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# Indian Pacing and Electrophysiology Journal

journal homepage: [www.elsevier.com/locate/IPEJ](http://www.elsevier.com/locate/IPEJ)

## Pseudo cryomapping for ablation of atrioventricular nodal reentry tachycardia: A single center North American experience



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### ARTICLE INFO

#### Article history:

Received 8 March 2016

Received in revised form

27 November 2016

Accepted 25 December 2016

Available online 6 January 2017

#### Keywords:

Cryoablation

AVNRT

AV nodal reentry

Cryomapping

Catheter ablation

### ABSTRACT

**Background:** Most literature for cryoablation of atrioventricular nodal reentry tachycardia (AVNRT) is based on  $-30$  degree celsius cryomapping with 4 & 6 mm distal electrode catheters. The cryomapping mode is not available on the 6 mm cryocatheter in the United States. We describe a technique for 'pseudo' mapping at  $-80^\circ$  using a 6 mm cryocatheter and report on short and long term outcomes.

**Methods:** A retrospective analysis of all index cases ( $n = 253$ ) of cryoablation of AVNRT at a single North American institution during the period of 2003–2010 was performed. The majority of cases utilized a 6 mm distal electrode tip catheter. Long term follow up ( $2.4 \pm 1.8$  years) was performed via review of the medical record and by questionnaire or telephone if necessary.

**Results:** Acute ablation success was achieved in 93% of cases, with transient conduction defects noted in 39% of cases, and long term conduction defects in 1.6% of cases (4 patients with PR prolongation, 2 of which were permanent). General anesthesia, male gender and presence of structural heart disease were more common in the acute failure cohort. The recurrence rate for AVNRT was 8%. These patients tended to be younger and had more transient A-V conduction defects during the index procedure than those without a recurrence.

**Conclusions:** In conclusion, anatomic cryoablation of AVNRT utilizing a 6 mm electrode catheter with mapping performed at  $-80^\circ$  Celsius is a safe procedure with good long term efficacy. Transient A-V block during the index procedure increases the risk of late recurrence.

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### 1. Introduction

Cryoablation is an accepted tool for catheter ablation [1], but widespread use in the treatment of atrio-ventricular nodal re-entry tachycardia (AVNRT) has been limited by perceptions concerning efficacy. Several studies have suggested that acute success rates with cryoablation are almost equivalent to radiofrequency ablation; however, long term recurrence rates may be significantly higher [2–4]. Cryomapping, a mode of reversible thermal lesion mapping performed by lowering catheter tip temperature to  $-30^\circ$  Celsius (C), can be performed with both the 4 and 6 mm distal electrode tip catheters in Europe and Asia. In the United States, both catheters

are available, but only the 4 mm supports the cryomapping mode. As such, much of the worldwide published literature on cryoablation using a 6 mm cryomapping capable catheter tip is not relevant to the technology utilized in the United States. Early experience suggesting a lower success rate for 4 mm tip cryoablation compared to radiofrequency (RF) ablation, resulted in many abandoning the cryoablation modality altogether, while propelling many users of cryoablation to utilize 6 mm catheters [5–7].

We have employed cryoablation almost exclusively for AVNRT ablation over the last 8 years, most recently utilizing a modified approach of pseudo-cryomapping at  $-80^\circ$  Celsius with the 6 mm catheter tip. This study describes our technique, and the acute and long term success rates, in a relatively large cohort from a single North American academic medical center. It illustrates that pseudo-cryomapping is a safe approach and that the 6 mm catheter is not statistically more efficacious than the 4 mm catheter in long term follow up.

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Peer review under responsibility of Indian Heart Rhythm Society.

## 2. Methods

### 2.1. Recruitment

We retrospectively analyzed consecutive cryoablation procedures for AVNRT, performed between October 2003 and April 2010. Both pediatric and adult patients were included in the analyses. The procedure was performed by one of six electrophysiologists, utilizing a similar basic protocol. Collected study data included: fluoroscopy time, sedation type (conscious sedation or general anesthesia), development of transient or permanent AV block, acute procedural outcome, and presence or absence of dual AV nodal physiology at the end of the procedure. Only the index procedure was included in the analysis, and in cases where an upgrade was made from a 4 mm tip catheter to a 6 mm tip catheter, the case was categorized as a 6 mm tip case. Long term follow up was performed by review of the patient medical record, a mailed questionnaire, and telephone contact with patients. Our institutional internal review board (Committee for the Protection of Human Subjects) approved this research study.

### 2.2. Cryoablation technique

Most procedures in adult patients were performed with moderate sedation in the post absorptive state. Most pediatric procedures were performed under general anesthesia. Antiarrhythmic medications were usually held for several half lives prior to the study. Quadripolar catheters were placed in the right atrium, right ventricle, and His bundle position and a decapolar catheter was used to cannulate the coronary sinus (usually via the right internal jugular vein). A routine electrophysiology study was then performed, with atrial and ventricular overdrive pacing, programmed electrical stimulation of the atrium and ventricle, and para-Hisian pacing as appropriate. The diagnosis of AVNRT was made with traditional criteria including a septal VA interval less than 70 ms in tachycardia and a V-A-H-V response to ventricular entrainment. When AVNRT was confirmed, a cryoablation catheter (7 F, Freezor 4 mm tip or Freezor Max 6-mm tip, CryoCath, Montreal, Canada) was advanced via the femoral vein, sometimes with the use of a stabilizing long sheath (Daig SRO).

Typically, the slow pathway was mapped with the ablation catheter starting at the tricuspid annulus near the level of the coronary sinus ostium and proceeding either inferiorly (toward the coronary sinus ostium) or superiorly (toward the His bundle), but only rarely higher than the mid-septum. Three-dimensional electroanatomic mapping with EnSite Nav-X (St Jude Medical) was typically used. If a slow pathway potential was not readily identified, an anatomic-based approach was performed. After a suitable site for ablation was identified, the cryoablation catheter was cooled to target temperature ( $-30^{\circ}\text{C}$  for the 4 mm tip catheter in 'map' mode, and  $-80^{\circ}\text{C}$  for the 6 mm tip catheter), with close monitoring of AV conduction. If AV conduction remained stable for 60 s, either a full lesion (4–6 min total) was commenced or, if SVT was inducible, the cryocatheter was typically warmed and moved to a new location. A similar strategy was used if cryoablation was performed during SVT. Once AVNRT was not inducible, a full 4–6 min lesion was applied, typically followed by several 'consolidation' lesions contiguous to the successful area. Often, the first consolidation lesion was delivered at the same site as the successful index lesion, in a 'freeze-thaw-freeze' manner. A waiting period of 30–60 min was usually employed, with attempted induction of SVT on isoproterenol. If tachycardia was still non-inducible, the procedure was terminated. A single echo beat was considered an acceptable endpoint, if AVNRT was non-inducible.

### 2.3. Follow up

Post ablation, all patients were hospitalized and monitored overnight on telemetry. Recurrent SVT was defined as either electrocardiographic recurrence consistent with AVNRT, or recurrence of typical symptoms even in the absence of documented SVT.

### 2.4. Statistical analysis

The results of the study are displayed as mean  $\pm$  standard deviation, counts, or percentages. The Student's t-test and chi square test were used for comparison of continuous and categorical variables respectively. All tests were two-tailed, with a p value of  $<0.05$  considered statistically significant.

## 3. Results

### 3.1. Patient population (Table 1)

253 consecutive cases of cryoablation of AVNRT were performed during the study period of October 2003 to early 2010. Only 18 patients (7%) were lost to follow up. The majority of patients were female and without structural heart disease. Pediatric patients comprised 12% of the total cohort with an average age of 15.1 years. Atypical AVNRT was diagnosed in 4 patients. In 10 patients, AVNRT was not inducible; in 9 of these patients, there was evidence of dual AV nodal physiology on the basis of a jump in AH interval, PR longer than RR or av nodal echo beats. In 1 patient, the clinical SVT was deemed to be a short RP tachycardia, and empiric cryoablation was performed in the absence of documented dual av nodal physiology. Acute procedural success was achieved in 93% of patients. Transient AV conduction abnormalities (non-permanent first, second or third degree heart block), were seen in 39% of patients, primarily as PR prolongation. PR prolongation persisted in 4 of 253 patients (1.6%).

### 3.2. Acute success (Table 2)

Excluding patients lost to follow up, acute procedural success was achieved in 93% of the patients. Patients with acute failure were more likely to be male, have structural heart disease, receive general anesthesia and longer fluoroscopy times. Transient AV conduction abnormalities occurred more frequently in the acutely successful group (39% versus 29%) but this difference was not statistically significant.

### 3.3. Long term follow-up (Table 3)

The mean duration of follow up was  $2.4 \pm 1.8$  years and the recurrence rate was 8%. Patients with long term recurrence all had

**Table 1**  
Patient population.

Total number of cases	253
Cases with long term follow up data	235
Average Age	$47 \pm 21$
% Male	37%
Pediatric Patients	12%
Heart Disease	14%
4 mm Tip	10%
General Anesthesia	31%
Fluoro Time (minutes)	$31 \pm 22$
Acute Success	93%
Transient AV block	39%
Persistent PR prolongation	1.6%

Data are expressed as mean  $\pm$  one standard deviation.

**Table 2**  
Acute success.

	Acute Success (n = 218)	Acute Failure (n = 17)	p value
Male Gender	37%	65%	0.036
Age (years)	48 ± 21	57 ± 16	0.826
Fluoro Time (min)	29 ± 20	46 ± 25	0.0065
General Anesthesia	30%	50%	0.0009
LVEF	62 ± 9	61 ± 10	0.76
Heart Disease	26 (12%)	7 (41%)	0.004
4 mm tip	20 (9%)	3 (18%)	0.22
ECHO BEATS	39 (18%)	n/a	
1° AV BLOCK (TRANS.)	49 (22%)	2 (12%)	0.377
2ND° AV BLOCK (TRANS.)	19 (9%)	2 (12%)	0.679
3RD° AV BLOCK (TRANS.)	19 (9%)	2 (12%)	0.679
Any Transient AV Block	86 (39%)	5 (29%)	0.152
Persistent PR prolongation	4	0	1.0

Data are expressed as mean ± one standard deviation.

apparent success at the initial procedure. Patients with recurrent SVT were younger, had longer fluoroscopy times, and were more likely to have transient AV block during ablation (73% versus 38%). There was a greater incidence of echo beats at the end of the procedure (19% vs. 6%) in the long term success group, but this difference was not statistically significant. The persistent PR prolongation noted during the index ablation returned to baseline in two of the four patients, at one day and one month (or less) respectively.

In the other two patients, PR prolongation was permanent and remained stable for 6 and 4 years respectively. The first patient underwent ablation in the mid-septum, increasing the PR interval from 170 ms to 270 ms acutely; the PR interval was 300 ms 4 months later and 262 ms 6 years later. The second patient underwent ablation near the His bundle, with acute PR prolongation from 176 ms to 364 ms; the PR interval was 302 ms 3 months later and again 302 ms 4 years later. Neither of these patients had recurrent SVT. No patients have required pacemakers as a result of the cryoablation procedure.

### 3.4. 4 mm versus 6 mm tip catheters

The 4 mm catheter was used exclusively in only 23 cases (10% of total). In five procedures, an upgrade from a 4 mm to a 6 mm catheter tip was performed; these cases were characterized as 6 mm catheter cases. In these 5 procedures, 3 were acutely successful with the 6 mm catheter and 2 required radiofrequency ablation resulting in success. All of these patients were successfully ablated long term. The 6 mm catheter tip was acutely more

effective than the 4 mm catheter tip, but this did not reach statistical significance. The long term recurrence rates were roughly equivalent, and the overall success rates were also not statistically different, with an overall success rate (including acute failures) of 78% for the 4 mm catheter and 86% for the 6 mm catheter.

### 3.5. Pediatric versus adult AVNRT

Pediatric cases represented 13% of all AVNRT ablations during the study period. Acute success was seen in 94% of pediatric cases with a 20% recurrence rate. The 4 mm catheter was used in 2 of the 6 patients with long term recurrence. Transient AV block was present in 65% of the pediatric cases and there was absence of echo beats at the culmination of all cases. There was almost exclusive use of general anesthesia for the pediatric cases (96% of pediatric cases).

### 3.6. Acute failures

Cryoablation was acutely unsuccessful in ablating AVNRT in 17 of the 253 patients (7%). Radiofrequency ablation was performed in 13 of these patients at the index procedure, with acute success in 11; one patient underwent an unsuccessful radiofrequency catheter ablation at a later date. Three patients did not undergo further ablation after the initial attempt at cryoablation failed, and they were managed medically.

Of the three patients who failed radiofrequency catheter ablation, one was managed medically and in the other two the fast pathway was intentionally modified using cryoablation. In one of these fast pathway cryoablation patients, the PR interval increased from 135 to 200 ms during the procedure without recurrent SVT. The second patient undergoing fast pathway cryoablation had an increase in PR interval from 220 to 250 ms with elimination of retrograde conduction during the procedure and with no SVT during follow-up.

In the 11 patients who had an acutely successful radiofrequency catheter ablation after failing cryoablation during the index procedure, no recurrent SVT was seen in the 8 patients in whom long term data were available.

### 3.7. Repeat procedures due to late recurrence

18 patients developed recurrent AVNRT during long term follow up. Repeat cryoablation was performed in 8 of these with acute and chronic success in all but one of the eight patients. The single cryoablation failure at the repeat procedure had acute success with radiofrequency ablation at the same procedure, but then had recurrent symptoms and was managed medically. One patient had

**Table 3**  
Long-term follow-up.

	Long Term Success	Recurrence	p value
Number of cases	200 (92%)	18 (8%)	
Male Gender	39%	17%	0.074
Age (years)	49 ± 21	33 ± 17	0.001
Fluoro Time (min)	28 ± 19	44 ± 28	0.003
General Anesthesia	28%	39%	0.42
LVEF	62 ± 9	66 ± 5	0.087
Heart Disease	12%	11%	1.00
4 mm tip	10%	11%	0.69
ECHO BEATS	19%	6%	0.208
1° AV BLOCK (TRANS.)	21%	39%	0.14
2ND° AV BLOCK (TRANS.)	8%	17%	0.20
3RD° AV BLOCK (TRANS.)	9%	17%	0.22
Any Transient AV Block	38%	73%	0.006
Persistent 1st° AV BLOCK	2%	0	1

TRANS. = transient, 1st° = first degree.

a successful radiofrequency ablation as the initial approach at the repeat procedure, and has had no recurrence. The remaining nine patients were managed medically per patient preference.

## 4. Discussion

### 4.1. Safety and efficacy of “cryomapping” at $-80^{\circ}$

Radiofrequency catheter ablation of AVNRT is considered to be highly effective, but is complicated by inadvertent complete heart block in up to 1–2% of cases [3,8]. Cryoablation has been demonstrated to have an excellent safety profile in this regard [1–6]. Interestingly, when cryoablation has been used to intentionally create AV block, it has been difficult to do so [9]. This is due to the nature of the cryoablation lesion [10], which tends to be focal and well circumscribed due to adherence of the catheter to the ablation site. However, cryomapping at  $-30^{\circ}$  C may not predict AV block during subsequent cryoablation [11], presumably secondary to a larger volume of thermal damage created by a lower temperature lesion. Although not truly reversible, ‘pseudo-cryomapping’ at a temperature of  $-70$  to  $-80^{\circ}$  C may be more sensitive for predicting A-V conduction block during subsequent ablation, whereas cryomapping at  $-30^{\circ}$  C may be more specific at identifying the appropriate location of the slow pathway. This may in part explain why the recurrence rate among patients who left the lab “acutely successful” after use of the 4 mm tip catheter was similar to that of those with the 6 mm tip catheter ie. when success is achieved with the smaller catheter, the lesion may be more precisely located. The 4 mm tip catheter appears to be less successful overall, however, when compared to the 6 mm tip catheter, likely due to the smaller lesion size. The overall success of 78% for the 4 mm tip catheter and 86% for the 6 mm tip catheter was primarily driven by acute failures of the 4 mm tip catheter. The 4 mm catheter tip cases disproportionately represented our early cryoablation experience, so there may have been a learning curve effect. However, this discrepancy between catheters was underestimated by the fact that for purposes of data analysis, we counted five failed 4 mm tip cases as 6 mm tip cases, when the catheter was upgraded during the index procedure.

Studies have demonstrated acute success rates of approximately 93% for cryoablation versus 96% for radiofrequency ablation, with recurrence rates of 10% versus 4% respectively [12]. Our acute success rate of 93% is comparable.

One of the largest randomized studies [3] comparing a cryomapping capable 6 mm tip catheter with radiofrequency ablation for AVNRT showed a recurrence rate of 9% for cryoablation versus 4% for radiofrequency ablation at 6 months. Our study, although retrospective, has a longer duration of follow up (2.4 years  $\pm$  1.8 years) and is biased towards over-reporting of long term procedural failure as we considered recurrence of significant typical symptoms, even in the absence of arrhythmia documentation, as a recurrence of AVNRT. Despite this, the long term recurrence rate appears to be acceptable at 8%. Other recent studies suggest that improved outcomes with cryoablation of AVNRT, perhaps comparable to radiofrequency ablation, may be achieved with 8 mm tip catheters [13,14], linear ablation in the inferior portion of Koch's triangle [15], freeze-thaw-freeze cycles [16], and eliminating slow pathway conduction completely i.e. no jump or echo beats [17]. Data from the pediatric literature suggests that acute success can be seen in 96.2% of patients, with a triple freeze-thaw cycle [16]. In this group, the recurrence rate was 2.0% (1 patient).

### 4.2. Transient AV block and recurrence

Transient AV block during cryoablation for AVNRT has been reported in the literature, but our incidence of 39% is higher than the 23% reported by De Sisti et al. [18], in whose study it persisted up to 4 days post ablation (PR prolongation), even when using a cryomapping capable 6 mm catheter. Our incidence of transient AV conduction delay is similar to the study of Qureshi et al. [16], which utilized a triple freeze thaw cycle. Similar to our findings, no patients required permanent pacemaker implantation. This finding likely represents an aggressive approach with cryoablation, which includes utilizing several consolidation lesions and ablation in the mid-septum if necessary. The 6 mm catheter likely creates a larger lesion than the 4 mm catheter and this may encroach on the compact AV node, even when applied below the mid-septum. As our experience with cryo-ablation has evolved, it has become apparent that cryoablation-induced acute AV conduction abnormalities are usually a readily reversible phenomenon, if the lesion is aborted promptly when conduction delay develops. To this end we follow the AH interval closely during cryoablation, especially for the 1st minute (a cryo map surrogate), often using a ‘triggered’ mode on the recording system, alerting us to small changes (e.g. 10 ms) in AH interval. Cryoablation is typically terminated with the onset of AH interval prolongation. It should be noted that even with discontinuation of cryoablation at the onset of PR/AH prolongation, the transient conduction disturbance may progress until the septum has fully warmed, secondary to some latency of effect. After warming of the septum, attempted re-induction of tachycardia as well as evaluation of conduction in antegrade and retrograde directions is attempted, before consideration of further ablation. If tachycardia was re-inducible, once parameters were back to baseline, further ablation was performed. If tachycardia was non-inducible, up to a 60 min wait period on isoproterenol would be used, with further ablation performed if tachycardia was re-induced. A review of 6 radiofrequency ablation studies for AVNRT showed complete atrioventricular block requiring pacemaker implantation in up to 8% of cases [18], although in more recent studies this is closer to 2%. In our study, no pacemakers were necessary despite this relatively aggressive approach, even in the 13 patients that were switched at the initial ablation to a radiofrequency strategy for failure of cryoablation.

Transient AV block was more prevalent in patients with acute success than in acute failures (39% vs. 29%), though this did not reach statistical significance. Conversely, there was an almost two-fold higher incidence of AV block during the index procedure in patients with recurrence of symptoms during follow-up, compared to patients in remission (73% vs. 38%,  $p = 0.006$ ). This association may reflect operator reluctance to apply further consolidation lesions during the index procedure, after transient AV block has occurred. Transient AV block may also result in very short-term non-inducibility of AVNRT, and a premature endpoint to the procedure.

The long term recurrence rate in a subgroup with no echo beats and no transient AV block during ablation was only 4.8%. Patients with no echo beats at the end of the procedure who experienced transient AV block during cryoablation had a long term recurrence rate of 15%. Few studies have reported data on the incidence of transient AV block and the potential correlation with long term outcomes. De Sisti et al. reported a 23% atrioventricular block incidence, of up to 4 days post procedure, using a cryomapping capable 6 mm catheter. A prolonged PR interval (lasting up to 4 days, but generally resolving in a few minutes), rather than second or third degree A-V block, predicted recurrent SVT [19]. We hypothesize that transient AV block can result in temporary non-inducibility of SVT due to stunning of the compact AV node,

which is misleading as an ablation endpoint.

#### 4.3. Permanent PR interval prolongation

Permanent PR interval prolongation after attempted slow pathway cryoablation for AVNRT has been described in only a single case in the literature, to our knowledge [20]. Two of our 253 patients (0.8%) had permanent PR interval prolongation out to 4 and 6 years of follow-up, as a result of intentionally targeting the slow pathway at the mid-septum in one patient and superior to the mid-septum in another.

To our knowledge, there is only one other case of cryoablation of the fast pathway for AVNRT [21], our limited experience suggests that this may warrant further study in the minority of patients who fail a slow pathway ablation with cryoablation or radiofrequency ablation. Two patients had successful fast pathway modification with cryoablation after failing slow pathway ablation with both cryoablation and radiofrequency ablation. One patient had dramatic retrograde block in the fast pathway, and no change in the pre-ablation PR interval at 2 years of follow-up. The other patient had a 50 msec increase from the pre-ablation PR interval (135–184 msec) at 6 years of follow-up. Neither had recurrent SVT.

#### 5. Conclusion

Our large single-center experience of cryoablation for AVNRT demonstrates that a 'pseudo-cryomapping' approach, with a 6 mm catheter at  $-80^{\circ}$  can result in an acute procedural success rate of 93% with a low risk of permanent AV conduction abnormalities. Overall (acute and chronic) success rates with a 6 mm catheter tip are 86%, and this seems acceptable given the excellent safety profile. Cryoablation affords additional advantages with regard to patient comfort and operator stress, at the cost of a possible modest decrease in long term efficacy compared to radiofrequency catheter ablation. Given the difference between 4 and 6 mm catheter tip cryoablation success rates, we favor a strategy of using a 6 mm catheter, 'mapping' at  $-70$  to  $-80^{\circ}$  celsius, and aggressive ablation on the septum if necessary. Consolidation or freeze-thaw-freeze lesions may enhance success rates. Given the data on recurrence we now try to avoid PR prolongation or heart block during cryoablation. Thorough programmed stimulation to assess for inducible SVT is important, especially if transient heart block develops during the index procedure, as this may translate to a higher recurrence rate in long term follow up.

#### Ethics

This study complies with the declaration of Helsinki, the research protocol was approved by the local committee for the protection of human subjects and informed consent of the participants was obtained.

#### Conflicts of interest

There are no conflicts of interest.

#### Acknowledgements

There were no funding sources.

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