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Cryoablation for atrioventricular nodal reentry tachycardia: Role of “mapping” and “pseudo-mapping”



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The goal of catheter ablation is to create lesions that would cause local tissue destruction and thus eliminate or modify arrhythmia substrate. This is commonly accomplished by changing cellular temperature at two extremes by either heating or cooling with radiofrequency (RF) and cryothermal energy respectively. Both RF and cryoablation technologies are widely available. It is because of the “curative” outcome that catheter ablation therapy approach has become preferred, standard and guidelines recommended treatment modality for almost all types of supraventricular tachycardias (SVTs) including atrioventricular nodal reentry tachycardia (AVNRT) [1,2]. Both RF and cryoablation have significant differences in their biophysical mechanisms, efficacy and safety profile. Usage of RF and cryo ablation among electrophysiologists also differ significantly. The majority of pediatric electrophysiologists prefer cryoablation over RF for ablation of SVT, particularly AVNRT, in children. On the other hand, most adult electrophysiologists use cryoablation as an alternative to RF ablation, a practice which is even considered to be in accordance with the current practice guidelines [3]. Success and failure of ablation of any arrhythmia depends largely on detailed, meticulous, accurate and precise mapping based on the electrophysiological properties and characteristics of all components responsible for the genesis and perpetuation of arrhythmia. Furthermore, the role of mapping techniques to identify optimal location for application of curative ablation lesions in case of ablation of AVNRT in all age groups cannot be overemphasized given the potential risk of permanent and irreversible atrioventricular (AV) conduction block needing a lifelong pacemaker. In this regard, since cryoablation has an ability to demonstrate the functionality of prospective ablation sites without inducing permanent injury it has distinct advantage over RF ablation [4]. Conventionally, one could perform “ice mapping” or “cryomapping”, at temperature around -30° Celsius (C) before proceeding to “cryoablation” by application of cryothermal energy to cool down temperature around -80° C to create an effective tissue lesion. In many countries, available technology allows cryomapping part of the procedure with 4 mm and 6 mm tip

catheters (Freezor, CryoCath, Montreal, Canada), but in the USA cryomapping can be performed only with 4 mm tip catheters. This has led many US operators to either abandon using 6 mm tip catheter, or modify their approach when ablating AVNRT. In the current issue of the journal, V.K. Moondra and colleagues describe their approach in which “pseudo-cryomapping” was utilized during cryoablation of AVNRT [5].

In an attempt to perhaps understand complexities of “cryomapping” and “pseudo-cryomapping”, informative discussion regarding basic and currently understood biophysics of cryoablation and clinical evolution of cryoablation is noteworthy. During cryoablation, permanent tissue injury is induced by formation of ice crystals initially within the extracellular matrix followed by intracellular as cells are rapidly cooled to freezing temperatures. Among the intracellular organelles, mitochondria are particularly sensitive to ice crystals and are the first structures to suffer irreversible damage. The cell death occurs further from intracellular hyperosmolality and desiccation. When freezing is discontinued, the ablated tissue passively returns to body temperature, resulting in a “thawing effect.” This important aspect of cryoablation, in fact, causes the intracellular crystals to expand resulting in more cellular destruction. The size and density of ice crystals are dependent on proximity to the cryoenergy source, the local tissue temperature, the rate of freezing, electrode size and its orientation.

The safety and efficacy of cryoablation for SVTs was reported in a large multicenter randomized prospective trial, the “Frosty” trial [6]. The majority of study cohort comprised of patients with AVNRT, and they were the ones who showed statistically highly significant ($p < 0.001$) acute success rate of 91%, compared to 69% for those with accessory bypass tract mediated AV reentry and 67% for those requiring AV nodal ablation for atrial fibrillation. Subsequently, several randomized trials comparing cryoablation with RF ablation specifically for AVNRT, and their meta-analyses have shown equivalent acute success rate, albeit with a higher rate of recurrence during long-term follow-up [7–10]. One such meta-analysis of 14 studies that included 5 prospective randomized and 9 observational studies with 2340 patients showed that after a median follow-up of 10.5 months, freedom from recurrent AVNRT was achieved in 96.5% in the RF group, and in 90.9% in the cryoablation group (OR = 0.40, 95% CI 0.28 to 0.58, $P < 0.001$) [9]. Similar results of high acute success but recurrence even beyond 4 years have been shown in a large cohort of patients undergoing cryoablation for AVNRT [10]. In these trials even larger tip (6 and 8 mm) catheters besides regular 4 mm tip catheters were used, and yet there have been no reports of permanent AV block requiring implantation of permanent pacemakers in spite of transient and variable AV block seen during cryoablation procedure. Credit for such impeccable

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safety record of cryoablation is attributed to “cryomapping”, the technique which in its conventional manner has been well-described and is performed quite routinely [4].

One of the advantages that cryoablation has over RF ablation is that due to catheter adhesiveness during application of cryothermal energy, there is greater catheter stability and programmed stimulation may be performed during ablation. Successful ablation site could hence be identified if during atrial extrastimulus (A_1A_2) testing conduction block over slow pathway (SP) with preserved conduction over the fast pathway (FP) during drive train (A_1A_1) could be demonstrated (Fig. 1). Likewise, termination of AVNRT with progressive lengthening of the AH interval during cryomapping suggests good catheter location at the slow pathway area and one could proceed with application of a permanent cryoablation lesion. Cryomapping also allows surveillance of the integrity of FP conduction or compact AV node such that immediate rewarming must be performed if AV block occurs and/or PR interval prolongs during sinus rhythm between atrial extrastimulus testing or AH prolongation and/or block occurs during atrial drive train (Fig. 2).

To improve acute success rate and lessen long-term recurrence, several protocols besides application of bonus and linear lesions, freeze-thaw-freeze cycle protocol, several techniques including time to termination, and use of larger tip catheters have been adopted [11–13]. Induction of sustained AVNRT is a requisite for the “time to termination” technique. Suitable target site may be identified if during cryomapping at -30°C , AVNRT terminates promptly within 20 seconds; following which cryoablation for 4 minutes at -70 to -80°C may be continued [13]. As regards the use of larger tip (6 and 8 mm) catheters, inability of the cryoablation consoles to allow the cryomapping mode poses a serious limitation for cryoablation of AVNRT. Several operators have hence adopted to “pseudo-mapping”, a somewhat modified approach to cryomapping. The emphasis here is on the concept of “time to effect”, which is based on a premise that AVNRT should terminate immediately with formation of a larger ice-lesion within few seconds after the cryocatheter tips temperature drops as indicated by noise recording from the tip. Atrial pacing and programmed stimulation should then be started promptly. Even the number of pacing impulses during drive train (A_1A_1) and pause intervals between programmed stimulation may be abbreviated to allow more assessment time, such that if AVNRT is still inducible, further

application of cryo energy is stopped and catheter is repositioned up on rewarming. If, however, AVNRT is not inducible, cryoablation is continued with continuous monitoring of AV nodal conduction; and one may apply additional bonus lesion at the very location if necessary. The end-point of the procedure, of course, is non-inducibility of AVNRT.

In children, it is not merely because of miniaturization of cardiac anatomy, but also the issues of technical differences that ablation of AVNRT remains considerably complex; the goals being high success rate, low long-term recurrence, and no AV block needing implantation of permanent pacemaker. For AVNRT ablation, 3-dimensional electroanatomical mapping not only helps in anatomical delineation of various cardiac structures accurately but also allows voltage gradient mapping of Koch's triangle. Cryoablation of AVNRT in children has been shown to be very effective when performed in conjunction with 3-dimensional electroanatomical mapping to find typical ‘hump and spike’ electrograms of low-voltage connections, or ‘voltage bridges’, corresponding to the anatomic position of the slow pathway [14–16].

Pertaining to the study by V.K. Moondra et al.; [5], the authors describe their experience of cryoablation of AVNRT in a cohort of 253 patients, at a single center in the United States. In this retrospective study, the majority of patients were adults, but 12% were in the pediatric age group. While most ablations were performed with 6 mm tip catheters as initial choice, exclusive usage of 4 mm tip catheter was minimal at 10%. It is unclear whether all ablations were performed in conjunction with 3-dimensional electroanatomical mapping, and if so, whether beyond anatomical mapping more sophisticated voltage gradient mapping of the Koch's triangle was performed to delineate the slow pathway zone. The authors also do not provide much details on their own strategies of “pseudo-mapping”, but we assume them to be similar to the “time to termination” and “time to effect” as described [11–13]. The authors report acute success in 93% of cases, which is in line with what has been described in the literature [9]. Additionally, they report transient conduction defects in 39% of cases, and long term conduction defects in 1.6% of cases. The reported PR intervals are ≥ 300 ms in those patients with permanent conduction defects. In clinical practice, many such patients with marked PR interval prolongation become symptomatic with “pseudo-pacemaker syndrome” from detrimental hemodynamics resulting from atrial systolic contraction of the next cardiac cycle occurring during closed

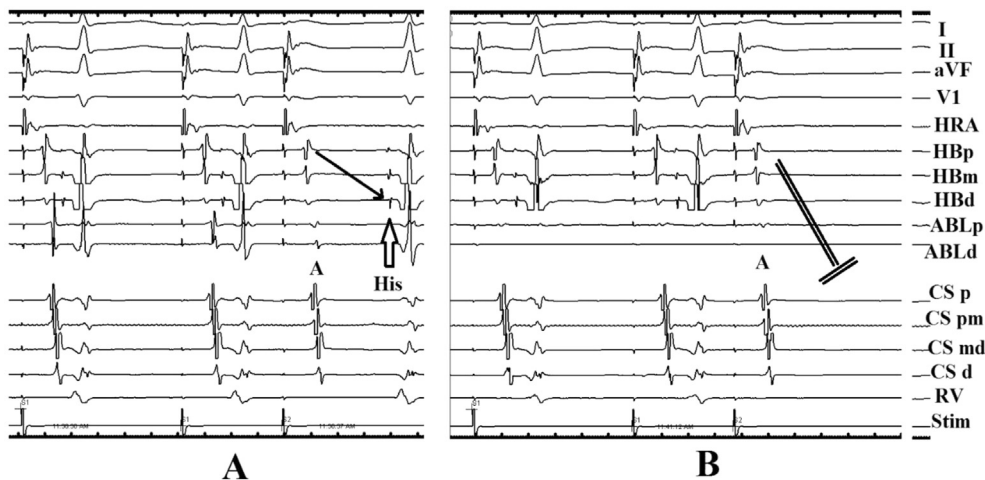


Fig. 1. Successful ablation site: During atrial extrastimulus (A_1A_2) testing conduction block over slow pathway (SP) with preserved conduction over the fast pathway (FP) during drive train (A_1A_1) is observed.

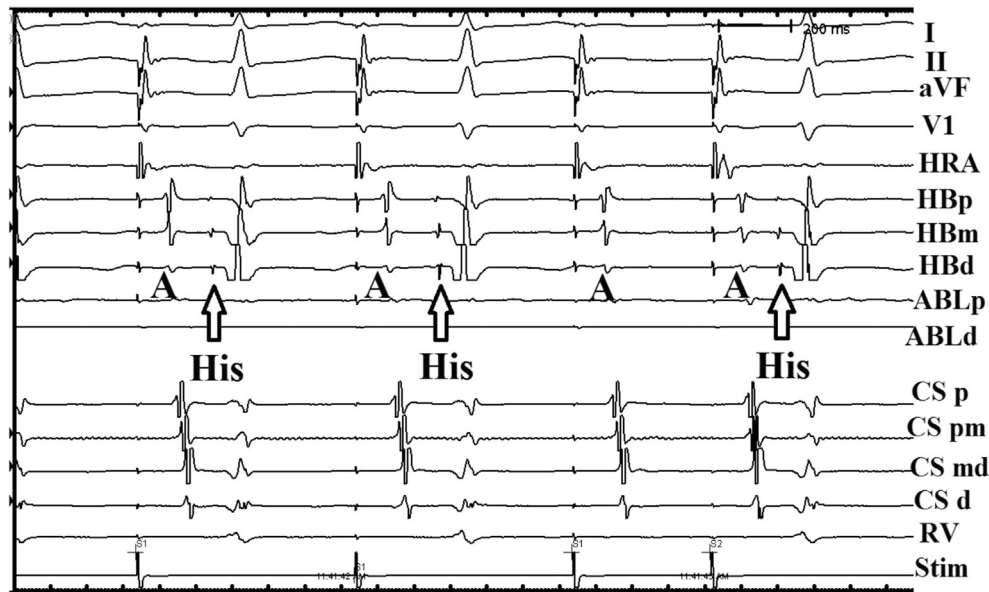


Fig. 2. Cryomapping shows progressive prolongation PR interval and AH interval with ensuing AV block indicating damage to FP conduction or compact AV node. Immediate rewarming must be performed (Fig. 2).

AV valves from the ventricular systole of the preceding cardiac cycle. Furthermore, prolonged telemetry monitoring and exercise stress test data regarding improvement or deterioration of the AV conduction during different autonomic state, especially in patients in whom cryoablation was performed near the His bundle would have helped in understanding the true extent of permanent conduction defects. Cryoablation of AVNRT using 6 mm tip catheter and utilizing “pseudo-mapping” did not improve the long-term recurrence rate substantially, i.e. 8% of patients had recurrence, and nearly 50% of whom required a repeat procedure, some with RF ablation.

One of the lessons that could be learnt from this study is that in spite of the advancement in our knowledge of the biophysics of ablation, mapping techniques, and catheter designs we still have several blind spots to overcome. We would like to believe that changes that occur at tissue level with application and up on discontinuation of cryoenergy whether after brief period at -80°C as in “pseudo-mapping” or -30°C as in “cryomapping” would be similar, completely reversible and entirely safe. To that end, it is reassuring to learn that even highly skilled operators who perform cryoablation almost exclusively for AVNRT now try to avoid PR prolongation or heart block during cryoablation given the recurrence rate in spite of it.

Disclosure for conflict of interest

None.

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