate and late outcome in 117 patients treated with cryoablation and RFCA at a single center. They reported acute success rates of 95% for CCA and 100% for RFCA. Recurrence rates at 1 year after an initially successful procedure were 8% for CCA vs. 2% for RFCA; their analysis did not disclose a statistically significant difference likely secondary to low statistical power (i.e., a possible Type II error). No permanent heart block occurred with either RFCA or CCA. Transient AV block occurred in similar proportions in both groups (10% for RFCA and 11% for CCA). However, a larger sample study would be necessary to optimally compare CCA to RFCA [33].

The technique for AVNRT cryoablation in children is evolving. In our EP lab a diagnostic electrophysiologic study is performed first, using antegrade and retrograde extrastimulus and decremental stimulation. We position a catheter in the coronary sinus as well as the RA, His and RV catheters from the outset. Sometimes the RA catheter is only used briefly to rule out a right sided accessory pathway with differential pacing, and then moved to the RV, with the remainder of atrial stimulation delivered through the coronary sinus catheter. If AVNRT is induced, the RV catheter is removed leaving only the His and CS catheters, and a 7 F quadrripolar deflectable cryoablation catheter with either a 4-mm or 6-mm tip electrode (CryoCath Technologies Inc., Montreal, Canada) is advanced to the right atrium through an 8 F SRO sheath (St. Jude Medical, California). We feel that limiting the catheters present during the ablation or when not needed reduces the chance of perforation to an even lower value. A 6-mm or 4-mm Cryo-tip is used according to the patient size with a 6-mm tip being used progressively more frequently as experience increases in both adults and in children; currently, we are comfortable using the 6-mm tip in patients larger than about 35 kg. The ablation catheter is placed in the area of the slow AV nodal pathway by an anatomic and electrophysiologic approach, positioning the catheter at about the level of the coronary sinus orifice or 4:00 in the left anterior oblique (LAO) view (in the superior or cranial aspect of the posterior septum) with a small atrial and large ventricular potential [34]. As most pediatric catheter ablations, especially age under 16, are performed with general anesthesia in our center, controlled ventilation is usually used at the initiation of a cryothermal lesion to maximize catheter stability by minimizing respiratory motion with apnea until the catheter is fully adherent to the myocardium. Occasionally, due to motion with the cardiac cycle (or respiration if apnea is not used), the catheter will adhere more superiorly or more inferiorly than desired and the lesion is terminated. Cryotherapy is applied during sinus rhythm at baseline (without isoproterenol) if AVNRT is inducible in this state, whereas if isoproterenol is needed for tachycardia induction the ablation is performed while continuing the isoproterenol infusion. Fluoroscopy is not needed after catheter adherence, limiting fluoroscopy time, which is especially critical in young patients. During cryotherapy, beginning after a temperature of about −60°C to −70°C is achieved and the catheter has become adherent, repeat atrial extrastimulus testing is conducted to document a change in AV nodal slow pathway conduction and lack of AVNRT inducibility. If using the 4-mm cryocatheter, we use the cryomapping mode to check for AV block during sinus rhythm or pacing and to look for a loss of slow pathway conduction prior to initiating the lower temperature cryoablation lesion. Cryoablation is delivered for a 4-minute lesion if an effect is noted in terms of loss of the jump, echo beats or inducibility; if no desired effect is observed the lesion is typically terminated prematurely after about 30–60 s. The peak nadir temperature achieved varies according to catheter contact and other factors and is usually −70°C to −75°C. One to three subsequent cryoablation lesions are placed by moving the catheter slightly superior to the initial site.

If ablation has been performed without isoproterenol and the tachycardia is rendered noninducible, isoproterenol is then begun to confirm the finding. If the initial lesion or lesions are unsuccessful the catheter is undeflected slightly, and moved more superiority (anteriorly in prior conventions) [35] to about 3:30 in the LAO view. Sequentially, ablation is continued slightly more superiority to about 3:00. If lesions in this region do not eliminate inducibility lesions are placed at about 3:30 with a larger atrial potential than with the first few CCA lesions, and, if necessary, sequentially at the mouth of and just inside the CS, inferior to the CS os at 4:30–5:00 with a larger V than A potential. If after...
one or more lesions the tachycardia remains inducible, catheter contact is checked, a different sheath used and consideration for ablation slightly higher at about 2:45 on the tricuspid annulus or even on the left mid-to posterior-septum although this is rarely needed.

Complications of cryoablation include those seen with RFCA except steam pops (which are not seen often with 4 mm RF catheters usually used for slow pathway modification), and include: hematoma, thromboembolism, cardiac tamponade, AV block, and very rarely: valvular injury, stroke, myocardial infarction or death. Coronary artery injury can be a serious complication, particularly when ablating within coronary sinus and coronary veins but is probably even less likely with cryoablation.

The gold standard to assess successful ablation is tachycardia noninducibility. Unlike with RFCA, junctional acceleration cannot be used as a marker for ablation success [16, 33, 36]. Aiming for complete elimination of slow pathway conduction versus modification of conduction, wherein only a single atrial echo is noted and not a second conducted impulse down the slow pathway, remains a controversy. Practically, we try to eliminate slow pathway conduction but do not perform more risky superior midseptal ablation (above about 3:00) if we have eliminated inducibility but have residual single atrial echoes in either children or adults.

However, in the pediatric as well as the adult population, AVNRT is sometimes noninducible, especially when the procedure is performed under general anesthesia or with deep sedation. If there is evidence of clinically documented, definite AVNRT (previously induced AVNRT at a prior procedure or a 12-lead ECG with pseudo r-prime wave for instance), some investigators have proceeded and we would as well proceed with AV nodal modification [37]. The endpoint for AV nodal modification using cryoablation in the situation of noninducibility remains a challenge. Ablation in the case of AVNRT noninducibility is easier if a jump, echo beats or PR interval greater than stimulus-stimulus interval is reproducibly found, but if none of these are found the ablation if performed will be empiric and without endpoint. Collins et al. [32] demonstrated that elimination of PR interval longer than RR, a marker of slow pathway conduction, after ablation was a useful surrogate for successful cryoablation as it was demonstrated for RFCA success as well [38]. They also demonstrated significant shortening of the maximal AH interval achieved with both atrial extrastimulus and incremental pacing in 35 children who underwent cryoablation for treatment of AVNRT. This was a consistent finding, observed in those with classically defined dual AV node physiology as well as those with continuous AV conduction curves.

Some centers perform ablation during sustained AVNRT, monitoring for tachycardia termination as a sign of potentially successful ablation. Importantly, while a break of AVNRT points to an effect and a good lesion location, termination does not usually equate with success allowing procedural termination. Although this approach carries the theoretical risk of AV nodal injury secondary to inability to continually assess antegrade AV nodal conduction, in reality when the AVNRT terminates one can ascertain whether block occurred in the slow or fast limb of the circuit and also monitor the antegrade fast pathway function immediately after the termination. If retrograde block (or even R-P prolongation) in AVNRT, or antegrade block or a non-physiological increase in the PR interval is observed the cryoablation should be immediately discontinued.

Prolongation of fast pathway ERP during successful cryolesions has been demonstrated [39]. Further studies will be needed to assess questions like how much of the AH prolongation can be tolerated during the cryolesion and how to determine success in patients with a continuous AH curve (i.e., absence of jump). Additional data on procedural success and freedom from long-term recurrence, especially with the 6 mm catheter and increased operator experience, viewed in comparison with RFCA will be helpful. While it is clear that AV block can occur with CCA of the slow pathway, confirmation of the rate being lower than for RFCA, especially with the 6-mm catheter would be beneficial.

**Conclusions**

Cryoablation offers an attractive alternative to RFCA for AVNRT with clear advantages in certain populations. The techniques are similar to those used for AVNRT but certain aspects differ, including inability to move the catheter during the lesion (cryoadherence), absence of junctional beats during ablation and (in most cases) reversibility of unintended AV nodal injury as discussed above.

**References**

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