Entrainment from the para-Hisian region for differentiating atrioventricular node reentrant tachycardia from orthodromic atrioventricular reentrant tachycardia

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Aims The difference between the stimulus-atrial and ventriculo-atrial intervals (SA–VA) and between the post-pacing interval and the tachycardia cycle length (PPI–TCL) during entrainment from the right ventricular apex distinguishes atrioventricular node reentrant (AVNRT) from orthodromic atrioventricular reentrant tachycardia (AVRT). We hypothesized that these features still apply when entrainment is performed from the para-Hisian region.

Methods and results Forty-seven supraventricular tachycardias (34 AVNRT/13 AVRT) were included. The SA–VA and PPI–TCL were obtained in all patients by using two right-sided diagnostic catheters. In 24 of them, these measurements were also performed upon His-bundle capture during entrainment. A paced QRS widening of ≥40 ms during entrainment, when compared with the tachycardia QRS width, identified absence of His-bundle capture, \( P < 0.001 \). A SA–VA >75 ms distinguished AVNRT from AVRT, \( P < 0.001 \) (sensitivity/specificity 97%/100%). A PPI–TCL <100 ms was diagnostic of AVNRT, \( P < 0.001 \) (sensitivity/specificity 97%/92%). Upon His-bundle capture, the SA–VA and PPI–TCL shortened in AVNRT (121 ± 23 to 66 ± 24 ms; 139 ± 30 to 85 ± 31 ms, respectively, \( P < 0.001 \)) and no longer differentiated AVNRT from AVRT.

Conclusion Para-Hisian entrainment without His-bundle capture distinguishes AVNRT from AVRT with the advantage of using only two diagnostic catheters.

KEYWORDS
Entrainment; His bundle; Atrioventricular node reentrant tachycardia; Orthodromic atrioventricular reentrant tachycardia; Accessory pathway

Introduction

Pacing from the right ventricular apex (RV) is an essential electrophysiological maneuver to differentiate atrioventricular nodal reentrant (AVNRT) from orthodromic atrioventricular nodal reentrant tachycardia (AVRT).1–6 Entrainment from the RV apex establishes the relative conduction time from the pacing site to the reentrant circuit, longer in AVNRT than in AVRT. As a result, a difference between the stimulus-atrial and the ventriculo-atrial intervals (SA–VA) of >85 ms, and between the post-pacing interval and the tachycardia cycle length (PPI–TCL) of >110–115 ms favours AVNRT as the tachycardia mechanism.3–4

The endocardial activation of the anteroseptal basal RV (para-Hisian region) starts 20–25 ms after the activation of the RV apex, in the absence of an accessory pathway (AP) with anterograde conduction capacities.7 Inversely, during entrainment from the para-Hisian region, the pacing site, although anatomically close, is electrically away from the tachycardia circuit in AVNRT patients, since ventricular activation travels towards the RV apex to engage the Purkinje network before reaching the AV node retrogradely. This principle may enhance the distinction between AVNRT and AVRT when entrainment is performed from the para-Hisian region. During entrainment or resetting from the His-bundle area, a >40 ms increase of the SA interval (△SA) upon loss of His-bundle capture favours AVNRT as the tachycardia mechanism.8 Noteworthy, varying the energy output during pacing for the achievement of loss of His-bundle capture may result in several degrees of local ventricular capture,

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His-bundle capture, and ‘pure’ His capture. Therefore, a precise identification of RV and RV plus His-bundle capture during para-Hisian entrainment appears obligatory, and is still lacking.

We hypothesized that established criteria differentiating AVNRT from AVRT (i.e., SA–VA and PPI-TCL) still apply when entrainment is performed from the para-Hisian region, with the advantage of using only two right-sided diagnostic catheters. We further aimed to determine the role of His-bundle capture during tachycardia entrainment as a critical factor for these electrophysiological features to have value.

Methods

Patient population

Fifty-five consecutive patients (30 female, mean age 49 ± 17 years) referred for electrophysiological study (EPS) and ablation of documented supraventricular tachycardia (SVT) or Preexcitation Syndrome were considered for inclusion. All patients gave written informed consent in accordance to our institutional guidelines. All but one had a single SVT mechanism, the remaining presenting with both AVRT and typical AVNRT. Patients in whom SVT could not be induced during the EPS or with atrial tachycardia were excluded, as well as those SVT that could not be entrained from the para-Hisian region.

Study protocol

The EPS was performed in the fasting state under conscious sedation. Two 6-French quadripolar catheters (interelectrode spacing 5 mm, C.R. Bard Inc., Murray Hill, NJ, USA) were inserted into the right femoral vein and advanced into the high right atrium (HRA) and the His bundle/proximal right bundle branch (HB–RB) area. Careful attention was given to minimize the atrial signal in the HB–RB catheter in order to ensure that the atrium was not captured during pacing, maintaining a HV interval of >30 ms in the absence of QRS aberrancy.

The surface ECG leads and bipolar intracardiac electrograms (filtered between 30 and 500 Hz) were recorded in the Lab Pro (C.R. Bard Inc., NJ, USA) system and analysed offline for the study analysis. Electronic calipers allowing 1 ms resolution were used at screen velocity of 100 mm/s for all measurements. Measurements were performed by two non-independent observers, and included in the data base after agreement between them. In case of disagreement, a third independent observer was used. The SVT mechanism was confirmed by established electrophysiological criteria and by elimination of the tachycardia after ablation plus inability to reindeer SVT with programmed stimulation within an observation period of 30 min.

Para-Hisian entrainment

Para-Hisian entrainment was attempted with and without HB–RB capture by pacing at 10–30 ms shorter than the TCL and was confirmed when the atrial cycle length accelerated to the pacing cycle length maintaining the same atrial sequence between the His and the HRA catheters, the tachycardia ongoing after pacing was discontinued. The following intervals were measured: (i) the TCL and the VA (between the onset of the QRS and the HRA electrogram); (ii) the A–A and the atrial sequence between the HB–RB and HRA catheters during overdrive pacing (in order to ensure para-Hisian entrainment); (iii) the SA (from the last stimulus to last entrained atrial depolarization in the HRA) and the PPI (from the last stimulus to the first RV electrogram in the first return beat); and (iv) the QRS width during tachycardia (QRS\textsubscript{tach}) and in the last entrained beat (QRS\textsubscript{entr} RV) or RV/HB–RB capture (QRS\textsubscript{entr} RV/HB–RB).

Statistical analysis

A test of normality was performed if considered necessary. Continuous variables (expressed as mean ± SD) were analysed using the Student t-test for independent or repeated measures as appropriate. Categorical variables were compared using \( \chi^2 \) or Fisher’s exact test as appropriate. A P-value of <0.05 was considered statistically significant.

Results

Nine of the 55 patients were excluded from the analysis because entrainment could not be performed for the following reasons: the tachycardia was not sustained (four patients), was repeatedly interrupted by ventricular pacing (four patients) or was haemodynamically not tolerated (one patient). As a result, 46 patients and 47 SVTs were included in the study analysis. Thirty-four patients presented with the slow–fast typical form of AVNRT and 13 with AVRT, 10 of which using a left free wall AP (LFWAP), 1 right posterosetal, 1 left posterosetal, and 1 para-Hisian. Five out of the 13 AVRT were using a concealed AP, and the remaining 8 presented with an AP with anterograde conduction properties. Only three patients had structural heart disease, consisting of moderate mitral regurgitation (one patient), ischaemic (one patient), and non-ischaemic (one patient) cardiomyopathy. The ablation was successful in all cases except one AVNRT patient, in whom the tachycardia was still inducible under isoproterenol infusion after ablation, but with no clinical recurrences. During a mean follow-up period of 8 ± 3 months no tachycardia recurrences were documented among our patient population.

Para-Hisian pacing (sinus rhythm)

Results are presented in Table 1. The QRS width during tachycardia was 89 ± 12 ms (range 78–120 ms), 142 ± 12 ms during RV pacing (range 124–166 ms), and 116 ± 12 ms during RV/HB–RB pacing (range 96–148 ms). When compared with the QRS width in tachycardia, the QRS was...
significantly longer upon both RV capture and RV/HB–RB capture, \(P < 0.001\). The QRS widening was significantly greater during RV capture as opposed to RV/HB–RB capture, \(P < 0.001\). Of note, a cut-off value of \(40\) ms for the QRS widening (when compared with the tachycardia QRS) reached highest discriminatory power to differentiate between RV and RV/HB–RB capture during para-Hisian pacing, \(P < 0.001\), with sensitivity of \(93\)%, specificity of \(94\)%, positive predictive value of \(100\)%, and negative predictive value of \(94\)% (Figure 1).

### Para-Hisian entrainment

Patients with AVNRT presented with a shorter VA than during AVRT (\(46 \pm 24\) ms vs. \(136 \pm 49\) ms, respectively, \(P < 0.001\)). No significant differences in the SVT cycle length were observed (\(350 \pm 74\) vs. \(327 \pm 73\) ms, \(P = 0.3\)).

#### Table 1  Para-Hisian pacing to identify the loss of His-bundle capture

<table>
<thead>
<tr>
<th>Patient (n)</th>
<th>QRStach (ms)</th>
<th>QRSRV (ms)</th>
<th>(\Delta QRSRV) (ms)</th>
<th>QRSRV/His (ms)</th>
<th>(\Delta QRSRV/His) (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>82</td>
<td>136</td>
<td>54</td>
<td>116</td>
<td>34</td>
</tr>
<tr>
<td>2</td>
<td>102</td>
<td>147</td>
<td>45</td>
<td>114</td>
<td>12</td>
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<tr>
<td>3</td>
<td>120</td>
<td>166</td>
<td>46</td>
<td>148</td>
<td>28</td>
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<tr>
<td>4</td>
<td>80</td>
<td>154</td>
<td>74</td>
<td>96</td>
<td>16</td>
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<tr>
<td>5</td>
<td>78</td>
<td>146</td>
<td>68</td>
<td>108</td>
<td>30</td>
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<tr>
<td>6</td>
<td>80</td>
<td>140</td>
<td>60</td>
<td>116</td>
<td>36</td>
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<tr>
<td>7</td>
<td>96</td>
<td>164</td>
<td>68</td>
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<td>8</td>
<td>80</td>
<td>130</td>
<td>50</td>
<td>110</td>
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<td>9</td>
<td>84</td>
<td>124</td>
<td>40</td>
<td>110</td>
<td>26</td>
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<td>10</td>
<td>84</td>
<td>135</td>
<td>51</td>
<td>108</td>
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<td>11</td>
<td>84</td>
<td>144</td>
<td>60</td>
<td>120</td>
<td>36</td>
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<tr>
<td>12</td>
<td>82</td>
<td>135</td>
<td>53</td>
<td>115</td>
<td>33</td>
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<tr>
<td>13</td>
<td>100</td>
<td>135</td>
<td>35</td>
<td>117</td>
<td>17</td>
</tr>
<tr>
<td>14</td>
<td>96</td>
<td>138</td>
<td>42</td>
<td>114</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>89 \pm 12</td>
<td>142 \pm 12</td>
<td>53 \pm 11</td>
<td>116 \pm 12</td>
<td>28 \pm 9</td>
</tr>
</tbody>
</table>

\(P\)-values < 0.05 are considered statistically significant. Values are expressed as mean \(\pm\) SD.

QRStach, QRS width during supraventricular tachycardia; QRSRV, QRS width during right ventricular pacing; \(\Delta QRSRV\), difference between QRSRV and QRStach (QRStach – QRSRV); QRSRV/His, QRS width during right ventricular plus HB-RB capture; \(\Delta QRSRV/His\), difference between QRStach and QRStach (QRSRV/His – QRStach).

* \(P\)-value when compared with the tachycardia QRS width.

** \(P\)-value when comparing the \(\Delta QRSRV\) with the \(\Delta QRSRV/His\).
respectively, during entrainment at lower energy output. As a result, the proposed cut-off value of >40 ms indeed identified absence of HB–RB capture in the overall analysis, \( P < 0.001 \), with sensitivity of 100%, specificity of 87%, positive predictive value of 89%, and negative predictive value of 100%.

**Entrainment without His-bundle capture**

Entrainment without HB–RB capture (presumed RV capture) was performed in all patients (Table 2). The SA–VA and the PPI–TCL values were significantly longer in AVNRT patients as opposed to AVRT: 121 \( \pm \) 23 vs. 49 \( \pm \) 19 ms and 139 \( \pm \) 30 vs. 75 \( \pm \) 25 ms, respectively, \( P < 0.001 \) (Figures 2 and 3). All but one patient with AVNRT and none with AVRT presented with an SA–VA difference of >75 ms. All but one patient with AVNRT and none except one with AVRT presented with a PPI–TCL difference of >100 ms. Thus, a cut-off value of >75 ms for the SA–VA and >100 ms for the PPI–TCL distinguished AVNRT from AVRT, \( P < 0.001 \), with a sensitivity of 97 and 97%, specificity of 100 and 92%, positive predictive value of 100 and 97%, and negative predictive value of 93 and 92%, respectively (Figure 4). When analysed separately, significantly shorter SA–VA and PPI–TCL were observed during AVRT using a septal AP (only three cases) when compared with AVNRT (31 \( \pm \) 27 vs. 121 \( \pm \) 23 ms, \( P < 0.001 \); 49 \( \pm \) 36 vs. 139 \( \pm \) 30 ms, \( P < 0.001 \), respectively) with no overlap between patients.

**Entrainment with His-bundle capture**

Entrainment with His-bundle capture was performed in 24 patients (Table 3). The SA and PPI significantly shortened in AVNRT patients upon RV/HB–RB capture, when compared with RV capture: 114 \( \pm \) 31 vs. 165 \( \pm \) 35 ms, \( P < 0.001 \); and 428 \( \pm \) 81 vs. 493 \( \pm \) 92 ms, \( P = 0.012 \), respectively. As a result, the SA–VA and PPI–TCL values shortened: 66 \( \pm \) 24 vs. 121 \( \pm \) 23 ms; and 85 \( \pm \) 31 vs. 139 \( \pm \) 30 ms, respectively, \( P < 0.001 \). As for AVRT patients, the SA–VA and PPI–TCL did not significantly shorten upon His-bundle capture: 35 \( \pm \) 22 vs. 49 \( \pm \) 19 ms, \( P = 0.204 \); and 55 \( \pm \) 32 vs. 75 \( \pm \) 25 ms, \( P = 0.172 \), respectively. Although the SA–VA value was still longer in AVNRT as opposed to AVRT patients (66 \( \pm \) 24 vs. 35 \( \pm \) 22 ms, \( P = 0.016 \)), the important overlap between the two groups precluded for the definition of a discriminatory cut-off value confirming AVNRT as the tachycardia mechanism. Similarly, the PPI–TCL value no longer distinguished AVNRT from AVRT upon His-bundle capture during tachycardia entrainment: 85 \( \pm \) 31 vs. 55 \( \pm \) 32 ms, \( P = 0.074 \).

**Discussion**

**Major findings**

Our study demonstrates that para-Hisian entrainment without His-bundle capture distinguishes AVNRT from AVRT. A SA–VA difference of >75 ms and PPI–TCL of >100 ms mostly identify AVNRT as the tachycardia mechanism, \( P < 0.001 \). This study first quantifies the degree of QRS widening when compared with the tachycardia QRS to determine the absence of His-bundle capture during para-Hisian entrainment (\( \Delta \)QRS\(_{\text{entr}} \)) of \( >40 \) ms. Importantly, these electrophysiological features do not apply when the His bundle is captured (\( \Delta \)QRS\(_{\text{entr}} \)) (<40 ms), and thus a precise identification of the absence of HB–RB capture appears compelling. At high-energy output (His-bundle capture), retrograde atrial activation proceeds directly over the AV node in AVNRT patients, avoiding the necessity of engaging the Purkinje network distally in the RV apex before reaching the AV junction. As a result, the SA–VA and PPI–TCL intervals shorten during AVNRT and no longer distinguish AVNRT from AVRT.

These maneuvers were performed by using only two right-sided diagnostic catheters with its subsequent cost-effectiveness and clinical benefits. However, it is suggested that additional diagnostic catheters should be positioned if considered necessary to confirm the SVT mechanism, especially when several retrograde pathways are suspected, and for guiding the ablation procedure.

**Previous studies**

Reddy et al.\(^8\) described the para-Hisian entrainment as a novel maneuver to differentiate AVNRT from AVRT. Unlike para-Hisian pacing (sinus rhythm), para-Hisian entrainment confirms either the AV node or an AP as the retrograde limb of the tachycardia circuit.\(^10\) In this study, a >40 ms increase in the SA interval (\( \Delta \)SA) upon the loss of HB–RB capture was associated to AVNRT. Our study contributes to precisely identify the loss of His-bundle capture during para-Hisian entrainment on the basis of the paced QRS widening, and additionally includes the SA–VA and PPI–TCL values as useful features to differentiate AVNRT from AVRT from the para-Hisian region.

The obtained cut-off values for the SA–VA and the PPI–TCL favouring AVNRT in the present study are lower than those obtained during entrainment from the RV apex.\(^3,4\) The inclusion of patients with atypical AVNRT (fast-slow), with decremental retrograde conduction properties, could have contributed to the longer mean SA–VA and PPI–TCL values obtained in AVNRT patients, and the higher cut-off values for the SA–VA and PPI–TCL, when compared with our study.\(^3\) Of note, the para-Hisian region is electrically further away than the RV apex from the AVNRT circuit, and closer to the atrio-ventricular annulae, where APs are found, including LFVAP, in which fast conduction through the interventricular septum may be responsible for the shorter SA and PPI intervals obtained.\(^7\) This also may have played a role in the lower cut-off values for the SA–VA and PPI–TCL observed and also in the almost absence of overlap in SA–VA values between AVNRT and AVRT using a

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**Table 2** Tachycardia entrainment from the para-Hisian region without His-bundle capture

<table>
<thead>
<tr>
<th>Interval (ms)</th>
<th>AVNRT (n = 34)</th>
<th>AVRT (n = 13)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCL (range)</td>
<td>350 ( \pm ) 74 (246–600)</td>
<td>327 ( \pm ) 73 (228–500)</td>
<td>0.318</td>
</tr>
<tr>
<td>VA (range)</td>
<td>46 ( \pm ) 24 (0–110)</td>
<td>136 ( \pm ) 49 (58–220)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SA (range)</td>
<td>165 ( \pm ) 35 (100–252)</td>
<td>188 ( \pm ) 54 (102–270)</td>
<td>0.175</td>
</tr>
<tr>
<td>PPI (range)</td>
<td>493 ( \pm ) 92 (340–734)</td>
<td>403 ( \pm ) 85 (288–596)</td>
<td>0.004</td>
</tr>
<tr>
<td>SA–VA (range)</td>
<td>121 ( \pm ) 23 (70–182)</td>
<td>49 ( \pm ) 19 (0–72)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PPI–TCL (range)</td>
<td>139 ( \pm ) 30 (76–198)</td>
<td>75 ( \pm ) 25 (8–106)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

P-values <0.05 are considered statistically significant. Values are expressed as mean \( \pm \) SD.

AVNRT, ativoventricular node reentrant tachycardia; AVRT, orthodromic ativoventricular tachycardia; PPI, post-pacing interval; SA, stimulus-atrial interval; TCL, tachycardia cycle length; VA, ventriculo-atrial interval.
LFWAP in comparison with other studies in which entrainment or resetting is performed from the RV apex.4,5

Study limitations
In this study, a limited number of AVRT, especially those using a septal AP, were included. However, this fact did not preclude for the identification of SA–VA and PPI–TCL highly specific cut-off values distinguishing AVRT from AVNRT. Although the number of AVRT patients in whom entrainment was performed with HB–RB capture is limited, we believe retrograde conduction over an AP should not be significantly affected by whether the His bundle is captured or not during entrainment, and thus the inclusion of additional AVRT patients with HB–RB entrainment should not modify our results.7,10 Our AVRT population is mainly representative of patients with non-septal APs, and the validation of the SA–VA and PPI–TCL cut-off values for patients with septal APs, although statistically enough in our analysis may need further investigation.

The analysis of the QRS widening to determine absence of His-bundle capture during para-Hisian pacing was not performed in a separated cohort of patients and may appear statistically redundant. Nevertheless, in the overall analysis
the obtained cut-off value was confirmed as valuable for identifying absence of HB–RB capture equally with a high discriminatory power. The measurement of the QRS widening during para-Hisian pacing and entrainment to identify absence of His-bundle capture may be limited by the presence of overlap among patients. As a result, an absolute value of the QRS width during RV or RV/HB–RB capture cannot be determined by this study. Regardless, we believe the proposed cut-off value of $\geq 40$ ms related to the tachycardia QRS width is a reasonable reference to distinguish the absence of His-bundle capture during para-Hisian pacing/entrainment.

The QRS aberrancy during tachycardia may limit the assessment of RV vs. RV/HB–RB capture during para-Hisian entrainment. Among our population, five patients presented with transitory bundle branch block during SVT, but measurements could be performed without QRS aberrancy in all patients.

Measurements were performed by two non-independent observers, and therefore interobserver variability was not analysed in this study.

The assessment of tachycardia entrainment by using two right-sided diagnostic catheters may have limitations. The EPS included the investigation of additional retrograde pathways after ablation, and the favourable outcome of ablative therapy observed in our population appears to validate the SVT differential diagnosis performed during our study protocol.

Our criteria have not been validated in patients with AVRT using APs with decremental properties, neither in patients with atypical AVNRT. Whether the described electrophysiological features apply to these patients remains unclear.
Conclusions

Para-Hisian entrainment without His-bundle capture distinguishes AVNRT from AVRT. An SA–VA of >75 ms and PPI–TCL of >100 ms is highly specific of AVNRT. The absence of His-bundle capture during entrainment is defined by a /C21 40 ms increase in the QRS width, when compared with the tachycardia QRS. This maneuver can be performed with the use of only two right-sided diagnostic catheters.

Conflict of interest: none declared.

References


Figure 4 The SA–VA and PPI–TCL cut-off values to distinguish between AVNRT and AVRT. The individual values and mean values ± SD of the stimulus-atrial–ventriculoatrial (SA–VA) and post-pacing interval–tachycardia cycle length (PPI–TCL) are represented. The line drawn at 75 ms for the SA–VA and 100 ms for the PPI–TCL represents the discriminatory value distinguishing AVNRT from AVRT patients, P < 0.001.

<table>
<thead>
<tr>
<th>Interval (ms)</th>
<th>AVNRT (n = 19)</th>
<th>AVRT (n = 5)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SA (range)</td>
<td>114 ± 31 (38–182)</td>
<td>186 ± 71 (120–270)</td>
<td>0.084</td>
</tr>
<tr>
<td>PPI (range)</td>
<td>428 ± 81 (302–584)</td>
<td>354 ± 49 (280–396)</td>
<td>0.066</td>
</tr>
<tr>
<td>SA–VA (range)</td>
<td>66 ± 24 (20–116)</td>
<td>35 ± 22 (0–56)</td>
<td>0.016</td>
</tr>
<tr>
<td>PPI–TCL (range)</td>
<td>85 ± 31 (30–158)</td>
<td>55 ± 32 (0–80)</td>
<td>0.074</td>
</tr>
</tbody>
</table>

P-values <0.05 are considered statistically significant. Values are expressed as mean ± SD.

AVNRT, atrioventricular node reentrant tachycardia; AVRT, orthodromic atrioventricular tachycardia; PPI, post-pacing interval; SA, stimulus–atrial interval; TCL, tachycardia cycle length; VA, ventriculo-atrial interval.

Table 3  Tachycardia entrainment from the para-Hisian region with His-bundle capture