# Targeting an electrotonic effect with ablation: Management of a symptomatic long PR interval

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## Introduction

Marked PR prolongation is an uncommon presentation of dual atrioventricular (AV) nodal physiology and may cause "pseudo-pacemaker syndrome." The usual explanation for a prolonged PR interval in this context is persistent anterograde conduction over the slow pathway, perpetuated by retrograde concealed conduction into the fast pathway, but significant impairment in anterograde fast pathway conduction is also possible. An "electrotonic" interaction between the slow and fast pathways is the putative reason why the effective refractory period of the fast pathway decreases after ablation of the slow pathway, and this electrotonic effect may also impair fast pathway conduction velocity.[1,2]

## Case report

A healthy 28-year-old male subject presented with exertional fatigue, palpitations, and dyspnea. His resting electrocardiogram (ECG) revealed a markedly prolonged PR interval (Figure 1A) of 460 ms. During an exercise stress test, his baseline PR interval was at the upper limit of normal, and it slightly shortened at maximal exercise. In early recovery, however, while still in sinus tachycardia at 120 beats per minute, his PR interval became markedly prolonged (Figure 1B). Additionally, he would have an occasional blocked premature atrial contraction (PAC), followed by 1 conducted beat with an upper normal PR interval, and then all subsequent beats again conducted with a markedly prolonged PR (Figure 1C). Given the suspicion of dual AV nodal physiology and significant exertional symptoms that seemed to be caused by pseudo-pacemaker syndrome, the patient was taken for an electrophysiology (EP) study and planned cryoablation of a suspected slow AV node pathway.

At the start of the EP study, baseline measurements were made in sinus rhythm, including a markedly prolonged AH interval of 358 ms and a normal HV interval of 45 ms. Atrial pacing demonstrated AV Wenckebach at a cycle length of 700 ms. Atropine was given, which caused progressive shortening of the AH interval from 358 ms down to 125 ms over a period of 30 seconds without any sudden AH changes. With the administration of isoproterenol, there was further AH shortening down to 69 ms. While the patient was on isoproterenol, single atrial extrastimuli revealed dual AV nodal physiology, with a 133 ms jump in the AH interval after a 10 ms decrement in the atrial extrastimulus. No tachycardia could be induced with programmed stimulation. After the isoproterenol was stopped, the AH interval prolonged to 325 ms, even while the atropine should still have been pharmacologically active.

Given the demonstration of dual AV node physiology, and the ability of the AH interval to shorten to normal, the decision was made to proceed with slow pathway ablation,

### KEY TEACHING POINTS

- Marked PR prolongation, related to dual atrioventricular (AV) node physiology, can cause "pseudo-pacemaker" syndrome from atrial contraction occurring during ventricular systole of the previous beat.
- In addition to perpetual conduction down a slow AV node pathway, PR prolongation can also be due to slowed conduction over an impaired fast pathway.
- There exists an electrotonic interaction between the slow and fast AV node pathways that results from a voltage gradient between the 2 pathways related to the altered timing of conduction in each pathway. Elimination of this electrotonic interaction is thought to be the reason why the fast pathway refractory period improves after slow pathway ablation.
- Improvement in fast pathway conduction velocity can also occur after slow pathway ablation, likely related to this same mechanism of elimination of an electrotonic interaction.

**KEYWORDS** Cryoablation; Electrotonic effect; Prolonged PR interval; Pseudo-pacemaker syndrome; Slow pathway ablation
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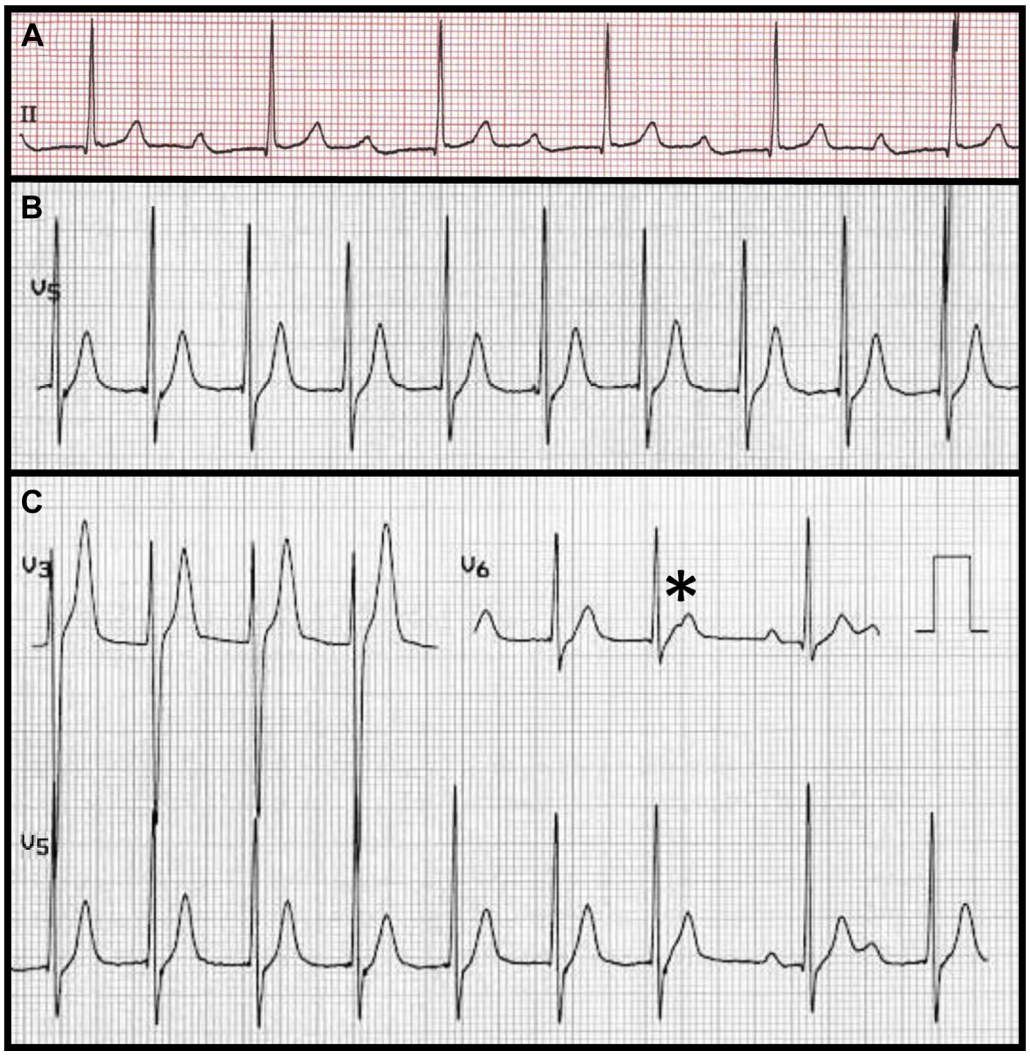


**Figure 1** **A:** Baseline electrocardiogram with a markedly prolonged PR interval (>400 ms). **B:** PR prolongation seen in the recovery phase of the treadmill test with the P wave superimposed on the T wave. **C:** After a blocked premature atrial contraction (*asterisk*), the PR normalized for 1 beat, followed by return of marked PR prolongation.

presuming that the presence of the slow pathway was directly implicated in the impairment of AV conduction. Cryoablation (Freezor Max 6-mm-tip catheter; CryoCath, Montreal, Canada) was chosen to minimize the risk of causing irreversible damage to AV conduction. During the first cryoablation lesion, the AH interval slightly shortened from 325 ms to 300 ms. During the second cryoablation lesion, the AH interval gradually and progressively shortened from 300 ms to 168 ms, without any sudden changes or "reverse jumps" over the 4-minute freeze (Figure 2A). During the fifth cryoablation lesion, just inside the coronary sinus ostium, the AH gradually and progressively shortened from 174 ms to 110 ms, again without any sudden changes. In total, cryoablation at the anatomic AV node slow pathway location (Figure 3A) progressively shortened the AH interval from 325 ms down to 110 ms (Figure 3B), always in gradual increments of 2–15 ms per beat, with most of the shortening during effective lesions seen in the first 30 seconds of cryo delivery (Figure 2B). In all, we administered 7 4-minute-long cryoablation lesions and 3 additional lesions of 90 seconds or less, which were stopped early owing to incomplete cooling or lack of effect. At the conclusion of the case, the AH interval was 125 ms, the PR interval was 205 ms (Figure 3C), and an EP study on isoproterenol revealed an AV Wenckebach cycle length of 370 ms and an AV nodal fast pathway effective refractory period of 400/250 ms. A month later, the PR interval had prolonged to 250 ms (Figure 3C); and 4 months after the ablation, an ECG demonstrated 2 different populations of PR intervals, with subtle lengthening of the "shorter" PR interval followed by a sudden "jump" to the longer interval during sinus rhythm, suggesting the return of dual AV node physiology (Figure 3D). The patient opted for conservative management given sustained clinical improvement in exertional symptoms.

## Discussion

In patients with a baseline long PR interval and dual AV node physiology, it may be difficult to determine if conduction is occurring over an impaired fast pathway or if the impairment

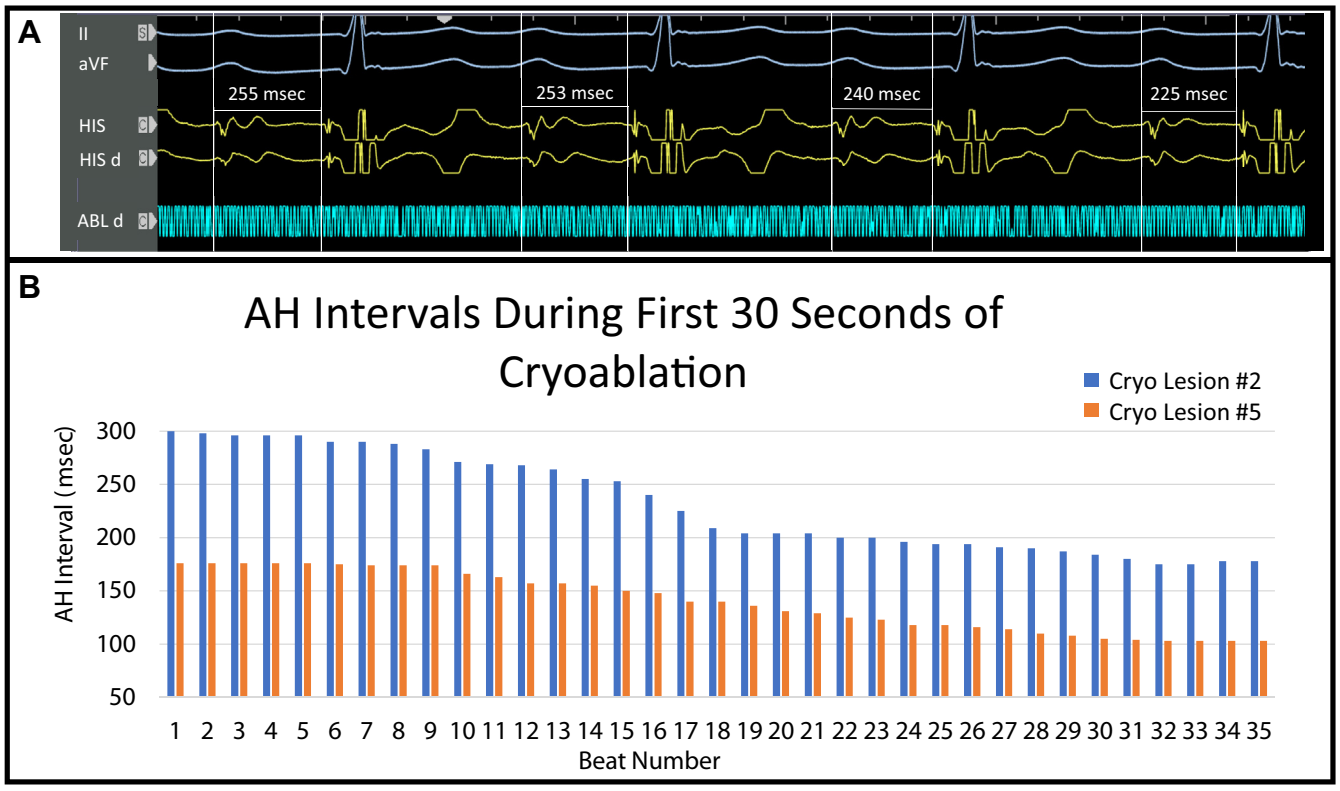


**Figure 2** **A:** Gradual AH interval shortening occurring during the second cryoablation lesion. **B:** Gradual AH interval shortening occurred predominantly during the first 30 seconds of cryo application (depicted here for the second and fifth cryo lesions).

in fast pathway conduction is allowing conduction to proceed over the slow pathway, which persists owing to concealed retrograde conduction into the fast pathway. There exists an "electronic interaction" whereby delayed conduction in the slow pathway leads to a voltage difference and resultant current in the surrounding syncytium that prolongs repolarization of the fast pathway.[3] This is the putative mechanism whereby ablation of the slow pathway leads to shortening of the fast pathway effective refractory period independent of autonomic tone,[2–4] and improvement in fast pathway conduction velocity has also been described.[1,5] In the series from Natale and colleagues,[1] patients with AV nodal reentrant tachycardia (AVNRT) and a baseline prolonged PR had an average PR interval shortening after slow pathway radiofrequency (RF) ablation of around 70 ms with a maximal shortening of 140 ms, much less than the 255 ms shortening seen in our case. One group found a marked and immediate improvement of baseline PR interval after slow pathway RF ablation in 2 patients with AVNRT; however, the authors concluded that baseline conduction was occurring over the slow pathway.[6]

In our case, the appearance of 2 populations of PR intervals prior to the ablation procedure suggested dual AV nodal physiology, and the predominant PR interval was markedly prolonged (>400 ms). Although this finding was initially thought to represent slow pathway conduction, the subsequent EP study and observations during slow pathway cryoablation demonstrated that a more likely explanation was impaired conduction down a "fast" pathway. After administration of atropine and isoproterenol, the PR interval shortened in a gradual, beat-to-beat progression rather than a sudden "reverse jump" that might be expected if anterograde conduction were to shift from the slow to the fast pathway. The subsequent observation of an AH jump during programmed atrial extrastimulation suggested that conduction was indeed occurring anterogradely over the fast pathway after the gradual AH shortening. During cryoablation of the slow pathway in the inferior triangle of Koch, a progressive shortening of the PR interval was seen. If the baseline long AH interval were explained by conduction down the slow pathway with retrograde concealment into the fast pathway, one would expect the AH to initially prolong during slow pathway cooling, and then suddenly shorten within a single beat as conduction switched back to the fast pathway. Instead, the gradual AH shortening that occurred was likely due to the gradual elimination of the electrotonic interaction between the slow and fast pathways, allowing for progressive improvement in fast pathway conduction. It should be noted that the degree of fast pathway conduction improvement may be related in part to this patient's young age, as there is evidence that the improvement in fast pathway refractory period is more dramatic in the pediatric population, indicating a more robust electrotonic interaction and greater functional impairment in young patients.[7] Because of its gradual nature, cryoablation allowed for unique observations in this case that would have not been feasible with RF ablation. If ablation had been performed with RF, the appearance of junctional beats during energy

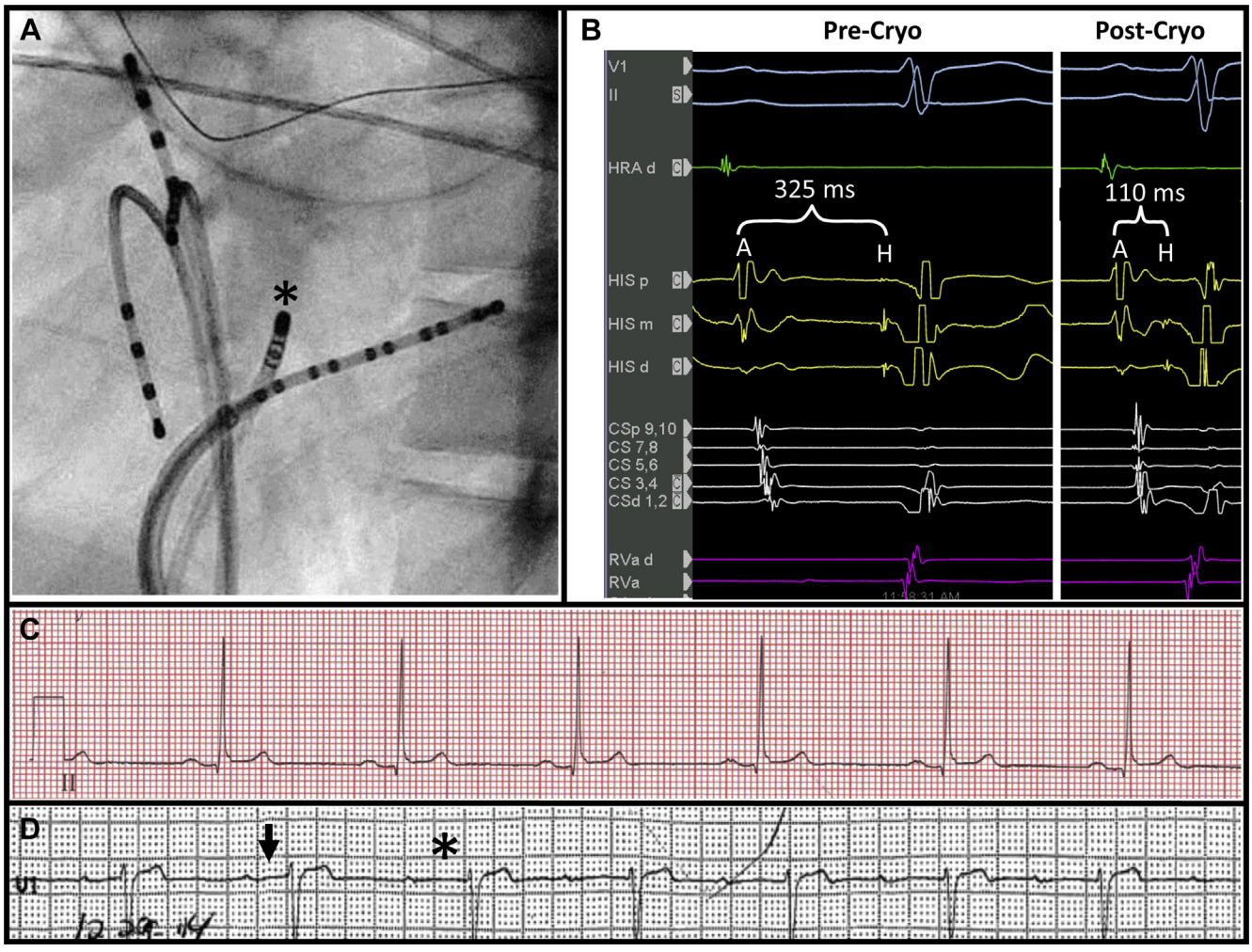


**Figure 3** **A:** Left anterior oblique view of cryoablation catheter position during slow pathway ablation (*asterisk*). **B:** AH interval before (Pre-Cryo) and after cryoablation (Post-Cryo). **C:** Marked PR interval improvement to 205 ms at the conclusion of the case. **D:** Four months after ablation, resting electrocardiogram showed 2 populations of PR intervals with initial subtle PR prolongation to 290 ms (*arrow*) followed by a "jump" to 420 ms (*asterisk*).

delivery would hinder continuous and sequential assessment of anterograde AV nodal conduction. In addition, the sudden shortening of the PR interval that would likely have been seen with RF would have made it difficult to discriminate between elimination of concealed retrograde fast pathway conduction and modification of electrotonic interactions.

In order to explain the findings of the exercise stress test, where the PR interval was initially normal and then became markedly prolonged early in recovery, we postulated that anterograde conduction over the fast pathway was always occurring, but that the presence or absence of an electrotonic interaction with the adjacent slow pathway impacted the PR interval. Figure 1C shows a persistently prolonged PR interval except for a single beat that follows a nonconducted PAC. The mechanism for this isolated normal PR interval may be block in the fast pathway but anterograde concealed conduction (and block) in the slow pathway during the PAC, resulting in the subsequent sinus beat blocking in the slow and conducting only down the fast, which is thus unimpaired by electrotonic interaction. On subsequent beats, conduction down both fast and slow pathways could reestablish the electrotonic impairment of fast pathway conduction velocity and lengthening of the PR, or, if there had been retrograde concealed conduction into the slow pathway after the first sinus beat, a normal PR could be further sustained owing to a linking phenomenon that would be contingent on sinus rate and autonomic tone. If the majority of slow pathway tissue were depolarized in a retrograde fashion, temporally dissociated from fast pathway anterograde conduction that had already occurred, any electrotonic effect on the fast pathway might be minimized as long as that activation sequence perpetuated. The simpler explanation that there was a jump from fast to slow pathway on the second beat after the blocked PAC seems less likely, given that the fast pathway would have to be refractory at a cycle length of greater than 500 ms while exercise-induced sympathetic tone was present. Fast pathway conduction, however, was found to be much better than that during the EP study on isoproterenol.

We also considered whether cryoablation of parasympathetic nerve inputs at the inferior triangle of Koch could explain improvement in conduction velocity of a fast

pathway that was under the influence of excessive vagal tone. Although 1 of the parasympathetic ganglia innervating the AV node is near the coronary sinus ostium and could be damaged by slow pathway ablation, case reports of cardioneuroablation have only demonstrated marked improvement in AV nodal conduction with more extensive ablation targeting additional ganglia in the high posterior portions of the right and/or left atrium.[8] A canine model of slow pathway ablation showed an attenuation of the effects of vagal stimulation on AV nodal effective refractory period; however, there was no significant change in the baseline AH interval.[9] Additionally in our case, the fact that the AH interval prolonged back to the presenting duration despite ongoing systemic atropine effect argues against a pure parasympathetic input explanation.

In follow-up, the beneficial effect of cryoablation seemed to be at least partially reversible, as evidenced by at least intermittent recurrence of a prolonged PR interval. Although the amount of cryothermal energy delivered was adequate to achieve immediate clinical endpoints, the prolongation of the PR interval on the 4-month ECG is likely explained by partially reversible tissue injury, which is known to be more prominent with cryoablation than with RF. It is not clear whether the dramatically prolonged PR on that particular ECG represented a switch from fast to slow pathway conduction or a sudden slowing of conduction down the fast pathway, possibly from recurrent electrotonic interaction with the slow pathway.

## Conclusion

A young patient with a markedly prolonged PR interval causing pseudo-pacemaker syndrome underwent slow pathway cryoablation, resulting in normalization of the PR interval and improvement in symptoms. Gradual improvement in the AH interval occurred during cryoablation of the slow pathway, likely owing to gradual elimination of an electrotonic effect between the slow and fast pathways, allowing for progressive improvement in fast pathway conduction. More evidence is needed before our unique findings and management can be applied to other patients with a long PR interval in the absence of AVNRT.

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