

# Differential Responses of the Septal Ventricle and the Atrial Signals During Ongoing Entrainment

## A Method to Differentiate Orthodromic Reciprocating Tachycardia Using Septal Accessory Pathways From Atypical Atrioventricular Nodal Reentry

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**Background**—Differential diagnosis between tachycardia mediated by septal accessory pathways (AP) and atypical atrioventricular nodal reentry can be challenging. We hypothesized that an immediate versus delayed pace-related advancement of the atrial electrogram, once the local septal parahisian ventricular electrogram (SVE) has been advanced, may help in this diagnosis.

**Methods and Results**—We focused on differential timing between SVE and atrial signals at the initiation of continuous right ventricular apical pacing during tachycardia. SVE advancement preceding atrial reset was defined as SVE advanced by the paced wave fronts while atrial signal continued at the tachycardia cycle. We analyzed 51 atypical atrioventricular nodal reentry (45% posterior type) and 80 AP tachycardias (anteroseptal [10], parahisian [18], midseptal [12], and posteroseptal [40]). SVE advancement preceding atrial reset was observed in 98% of atrioventricular nodal reentries during  $4 \pm 1.1$  cycles; this phenomena was observed in 6 (8%) of the atrioventricular reentrant tachycardia mediated by septal AP ( $P < 0.001$ ; sensitivity 98%; specificity 93%; positive predictive value 90%; negative predictive value 99%) and lasted 1 single cycle ( $P < 0.001$ ). Right posteroseptal AP tachycardias were distinctly characterized by atrial reset preceding SVE advancement (with ventricular fusion; specificity 100%; positive predictive value 100%). In 11 cases, it was impossible to achieve sustain entrainment. In all of them, the differential responses at the entrainment attempt allowed for appropriate diagnosis.

**Conclusions**—The differential response of the SVE and the atrial electrogram at the initiation of continuous right ventricular apical pacing during tachycardia effectively distinguishes between atypical atrioventricular nodal reentry and atrioventricular reentrant tachycardia mediated by septal APs. (*Circ Arrhythm Electrophysiol.* 2015;8:1201-1209. DOI: 10.1161/CIRCEP.115.002949.)

**Key Words:** accessory pathway ■ atypical nodal reentry ■ diagnostic method ■ differential diagnosis  
■ entrainment attempt ■ supraventricular tachycardia

Septal accessory pathways (APs) and atypical atrioventricular nodal reentry (AVNRT) commonly mediate supraventricular tachycardia with concentric atrial activation and long ventriculoatrial (VA) intervals. Several diagnostic maneuvers can aid differential diagnosis, including a return cycle after continuous entrainment from the right ventricular apex (RVA),<sup>1,2</sup> tachycardia resetting with

electrocardiographic fusion,<sup>3,4</sup> and even responses to single ventricular extrastimulus.<sup>5</sup> However, it has been reported that  $\leq 15\%$  to 20% of the tachycardia mechanism could be interrupted by the entrainment maneuvers.<sup>5</sup> In these instances, the utility of RVA pacing during tachycardia at the beginning of the entrainment attempt has received less attention as a diagnostic technique. Recently, AlMahameed et al elegantly

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### WHAT IS KNOWN

- To differentiate between tachycardia mediated by septal accessory pathways or atypical atrioventricular nodal reentry commonly require for extensive differential diagnosis.
- The entrainment attempt from the right ventricular apex retrieves important clues.

### WHAT THE STUDY ADDS

- A new analysis to distinguish between tachycardia mediated by septal accessory pathways and atypical atypical atrioventricular nodal reentry is described and compared with standard methods and maneuvers.
- The study displays that the course of changes in the local time of activation induced by the entrainment attempt at the septal ventricle, and the atrial signals are related to the tachycardia mechanism, with potential for diagnostic improvements.

described the concept of the transitional zone (TZ) as the sequence of interactions between the first train stimulus and the corresponding tachycardia wave fronts, allowing progressive fusion of the QRS complex.<sup>4</sup> Perturbation of atrial timing during this TZ is a specific feature of macroreentry, with the ventricle being part of the circuit, allowing for the fusion of the ventricle while resetting the atrium. Another similar way to demonstrate it is a single ventricular extrastimuli delivered during refractory His or displaying fusion at the surface ECG<sup>6</sup> because even one beat of reset/entrainment (whether single extrastimuli or onset of pacing) is diagnostically sufficient. Also, Dandamudi et al described that the time-dependent pattern of resetting the atrium by RVA pacing yielded appropriate diagnostic discrimination even if the tachycardia mechanism was interrupted.<sup>7</sup>

Here we describe a complementary diagnostic method based on the differential timing between the septal ventricular electrogram (SVE) and the atrial signals during continuous ventricular pacing from the RVA. We analyzed the responses in the clinical scenario of 2 tachycardia mechanisms that require extensive electrophysiological investigation, atypical AVNRT, and atrioventricular reentrant tachycardia (AVRT) mediated by septal AP. Our principle for this approach is that SVE could be advanced by the paced wave front without perturbing the atrial timing, and without resetting the tachycardia cycle, only if the responsible mechanism is an AVNRT; however, the latter is not an expected phenomena in AVRT mediated by septal APs because the interaction of the paced wave front with the ventricular insertion of the AP at the septum must immediately reset the tachycardia cycle length.<sup>8</sup>

## Methods

### Study Population and Inclusion Criteria

We evaluated the clinical profile of the patients included in the database of our Electrophysiology Laboratories. Retrospectively, patients

referred because of paroxysmal supraventricular tachycardia were analyzed if pacing from the RVA was delivered, faster than the tachycardia cycle length, in an attempt to entrain the tachycardia mechanism. Of those, our study focused on patients developing tachycardia with concentric atrial activation and mediated by septal APs (ortodromically) or atypical AVNRT (earliest VA intervals >70 ms).<sup>9</sup> Patients with APs with decremental conduction properties were excluded from the analysis. Only patients with a certain diagnostic and successful ablation were included.

### Electrophysiological Procedure and Tachycardia Diagnosis

After obtaining written informed consent, an electrophysiological study was performed with patients in the fasting, unsedated state. Inserted through the right femoral vein, 2 diagnostic catheters were placed at the high right atrium (HRA) and the RVA and a 4-mm ablation catheter was placed at the level of the antero-septal tricuspid valve to record the His bundle signal and the parahisian atrium and ventricle. Bipolar signals were stored on conventional recording systems (Prucka Cardiolab, General Electric Medical Systems, Milwaukee, WI; EPTracer, Cardiotek, Maastricht, The Netherlands). Signals were band-pass filtered between 30 and 500 KHz and recorded at 100 to 200 mm/s using the integrated calipers for measurements. Under these conditions, the expected accuracy of the measurements is considered to be <5 ms.<sup>10</sup> Changes in the local time of activation of the SVE and atrial signals during the entrainment attempt were considered to occur only if >15 ms. If there was some irregularity in the tachycardia cycle length (here defined as beat-to-beat variability exceeding 15 ms), any advancement of the atrial or the ventricular signals was measured considering the shortest tachycardia cycle length as a reference.<sup>5</sup> For appropriate timing at the bipolar records, we consistently selected for measurement the point at which the largest rapid deflection crosses the baseline or the peak of the largest deflection because they more or less correspond with the maximum dV/dr (intrinsicoid deflection) of the unipolar records.<sup>10</sup> If the signal was fragmented (multicomponent electrogram), and no clear deflection behaved as the largest, we selected the peak of the first positive deflection of the electrogram for timing. Bipolar pacing was performed at twice diastolic threshold from the distal electrode pair.

Sustained supraventricular tachycardia was induced using conventional atrial and ventricular stimulation protocols. By using the ablation catheter, we explored the coronary sinus and the tricuspid annulus to determine concentric sequences of activation during tachycardia. Of those, we excluded atrial tachycardia for analysis, characterized by a common VAAV response after entrainment from the RVA, absence of VA linking (ie, variable AH and VA intervals), changes in H-H or V-V intervals that were preceded by changes in A-A intervals, or AV dissociation with rapid RVA pacing at a cycle length between 200 and 250 ms during tachycardia as described elsewhere.<sup>1</sup> After that, the exact mechanism of the tachycardia was determined based on previously described maneuvers.<sup>2</sup> Despite both types being included, posterior type AVNRT (versus anterior) was defined by the earliest retrograde atrial activation recorded at the ostium of the coronary sinus. Septal APs were classified as antero-septal, parahisian, midseptal, or postero-septal according to the anatomic location of the catheter tip during successful ablation. The same criteria were followed to consider the left or right location of postero-septal APs.

### Entrainment Attempt and Definitions

After induction by programmed stimulation, entrainment of the tachycardia was attempted by pacing for several pulses from the RVA at a cycle length shorter than the tachycardia cycle length. For appropriate coupling, the first train beat was timed to the bipolar signal at the distal RVA electrode because it was the same bipole as that used for stimulation. Entrainment was confirmed when the atrial cycle length accelerated to the pacing cycle length without a change in the atrial activation sequence, and the tachycardia resumed after pacing was discontinued.<sup>3</sup> Resetting of the tachycardia mechanism

was confirmed when the atrial depolarization after RVA pacing was advanced by at least 15 ms followed by the entrainment/continuation of the tachycardia. Fusion at the 12 lead ECG records was evaluated during resetting or entrainment. Two experimented electrophysiologists independently examined all recordings.

To conduct the analysis, the train of stimulus from the RVA was analyzed during the first pacing beats in an attempt to interact with the tachycardia mechanism, previously described as TZ.<sup>4</sup> We analyzed the first atrial and SVE (parahisian) signals that are advanced for the paced wave fronts from the tachycardia cycle length (captured by the paced wave front). The presence of discordant timing between the corresponding atrial and SVE signals for at least 1 cycle was defined as a differential response. The differential response was considered to be SVE advancement preceding atrial reset when the SVE was advanced by the paced wave front, whereas the corresponding atrial activation remained at the tachycardia cycle length. In contrast, an atrial reset preceding SVE advancement response was confirmed when the atrial activation was advanced by the paced wave front, whereas the corresponding SVE continued at the tachycardia cycle length (which implies atrial reset with ventricular fusion). Finally, simultaneous SVE advancement and atrial reset was defined when the atrial signals and the SVE were simultaneously advanced by the paced wave front. The last 2 responses implied the reset of the tachycardia.

### Mechanistic Analysis

To provide for mechanistic insight, the time lapse and spatial distance from the stimulation point at the RVA to 2 different recording sites, located at the parahisian and the right posteroseptal ventricle, were measured in terms of conduction time and linear longitudinal distance. For the latter, we performed measurements in a subset of patients using the CARTO system (Measure Distance; Biosense Webster). In addition, activation time from the onset of the QRS complex to the local ventricular electrogram at the parahisian and the right posteroseptal location was measured during sinus rhythm.

### Statistical Analysis

Categorical variables were summarized by percentages and quantitative variables by mean and standard deviation (SD). Percentages were compared between groups using the  $\chi^2$  test, and means were compared between groups by using the *t* test. In the case of paired data, means were compared between groups by paired *t* test. The predictive performance of maneuvers was assessed by receiver operating characteristic analysis. The area under the curve between methods was compared using the DeLong method.<sup>11</sup> Positive predictive values and negative predictive values were compared between methods using the standard 2 related proportional test.<sup>12</sup> Agreement between investigators was measured by the concordance correlation coefficient ( $\kappa$  statistic). Analyses were performed with SPSS version 20 (SPSS Inc., Chicago, IL), R version 3.1 (www.r-project.org),

and Epidat 4.1 (www.sergas.es). Statistical significance was declared when  $P < 0.05$ .

## Results

### Patients and Tachycardia Characteristics

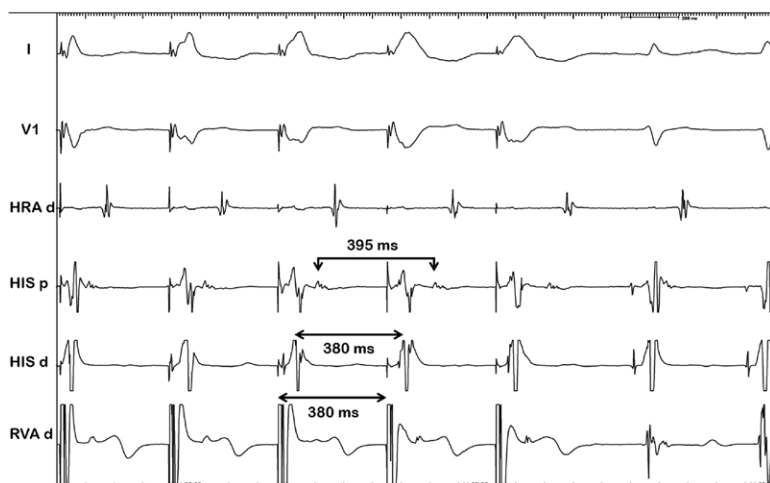
We analyzed 131 patients: 51 (39%) with atypical AVNRT and 80 (61%) with orthodromic AVRT mediated by septal APs. Mean age was  $45.6 \pm 19.7$  years, and 65 (49.6%) of the patients were women. AVNRTs displayed a VA interval of  $152 \pm 63$  ms measured to the HRA and a shorter VA interval of  $129 \pm 54$  ms displayed at the septum. The AVNRTs included 23 (45%) posterior-type forms, as defined by earliest atrial activation at the ostium of the coronary sinus. The location of the APs was anteroseptal in 10 cases (12.5%), parahisian in 18 cases (22.5%), midseptal in 12 cases (15%), and posteroseptal in 40 cases (50%). Posteroseptal APs were found at the right posteroseptum in 27 cases (67.5%) and at the left posteroseptum in 13 cases (32.5%). The VA interval measured to the HRA was not significantly longer during AVRT ( $161 \pm 36$  ms) than during AVNRT ( $P = 0.393$ ), but there were significant differences in the tachycardia cycle length (AVNRT  $400 \pm 78$  ms versus AVRT  $340 \pm 51$  ms;  $P < 0.001$ ).

### Tachycardia Responses to the Entrainment Attempt

RVA stimulation was performed  $28.1 \pm 13$  ms faster than the tachycardia cycle length. Failure for sustain entrainment of the tachycardia was observed in 11 patients (8%); 5 patients with AVNRT and 6 patients with AVRT (see below for details). When determined ( $n = 120$ ), corrected return cycle length after entrainment from RVA was longer for AVNRT ( $177 \pm 35$  ms versus  $44 \pm 22$  ms;  $P < 0.001$ ). Also, the differences between the time interval from the stimulation spike to the HRA signal during entrainment and from the QRS onset (SA-VA) were longer for AVNRT ( $156 \pm 37$  ms versus  $27.3 \pm 21$  ms;  $P < 0.001$ ).

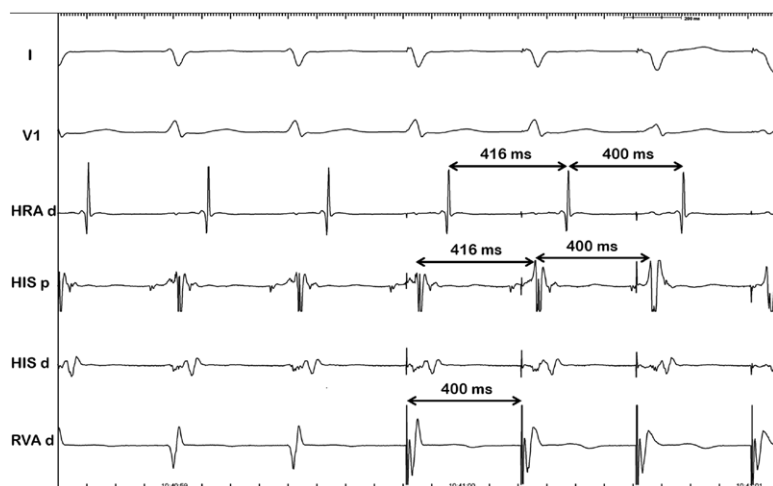
### Characteristic Responses of AVNRT

Independently of the location of the earliest atrial activation (posterior versus anterior), AVNRT usually exhibited transient SVE advancement preceding atrial reset in response to the first pacing beats from the RVA ( $n = 50$ ; 98%). Figure 1 displays a representative example in which the atrial timing remains at the tachycardia cycle length, despite the parahisian



**Figure 1.** SVE advancement preceding atrial reset during AVNRT. During the entrainment attempt, the parahisian ventricular signal is advanced to the stimulation cycle length (380 ms), whereas the corresponding atrial signals remain at the tachycardia cycle length (395 ms). Note that entrainment was not ultimately achieved at the end of the train, thus explaining the additional value of the observed response. AVNRT indicates atrioventricular nodal reentry tachycardia; HRA, high right atrium; RVA, right ventricular apex; and SVE, septal ventricle electrogram.





**Figure 2.** Simultaneous SVE advancement and atrial reset during the entrainment attempt of AVRT mediated by a parahisian AP. As soon as the parahisian ventricular signal is advanced from the tachycardia cycle length (416 ms) to the pacing cycle (400 ms), the same phenomena is observed at the corresponding atrial signals. A refractory His bundle is observed, thus confirming the presence of an AP. AP indicates accessory pathway; AVRT, atrioventricular reciprocating tachycardia; HRA, high right atrium; and RVA, right ventricular apex.

SVE having been captured by the pace wave front. It is noteworthy that after the last paced pulses sustain entrainment was not achieved, the SVE advancement preceding atrial reset is independently observed. Overall, the mean number of SVE that was consecutively advanced from the paced wave front without perturbing the atrial timing or interrupting the tachycardia mechanism was  $4 \pm 1.1$  (range 2–6). Only 1 case showed simultaneous SVE advancement and atrial reset, a response that was immediately followed by the entrainment of the tachycardia.

### Characteristic Responses of AVRT

The behavior of AVRT was highly dependent on the location of the AP in the septum. The most frequent response of anterosseptal, parahisian, and midseptal APs was the simultaneous SVE advancement and atrial reset ( $n=38$ ; 95%), indicating that as soon as the parahisian ventricular septum was advanced by the paced wave front, the atrial timing was simultaneously shortened by the paced wave front (Figure 2). Only 2 cases showed SVE advancement preceding atrial reset during 1 single cycle, a response that was immediately followed by the entrainment of the tachycardia.

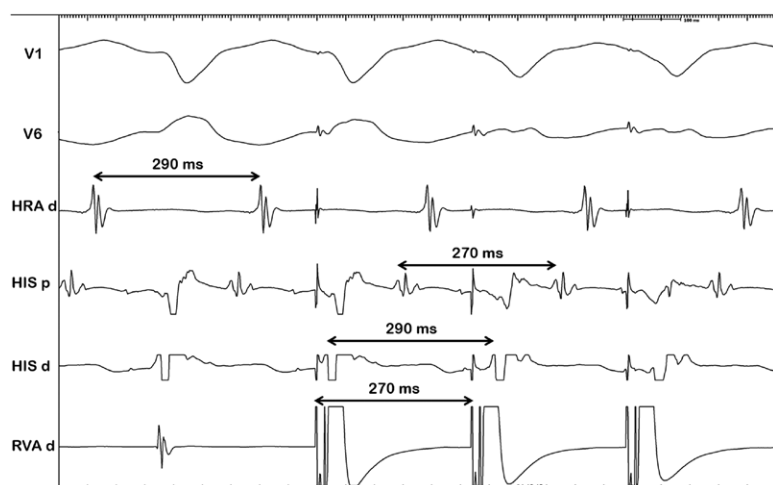
Atrial reset preceding SVE advancement was observed exclusively during AVRT mediated by right posteroseptal APs when compared with other septal locations ( $P<0.001$ ).

Figure 3 clearly exemplify the response and demonstrates how the phenomena accounts for one single cycle. This type of response accounted for 19 of 27 right posteroseptal APs (70%), and, as expected, it was observed only during one single cycle in all of the cases, giving rise to sustain entrainment or the interruption of the circuit. The other 8 cases showed simultaneous SVE advancement and atrial reset, as expected for the tachycardia mechanism.

Left posteroseptal APs behaved differently, and the incidence of SVE advancement preceding atrial reset, never observed in right posteroseptal APs, accounted for 4 cases (31%). As for other locations, the phenomenon was observed during one single cycle and was followed by sustain entrainment of the tachycardia. The other 9 cases (69%) displayed simultaneous SVE advancement and atrial reset. Atrial reset preceding SVE advancement was never achieved in this tachycardia mechanism.

### Tachycardia Responses When Sustain Entrainment Was Not Achieved

As stated earlier, the tachycardia mechanism was interrupted in 11 patients during overdrive pacing. As a consequence, the mechanism was entrained even if for only one beat, but it did not allow for the analysis of postpacing responses (ie, return



**Figure 3.** Atrial reset preceding SVE advancement during the entrainment attempt of AVRT mediated by a right posteroseptal AP. After the second paced beat, the parahisian atrial signal is advanced to the stimulating frequency (270 ms), whereas the corresponding parahisian ventricular signal remains at the tachycardia cycle length (290 ms). A refractory His bundle is observed, thus also confirming the presence of an AP. However, the response additionally enables rapid location of the AP to the right posteroseptal area. AP indicates accessory pathway; AVRT, atrioventricular reciprocating tachycardia; HRA, high right atrium; RVA, right ventricular apex; and SVE, septal ventricle electrogram.



**Figure 4.** SVE advancement preceding atrial reset during AVNRT. During the entrainment attempt, the parahisian ventricular signal is advanced to the stimulation cycle length (380 ms), whereas the corresponding atrial signals remain at the tachycardia cycle length (415 ms). Of note, the His signal was not appropriately recorded, and the tachycardia was interrupted in the retrograde limb without entrainment (red dot). Both circumstances reflect the additional value of the differential response. AVNRT indicates atrioventricular nodal reentry tachycardia; HRA, high right atrium; RVA, right ventricular apex; and SVE, septal ventricle electrogram.

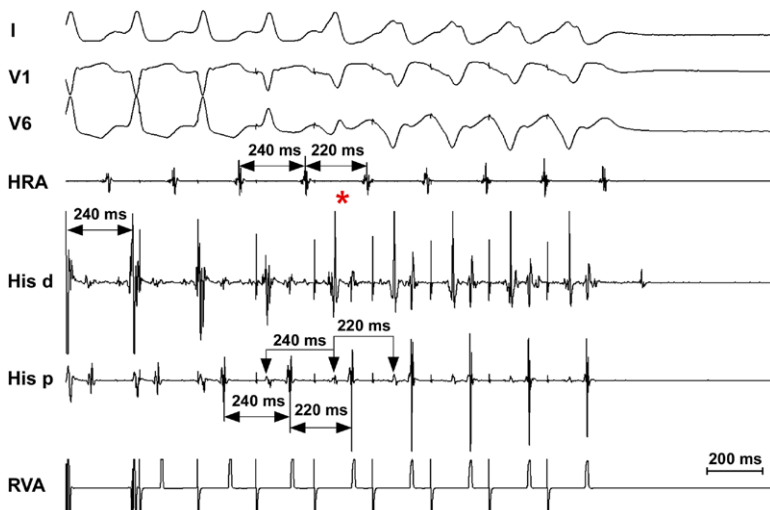
cycle). Interestingly our approach proved to be useful in these particular cases because the responses observed during the entrainment attempt remained diagnostic of the tachycardia mechanism. As it is exemplified in Figure 4, the maneuver appropriately worked in those cases of AVNRT where the entrainment attempt interrupted the tachycardia during stimulation ( $n=5$ ). In this representative example, the interruption of the tachycardia was observed because of a block in the retrograde limb. However, just before the block, the parahisian SVE was captured by the pace wave front during 5 cycles without perturbing the atrial cycle, thus allowing for appropriate diagnosis.

In those cases of AVRT, inability for sustain entrainment was mainly observed because of the interruption of the circuit during pacing in the anterograde limb ( $n=5$ ; 2 right posteroseptal AP, 2 parahisian AP, and 1 midseptal AP). However, the responses observed just before the interruption were congruent with the mechanism of the tachycardia, either simultaneous SVE advancement and atrial reset or atrial reset preceding SVE advancement. This is exemplified in Figure 5, where interruption in the anterograde limb of the tachycardia is demonstrated by the atrial reset preceding SVE advancement observed during one single cycle and refractory His. The example corresponds to an AVRT mediated by a right posteroseptal AP, highlighting the additional value of the response not only to confirm the presence of an AP but also helping to localize it at the right posteroseptal area. In 1 additional case, entrainment was not possible because of the inability to

pace regularly during the train. However, single extrastimulus delivered during tachycardia from the RVA allowed for the reset of the circuit during refractory His. The response observed during the maneuver was an atrial reset preceding SVE advancement, thus confirming the presence of a right posteroseptal AP.

### Diagnostic Yield of the Maneuver

As a diagnostic maneuver, SVE advancement preceding atrial reset displays high sensitivity and negative predictive value for AVNRT, supporting the diagnosis of AVRT when the phenomena is lacking (sensitivity 98%; specificity 93%; positive predictive value 89%; negative predictive value 99%). In addition, the high specificity and positive predictive value of the atrial reset preceding SVE advancement reveals this phenomena as diagnostic of AVRT mediated by a right posteroseptal AP (sensitivity 70%; specificity 100%; positive predictive value 100%; negative predictive value 93%). Overall, this data enhances credibility for the atrial reset preceding SVE advancement as demarking both the tachycardia mechanism and the location of the septal AP. Also, it is noteworthy that, if observed, SVE advancement preceding atrial reset during AVRT invariably accounts for 1 single cycle, whereas characteristically occurs for several cycles during AVNRT ( $4 \pm 1.1$  cycles;  $P < 0.001$ ). Interestingly, concordance in the interpretation of the different responses between observers was significantly high ( $\kappa$  statistic 0.94).



**Figure 5.** Atrial reset preceding SVE advancement during AVRT mediated by a right posteroseptal AP. During the entrainment attempt, the tachycardia was interrupted. At the beat marked with the red dot, atrial signals were advanced from the tachycardia cycle length (240 ms) to 220 ms (pacing cycle from the right ventricular apical [RVA] 210 ms). However, at the same beat, parahisian SVE remains at the tachycardia cycle length (240 ms). The phenomenon was observed during one single cycle-beat. Atrial reset during QRS fusion and refractory His confirms also the presence of an AP, but the atrial reset preceding SVE advancement additionally localize the AP to the right posteroseptal area. AP indicates accessory pathway; AVRT, atrioventricular reciprocating tachycardia; HRA, high right atrium; RVA, right ventricular apex; and SVE, septal ventricle electrogram.

**Table. Performance of Overdrive Pacing Maneuvers During Tachardia**

Observed Phenomena	AVNRT, N (%)	AVRT, N (%)	PPV, %	NPV, %	ROC (AUC $\pm$ SE)	Impossibility to Test, N (%)	$\kappa$ Statistic (Two Observers)
Atrial reset with ventricular fusion at the surface ECG	0 (0)	73 (91)	100, $P=0.989$	88, $P=0.946$	0.96 $\pm$ 0.02, $P=0.886$	0 (0)	0.61, $P<0.001$
Atrial reset with refractory His bundle	0 (0)	76 (99)	100, $P=0.995$	98, $P=0.166$	0.99 $\pm$ 0.01, $P=0.031$	6 (5)*	...
Simultaneous advancement or atrial reset preceding SVE advancement	1 (2)	74 (93)	99	89	0.95 $\pm$ 0.02	0 (0)	0.94
Corrected return cycle <110 ms	0 (0)	74 (100)	100, $P=0.995$	100, $P=0.062$	1, $P=0.015$	11 (8)†	...
SA-VA difference <90 ms	2 (4)	74 (100)	97, $P=0.991$	100, $P=0.061$	0.98 $\pm$ 0.02, $P=0.210$	11 (8)†	...

Diagnostic yield observed for responses analyzed during overdrive pacing from the RVA. Values were calculated to predict AVRT if the phenomena is observed. AUC indicates area under the curve; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver operating characteristic; RVA, right ventricular apex; and SVE, septal ventricle electrogram. All the  $P$  values are from testing the equality of PPV, NPV, AUC, and  $\kappa$ -statistic between each considered method and the reference one (simultaneous advancement or atrial reset preceding SVE advancement).

\*Impossibility to test because of no appropriate His bundle recording.

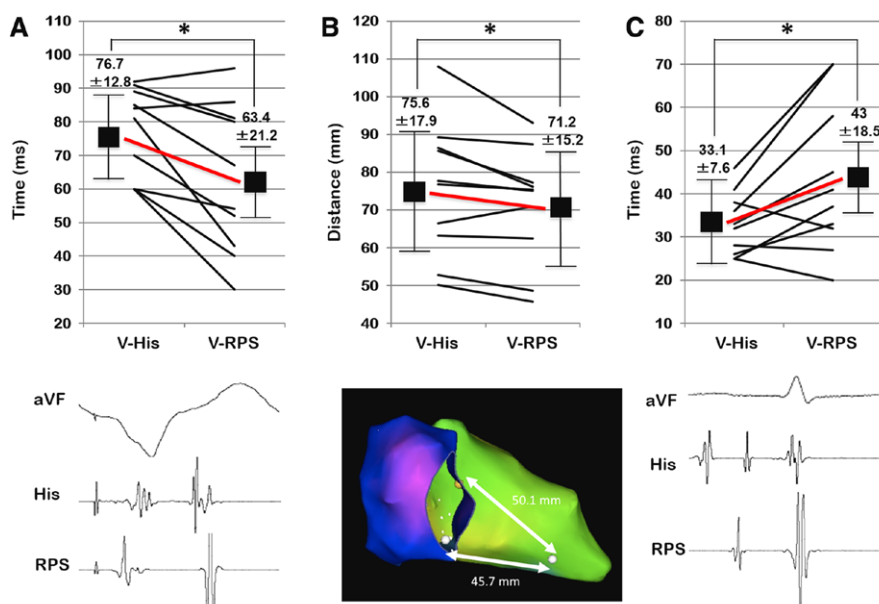
†Impossibility to test because of tachycardia interruption during pacing.

A comparison with previously described maneuvers is summarized in Table. To summarize briefly, appropriate diagnostic yield was high for all the analyzed maneuvers. In our sample, postpacing responses (ie, corrected return cycle and SA-VA) and atrial reset during refractory His bundle were impossible to test in 8% and 5% of the cases, whereas our maneuver and the atrial resetting with ECG fusion could be tested in all cases. Also, the analysis of the intracardiac signals we propose here had less variability between observers when compared with the analysis of the surface ECG fusion ( $\kappa$  statistic 0.94 versus 0.61;  $P<0.001$ ). Based on these data, we think that the relative utility of the observations found in our work increase the ability of the overdrive

pacing maneuvers to differentiate between atypical AVNRT and AVRT mediated by septal APs in difficult or unusual scenarios.

### Physiological Explanations to the Observed Responses

For mechanistic analysis, we evaluated local timings of the RV endocardium in 10 patients with structurally normal hearts referred for electrophysiology evaluation and 3D mapping because of left atrium tachycardias, left free wall Aps, and right ventricle outflow tract extrabeats. During RVA pacing, the stimulated wave front arrived first to the right posteroseptal



**Figure 6.** **A**, Time lapse from RVA stimulation to the parahisian and right posteroseptal ventricle, respectively (an example is showed in bottom). **B**, Longitudinal distance from the stimulation point at the RVA to the parahisian and right posteroseptal ventricle, respectively. An example of the CARTO measurements is showed at the bottom, where 3D maps correspond to the right atrium (blue) and left ventricle (green). Solid balls depicted location only points used for measurements (yellow balls correspond to His location; left white correspond to right posteroseptal ventricle; right white correspond to the stimulation point at the RVA). **C**, Time lapse from the QRS onset to the parahisian and right posteroseptal ventricle, respectively (an example is showed in bottom). RVA indicates right ventricular apex; V-His, his ventricle; and V-RPS, right posteroseptal ventricle.

ventricle than to the parahisian ventricle ( $63.4 \pm 21.2$  versus  $76.7 \pm 12.8$  ms;  $P=0.006$ ; Figure 6A). These data were also in accordance with the shorter longitudinal distance measured from the stimulation point at the RVA to the right posteroseptal ventricle compared with the parahisian ventricle ( $71.2 \pm 15.2$  versus  $75.6 \pm 17.9$  mm;  $P=0.032$ ; Figure 6B). In addition, measurements during sinus rhythm showed that time lapse from QRS onset to the parahisian ventricle was shorter than that to the right posteroseptal ventricle ( $33.1 \pm 7.6$  versus  $43 \pm 18.5$  ms;  $P=0.041$ ; Figure 6C). The latter allowed shorter coupling intervals during RVA stimulation to the right posteroseptal ventricle.

## Discussion

### Main Findings

This study expands the diagnostic value and reliability of the RVA overdrive pacing maneuvers to discern between atypical AVNRT and AVRT mediated by septal APs, a common diagnostic problem in clinical electrophysiology.<sup>13,14</sup> Focusing on those paced wave fronts that allow for what was previously described as TZ,<sup>4</sup> local responses of the SVE and atrial signals provide diagnostic clues for the differential diagnosis between both arrhythmia mechanisms even if the tachycardia was interrupted during overdrive pacing. Also, it is simple to analyze, displays low variability between observers, and is not dependent on the His bundle recording. Moreover, a different location of the AP at the septum implies a different pattern of responses. That allows for a distinctive behavior of those AVRT mediated by right posteroseptal APs consisting in atrial reset preceding SVE advancement, which remains diagnostic not only for the tachycardia mechanism but also for the anatomic location of the AP when analyzed under the standard position of the catheters for pacing and measurements.

### Rationale of the Study and Mechanism

Both atypical AVNRT and AVRT mediated by septal APs display long VA intervals, concentric activation of the coronary sinus, and earliest atrial activation that can be widespread along the septum depending on the location of the retrograde limb. Thus, recognition of the exact tachycardia mechanism generally requires additional diagnostic maneuvers. Methods based on physiological criteria generally look for binary responses that are compatible or not with the presence of a particular tachycardia mechanism. Examples are apex base stimulation,<sup>15</sup> parahisian pacing,<sup>16</sup> and tachycardia resetting during the His bundle's refractory period.<sup>6</sup> Consistent with Lockwood et al,<sup>8</sup> we postulated that with RVA overdrive pacing, the SVE at the His should be activated immediately before the reset of the atrium at the same site if there is a septal AP close enough to this region (this atrial reset is reflected if there is no atrial delay as there usually is not). In other words, SVE advancement preceding atrial reset is not compatible with the presence of a common septal AP that maintains the tachycardia mechanism because whenever the ventricular insertion of the AP at the septum is advanced from the RVA paced wave front, the atrial signal must also be advanced. On the contrary, with RVA overdrive pacing the SVE at the His may be activated first, even if there is no reset of the atrium at the same

site, in the absence of an AP (ie, AVNRT) or if there is an AP far enough away from the septal region (ie, free wall AP).

As a practical approach, we measured the responses at the level of the HRA, the parahisian atrium, and the parahisian ventricle during RVA stimulation because those areas are commonly explored during the electrophysiological procedures and enable quick diagnostic maneuvers to be performed. In these instances, SVE advancement preceding atrial reset by  $>1$  cycle is transiently observed during AVNRT until RVA wave fronts entrain the tachycardia circuit at the atrioventricular node. Our data are in accordance with AlMahameed et al, who have shown that AVNRT entrainment typically occurs after the TZ with no fusion in the surface ECG.<sup>4,17</sup> In our opinion, different mechanism may explain why the paced wave front reaches the parahisian ventricular myocardium before capturing the atrium through the conducting system. One involves the refractory His encountered by the late-coupled wave fronts at the beginning of the entrainment attempt. Another stems from the older discussion about the atrioventricular node final common pathway, which would be responsible for the delayed entrainment.<sup>6,7</sup>

In contrast, SVE advancement preceding atrial reset was rarely observed during AVRT mediated by anteroseptal, parahisian, and midseptal APs, thus reflecting the association between the high ventricular septum and the tachycardia mechanism. Only 2 cases revealed the unexpected phenomena during one single cycle. Although septal, and difficult to explain in other terms, we postulate that the ventricular insertion of the AP could be located at a deep level (in the midmyocardium), thus allowing some degree of spurious differential responses. In addition, those APs were identified at the level of their atrial insertion, and it is possible that a crossing tract remained unexplored.

Right posteroseptal APs merit special consideration. The specific response, characterized by atrial reset preceding SVE advancement, reflects the presence of ventricular fusion while the atrium is reset, thus confirming the presence of an AP.<sup>13</sup> The particular value of this response is that it is also specific in localizing the AP at the right posteroseptum. Several factors could favor this phenomenon. First, timing the coupling interval of the train to the bipolar signal of the RVA results in greater couplet stimulus to the right posteroseptum than to the parahisian SVE. This is because of the shorter activation time from the QRS to the parahisian electrogram than to the right posteroseptum. Second, because the right posteroseptal location is somewhat distant from the recorded ventricular signal at the parahisian level, it is possible to encounter the posterior right septum from RVA stimulation first if it is close (Figure 6). That allows the paced wave front to reset the atrial cycle length before the advancement of the parahisian SVE. As a result, the phenomenon consists of a reset of the atrium during ventricular pacing, without perturbing the parahisian SVE. Of note, 45% of our patients with atypical AVNRT showed earliest atrial activation at the ostium of the coronary sinus, making the differential diagnosis with right posteroseptal APs based on atrial activation sequence impossible. This enhances the additional value of the specific response.

Finally, left located APs could be a drawback for the technique. We postulate that because the left septum is far from



both the stimulated point and the recorded point in the right ventricle, SVE advancement preceding atrial reset may be observed during left posteroseptal Aps-mediated AVRT. It may also be explained by the dependency of the circuit on the left conducting system.<sup>3</sup> However, the fact that the response was observed during one single cycle denotes differences with AVNRT and allows for the diagnosis. As expected, atrial reset preceding SVE advancement was never recorded in this context.

### Comparison With Other Studies and Maneuvers

The TZ has been extensively analyzed by other authors, rendering appropriate diagnostic yield for discrimination between AVNRT and AVRT. The main findings to be addressed during the analysis are the pattern of perturbation of atrial timing during the overdrive pacing and its relation to fusion at the surface QRS. Both AlMahameed et al and Dandamudi et al observed that perturbation of atrial timing during this TZ is a specific feature of macroreentry with the ventricle being part of the circuit, allowing fusion of the ventricle while resetting the atrium. They also demonstrate that the time-dependent pattern of atrial resetting yielded appropriate diagnostic discrimination even if the tachycardia mechanism was interrupted. Our data are in agreement with those observations and also extend the reliability for differential diagnosis by displaying lower variability between observers when ventricular fusion is analyzed using intracardiac records instead of the surface ECG (Table). Recently, other authors have also focused on intracardiac responses to differentiate between AVRT and AVNRT, pointing out additional value beyond subjective comparisons of the surface ECG records. In this setting, Nagashima et al showed that anterograde His bundle or SVE capture during RV entrainment was diagnostic for AVRT using a septal AP.<sup>18</sup> However, they found that the response was indeterminate in  $\approx 25\%$  of patients. Instead, differential responses of the SVE and atrial signals, such as those proposed in our work, were consistently measured in all patients and without significant discrepancies between observers, probably displaying additional value for the relevant findings from Nagashima et al.

When compared with other maneuvers, we postulate that there are 3 possible scenarios in which the differential responses between the SVE and atrial signals may contribute to increasing the diagnostic yield of the overdrive pacing maneuvers (summarized in Table): (1) when the responses to entrainment cannot be studied because of interruption of the tachycardia, (2) when the quality of the His bundle signal is not appropriate for analysis (ie, when lost during pacing or in patients with displaced AV nodes/conduction system as those with congenital heart diseases), and (3) when subtle changes at the QRS morphology preclude consistent evaluation of fusion at the ECG records. Besides, this maneuver is simple to do and easy to interpret. Based on these data, we think that the relative utility of the observations found in our work increase the ability of the overdrive pacing maneuvers to differentiate between atypical AVNRT and AVRT mediated by septal APs under difficult and unusual scenarios.

### Limitations

Although the classification of responses is based on objective measurements, this study is not blinded with regard to the final diagnosis of the tachycardia mechanism. APs with decremental properties were not examined in this study, so the conclusions obtained cannot be applied. Also, free wall APs could theoretically present similar responses and should be differentiated from right septal APs. We emphasize that the results and interpretations described in this work applies under the septal location of the APs. Despite the fact that measurements were done at the bipolar records, changes in morphology can occur between consecutive beats, which may affect accuracy when determining changes in the local activation time. Regarding the longitudinal measurements, we are aware that distance is not at all linear in the endocardial surface. Because of that, measurements should be taken as an approximation of real conditions. Also, the limited number of cases included for this analysis prevents us from validating the hypothesis under different types of conduction abnormalities and heart disease. Evaluation of the number of cycles that display SVE advancement preceding atrial reset could be influenced by the pacing cycle and affect the results. Also, as the nature of the responses could be critically dependent on the position of the catheters and places for measurements, we cannot ascertain the validity of the responses under different settings for the electrophysiological procedure.

### Conclusions

Different patterns of local responses of the SVE and the atrial signals during the entrainment attempt effectively distinguish between atypical AVNRT and AVRT mediated by septal APs. In addition, atrial reset preceding SVE advancement is a specific response of AVRT mediated by a right posteroseptal AP compared with other septal locations. The predictive values of the responses remain valid even if sustain entrainment is not achieved or the tachycardia mechanism is interrupted. Furthermore, it is a simple maneuver and easy to interpret.

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### Disclosures

None.

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**Differential Responses of the Septal Ventricle and the Atrial Signals During Ongoing Entrainment: A Method to Differentiate Orthodromic Reciprocating Tachycardia Using Septal Accessory Pathways From Atypical Atrioventricular Nodal Reentry**

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