

Title: Prevalence and characteristics of atrioventricular nodal reentrant tachycardia with a bystander concealed nodoventricular/nodofascicular pathway

Short title: Prevalence & characteristics of AVNRT with NV/NF

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Abstract

Background: The concealed nodoventricular/nodofascicular (NV/NF) pathway is mostly a bystander, retrograde bypass tract connecting right ventricle/right bundle branch (RBB) and slow pathway (SP), which is observed in patients with atrioventricular nodal reentrant tachycardia (AVNRT). However, its prevalence and characteristics in response to pacing maneuvers have not been fully evaluated.

Objective: This study investigated the prevalence and characteristics of AVNRT with a bystander NV/NF-pathway.

Methods: We retrospectively reviewed 153 consecutive patients undergoing catheter ablation of AVNRT. Excluding 52 patients with inadequate electrophysiological data, 101 patients composed the study population.

Results: Three patients (3.0%) had bystander concealed NV/NF-pathways, all of which were connected to the SP. The tachycardia was typical SP/fast pathway (FP) AVNRT in two patients and atypical FP/SP AVNRT in one patient. In all cases, His-refractory ventricular extra stimuli (VESs) reset the AVNRTs with delay through the NV/NF-pathways. Ventricular overdrive pacing (VOP) in the early-phase also reset the AVNRT with delay. Earlier VESs and middle-phase of VOP did not reset the tachycardia, and further earlier VESs and late-phase of VOP reset the tachycardia with advance through

the RBB-His conduction.

Conclusion: A bystander NV/NF-pathway was not rare in patients with AVNRT. The VESs and VOP for the AVNRTs with the bystander NV/NF-pathways were characterized by the two-phase resetting phenomenon: initial transient resetting with delay through the NV/NF-pathway, and late resetting with advance through the RBB-His conduction.

Keywords: nodoventricular pathway; nodofascicular pathway; atrioventricular nodal reentrant tachycardia; His-refractory ventricular extra stimulation; ventricular overdrive pacing.

List of abbreviations

AVNRT	atrioventricular nodal reentrant tachycardia
CI	coupling interval
FP	fast pathway
NV/NF	nodoventricular/nodofascicular
PCL	pacing cycle length
SP	slow pathway
TCL	tachycardia cycle length
TPP	total pacing prematurity
VES/VESs	ventricular extra stimulus/stimuli
VOP	ventricular overdrive pacing

1 **Introduction**

2 The concealed nodoventricular/nodofascicular (NV/NF) pathway is a retrograde
3 bypass tract that connects the atrioventricular node, mostly slow pathway (SP), and the
4 right ventricular (RV) muscle/right bundle branch (RBB). Recently, it has been found to
5 participate in atrioventricular nodal reentrant tachycardia (AVNRT) as a bystander
6 pathway.^{1, 2} Although the catheter treatment of AVNRT with a bystander NV/NF-pathway
7 is anatomical SP ablation, just as the same as that of pure AVNRT, it is important to
8 evaluate the presence or absence of a NV/NF-pathway because it also causes orthodromic
9 reciprocating tachycardia (ORT). However, the prevalence of NV/NF-pathways in
10 AVNRT patients has not yet been reported.

11 Resetting of AVNRT with delay and/or termination of AVNRT without atrial capture
12 by His-refractory ventricular extra stimuli (VESs) are considered specific to AVNRT with
13 a bystander NV/NF-pathway.^{1, 2} However, its response to ventricular overdrive pacing
14 (VOP) has not yet been fully evaluated.

15 Therefore, we sought to investigate the prevalence and electrophysiological
16 characteristics of a bystander concealed NV/NF-pathway in patients with AVNRT.

Methods

Study population

We retrospectively reviewed 153 consecutive patients undergoing catheter ablation for AVNRT from February 2015 to December 2022 in Kyoto University Hospital. Excluding 4 patients without available electrophysiological study (EPS) data, 1 patient without His electrograms, 15 patients without inducible sustained tachycardia, 15 patients without adequate pacing maneuvers during tachycardia, 13 patients with cycle-length alternations during tachycardia, and 4 patients with AV block during tachycardia due to a lower common pathway (LCP), a total of 101 AVNRT patients composed the study population (Figure 1). The research protocol was approved by the ethics committee of Kyoto University Hospital, and all procedures were performed in accordance with the 1964 Helsinki Declaration. Written informed consent from each patient was waived because we used clinical information obtained in routine clinical practice. Instead, the right not to participate in the study was reserved in the form of opt-out in the outpatient department.

Electrophysiological study

The details of the baseline EPS are described in the Supplemental methods. After successful induction of the supraventricular tachycardia (SVT), VOP and VESs were

performed in all patients. In VOP, usually 10 stimuli were delivered with a pacing cycle length (PCL) of 15-30ms shorter than the TCL. When the atrium was not entrained, additional VOP with a larger number of stimuli or a shorter PCL was performed. The coupling interval (CI) of the VESs was reduced by 10ms until the RV was not captured owing to the effective refractory period (ERP).

ORT using an accessory pathway (AP) or a NV/NF-pathway was excluded based on the followings: 1) no retrograde AP conduction in the baseline EPS, 2) septal VA interval during tachycardia of $<70\text{ms}$,³ 3) post pacing interval (PPI)–TCL of $>125\text{ms}$,^{4, 5} and/or corrected PPI–TCL of $>110\text{ms}$,⁶ and 4) total pacing prematurity (TPP) of $>125\text{ms}$.⁷

The presence of a bystander concealed NV/NF-pathway was diagnosed by the followings: 1) His-refractory VESs reset the AVNRT with delay and/or 2) terminated the AVNRT without atrial capture.^{1, 2} Resetting of AVNRT with delay by His-refractory VESs was regarded as present when the A-A interval was prolonged by $\geq 4\text{ms}$ at ≥ 2 consecutive ventricular stimuli, with maximum A-A prolongation of $\geq 8\text{ms}$. Similar criteria were used for resetting with delay during VOP, i.e., prolongation of the A-A interval by $\geq 4\text{ms}$ at ≥ 2 consecutive ventricular stimuli, with no definition for maximum A-A prolongation.

Further details of EPS are described in the Supplemental methods.

Results

Among the 101 study patients undergoing catheter ablation for AVNRT, 3 patients (3.0%) had a bystander concealed NV/NF-pathway (Figure 1). The baseline and procedural characteristics as well as clinical outcomes, comparing 98 patients with pure AVNRT and 3 patients with AVNRT plus NV/NF-pathway, are shown in Supplemental Table 1. There were no remarkable differences between the groups including dominance of female patients and typical SP/first pathway (FP) AVNRT. No procedural complication occurred except for 1 complete AV block requiring permanent pacemaker in the pure AVNRT group. Five patients (5.1%) in the pure AVNRT group had arrhythmia recurrence, but none in the AVNRT plus NV/NF-pathway group.

Electrophysiological characteristics of the AVNRTs and the NV/NF-pathways of the 3 cases are summarized in Supplemental Table 2. Two patients had typical SP/FP AVNRT and one had atypical FP/SP AVNRT. The ventricular insertion was undistinguishable (NV/NF-pathway) and the atrial insertion was SP in all cases. At His-refractory VESs, the AVNRTs were reset with delay in all cases, while termination without atrial capture was observed only in one case. Importantly, resetting with delay was also observed during VOP in all cases. Plots of the delta A-A interval (A-A interval–TCL) at the VESs and VOP during the AVNRTs are shown in Figure 2, which could be characterized by the two-

phase resetting phenomenon: the initial transient resetting with delay through the NV/NF-pathways at the His-refractory VESs and early-phase of VOP (red dots), followed by no resetting at the earlier VESs and middle-phase of VOP (gray dots), and late resetting with advance through the RBB-His conduction at the further earlier VESs and late-phase of VOP (blue dots).

Further details of the 3 cases are shown below.

Case-1 (Typical SP/FP AVNRT with a bystander NV/NF-pathway connected to SP)

The patient was a 69-year-old woman. A short RP tachycardia was induced with AV jump. The earliest atrial activation site (EAAS) was His region and septal VA interval was <70ms. VOP showed resuming of SVT with an A-V pattern and long PPI-TCL (Figure 3). Thus, the SVT was diagnosed as typical AVNRT.

As shown in Figure 2A and Figure 4, the VESs during tachycardia showed the two-phase resetting. The His-refractory VESs with CIs of 366→346ms delayed His and atrial activation one cycle later, indicating that the VESs antegradely reset the typical AVNRT with delay through a bystander NV/NF-pathway connected to the SP (Figure 4A and 4B).

The earlier VESs with CIs of 336→306ms did not reset the AVNRT, probably due to the decremental conduction of the NV/NF-pathway (Figure 4C). The further earlier VESs

with CIs of ≤ 296 ms retrogradely advanced the atrial electrograms immediately after stimulation through the RBB-His conduction (Figure 4D).

The two-phase resetting was also observed in the VOP (Figure 2B and Figure 3). The A-A interval was initially prolonged through the NV/NF-pathway in the fused QRS zone. Then, the A-A interval returned to the TCL, finally being shortened to the PCL through the RBB-His conduction. TPP through the NV/NF-pathway ($TPP_{NV/NF}$) was 90ms, and TPP through the RBB-His conduction ($TPP_{RBB-His}$) was 162ms.

Case-2 (Typical SP/FP AVNRT with a bystander NV/NF-pathway connected to SP)

The patient was a 67-year-old woman. A short RP tachycardia with EAAS at His area and septal VA interval of <70 ms was induced along with AV jump. VOP showed resuming of SVT with an A-V pattern and long PPI-TCL (Figure 5). Thus, the tachycardia was diagnosed as typical AVNRT. Also, a long delta-HA interval suggested the presence of a long LCP.⁸

As shown in Figure 2C and Figure 6, the VESs showed the two-phase resetting. The His-refractory VESs with CIs of $444 \rightarrow 404$ ms delayed the His and atrial electrograms one cycle later, suggesting anterograde resetting of the typical AVNRT through a NV/NF-pathway connecting to the SP (Figure 6A and 6B). The earlier VESs with CIs of

394→364ms did not affect atrial activation, although His activation was retrogradely advanced through the RBB (Figure 6C). The discrepancy between the A-A and H-H intervals was considered due to the long LCP. The further earlier VESs with CIs of ≤ 354 ms advanced both the His and atrial electrograms through the RBB-His conduction (Figure 6D).

The two-phase resetting was also observed during the VOP (Figure 2D and Figure 5). The A-A interval was initially prolonged through the NV/NF-pathway, and then shortened to the PCL through the RBB-His conduction. $TPP_{NV/NF}$ was 72ms, while $TPP_{RBB-His}$ was 126ms. As observed at the earlier VESs (Figure 6C), there was discrepancy between the A-A and H-H intervals after S6 and S7, owing to the long LCP.

Case-3 (Atypical FP/SP AVNRT with a bystander NV/NF-pathway connected to SP and a posteroseptal accessory pathway)

We have previously reported this case.² The patient was a 37-year-old man. A 12-lead electrocardiogram (ECG) showed delta-waves, suggesting a posteroseptal AP. Four SVTs were induced. SVT-1a and SVT-1b were atypical FP/SP AVNRTs with a concealed NV/NF-pathway connected to the retrograde SP, with and without bystander preexcitation. SVT-2a and SVT-2b were ORTs with FP and SP acting as anterograde limbs of the re-

entry circuit, respectively.

VOP for the SVT-1a (Figure 7A) showed a pseudo-A-A-V pattern and long PPI-TCL, indicating that the SVT-1a was atypical FP/SP AVNRT.

The VESs for the SVT-1a are shown in Figure 2E and Figure 8. The His-refractory VESs with CIs of 290→230ms delayed subsequent atrial and His activation (Figure 8A and 7B), suggesting that the SVT-1a was retrogradely reset through a NV/NF-pathway connecting to the SP. The earlier VESs with CIs of 220→170ms did not affect the A-A intervals (Figure 8C), probably due to the decremental conduction of the NV/NF-pathway.

The further earlier VES with a CI of 160ms could not capture RV owing to the ERP (Figure 2E). In the VESs for the SVT-1b (Figure 2G and Figure 8), the His-refractory VESs with CIs of 278→248ms delayed the subsequent atrial and His electrograms through the NV/NF-pathway (Figure 8D and 8E). The following His-refractory VES with a CI of 238ms terminated the SVT-1b with VA block (Figure 8F).

Back in the VOP for the SVT-1a (Figure 7A), the A-A interval was initially prolonged through the NV/NF-pathway in the fused QRS zone. Then, the A-A interval returned to the TCL, finally becoming nearly equal to the PCL. The two-phase resetting was also observed in another VOP for the SVT-1a (Figure 7B).

Discussion

AVNRT is the most common type of SVT, accounting for approximately 70% of the entire SVT cases.⁹ Recently, a concealed NV/NF-pathway has been reported to participate in AVNRT as a bystander pathway,^{1,2} although its prevalence has not been reported. The present study for the first time showed the prevalence of bystander concealed NV/NF-pathways in a cohort of consecutive patients undergoing catheter ablation for AVNRT. The 3.0% prevalence of the bystander NV/NF-pathways shown in the present study is not rare, given the fact that AVNRT is the most common type of SVT. Because concealed NV/NF-pathways not only act as bystander bypass tracts but also cause ORT, aggressive induction of SVT after successful SP modification may be important in AVNRT patients with NV/NF-pathways.

The present study clearly demonstrated the two-phase resetting phenomenon at the VESs during the AVNRTs with the concealed NV/NF-pathways: the initial transient resetting with delay through the NV/NF-pathways at the His-refractory VESs, followed by no resetting at the earlier VESs, and late resetting with advance through the RBB-His conduction at the further earlier VESs. Importantly, the two-phase resetting was also observed during the VOP maneuvers in all 3 cases of the present study. The A-A interval was initially prolonged through the NV/NF-pathways (early-phase of VOP), and then

1 returned to the TCL (middle-phase of VOP), finally becoming equal to the PCL (late-
2 phase of VOP).

3 VOP during SVT is the cornerstone of the pacing maneuvers in the differential
4 diagnosis of SVT, especially for the separation of AVNRT and ORT using a septal AP or
5 a NV/NF-pathway.^{4,5} PPI-TCL of $>125\text{ms}$ strongly suggests AVNRT because its re-entry
6 circuit is remote from the RV apex compared to septal ORT or NV/NF ORT.^{4,5} However,
7 to assess PPI-TCL, VOP should be done until the atrium is entrained through the
8 retrograde limb of the re-entry circuit, which is sometimes frustrating. VOP with a PCL
9 slightly shorter ($\approx 10\text{ms}$) than the TCL and a number of stimuli of ≤ 10 often fails to entrain
10 the atrium, while VOP with a PCL far shorter ($>30\text{ms}$) than the TCL or a larger number
11 of stimuli (>10) often terminates the SVT. Thus, TPP has been proposed as an alternative
12 diagnostic tool to differentiate AVNRT and septal ORT. TPP is the sum of differences
13 between the TCL and PCL until the atrium is entrained or the SVT is terminated during
14 VOP. Therefore, both PPI-TCL and TPP represent the temporal distance between the RV
15 pacing site and the re-entry circuit, leading to the same cutoff values of $>125\text{ms}$ for
16 AVNRT.^{4,5,7} The advantage of TPP over PPI-TCL is that it can differentiate AVNRT and
17 septal ORT even when the SVT is terminated during VOP. However, TPP is affected by
18 transient resetting of AVNRT through a bystander decremental AP or NV/NF-pathway.

1 Actually, in all 3 cases of the present study, $TPP_{NV/NF}$ was far shorter than 125ms owing
2 to the transient resetting through the NV/NF-pathways. On the other hand, PPI-TCL was
3 far longer than 125ms in all 3 cases, correctly showing that the SVT was not septal ORT
4 but AVNRT. When the transient resetting through the NV/NF-pathway was neglected in
5 the TPP calculation, then $TPP_{RBB-His}$ was longer than 125ms in all 3 cases, consistently
6 with PCI-TCL (Supplemental Table 2).

7 The disappearance of the resetting of AVNRTs with delay through the NV/NF-
8 pathways at the earlier VESs can be explained by either of the followings: 1) the ERPs of
9 the SPs at the atrial insertion of the NV/NF-pathways, 2) the ERPs of the NV/NF-
10 pathways, and 3) the decremental conduction of the NV/NF-pathways.^{1, 5} However,
11 transient resetting of the AVNRTs with delay through the NV/NF-pathways was also
12 observed during VOP in all 3 cases of the present study. Because the PCL was constant
13 throughout the VOP maneuvers, the ERPs of the SPs or NV/NF-pathways cannot explain
14 the transient resetting with delay through the NV/NF-pathways during VOP. Thus, only
15 the decremental conduction property of the NV/NF-pathways can clearly explain the
16 transient resetting with delay at VESs and VOP. Theoretically, however, very slowly
17 conducting activation through the NV/NF-pathway can reach the SP and reset or
18 terminate AVNRT one cycle later. Actually, in a recent case report, His-refractory VESs

1 reproducibly terminated AVNRT without atrial capture one cycle later, suggesting the
2 existence of a very slowly conducting NV/NF-pathway.¹⁰ However, there have been no
3 other reports showing this kind of phenomenon. Also, in the VESs and VOP of the present
4 study, once the A-A interval returned to the TCL after the initial prolongation, no re-
5 prolongation was observed (Figure 2). Thus, most of slowly conducting excitations
6 through decremental NV/NF-pathways are considered unable to enter the re-entry circuit
7 owing to its relatively narrow excitable gap.

8 Further discussions are described in the Supplementary materials.

10 **Limitations**

11 The present study has several limitations. First, this was a retrospective cohort study
12 with limitations inherent to the observational study design. The decision-making for
13 pacing maneuvers during AVNRT was left to the discretion of the operators who were not
14 necessarily aggressive to find bystander NV/NF-pathways, possibly leading to
15 underestimation of the prevalence of the NV/NF-pathways. However, the present study
16 excluded patients with inadequate EPS data, and all the study patients underwent both
17 VESs and VOP during the AVNRTs. Second, because the degree of the A-A prolongation
18 through the NV/NF-pathway at the His-refractory VESs and VOP was modest, we cannot

1 exclude the possibility of cycle-length alternation of the tachycardia. However, A-A
2 prolongation of ≥ 4 ms at ≥ 2 consecutive ventricular stimuli was observed both in the VESs
3 and VOP in all patients. Furthermore, the maximum A-A prolongation at the His-
4 refractory VESs was ≥ 10 ms in all patients. Thus, we believe the presence of bystander
5 NV/NF-pathways in the 3 AVNRT patients of the present study was robust.

7 **Conclusions**

8 Bystander concealed NV/NF-pathways in association with AVNRT were not rare,
9 observed in 3.0% of patients. The two-phase resetting phenomenon, i.e., the initial
10 transient resetting with delay through the NV/NF-pathway and late resetting with advance
11 through the RBB-His conduction in response to VESs and VOP during tachycardia, is
12 crucial for the diagnosis of a bystander NV/NF-pathway with AVNRT.

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Figure legends.

Figure 1. Study flow chart.

AVNRT=atrioventricular nodal reentrant tachycardia;

NF=nodofascicular; NV=nodoventricular; SP=slow pathway.

Figure 2. Plots of the delta A-A interval at the VESs and VOP for AVNRT with a bystander concealed NV/NF-pathway.

Plots of the delta A-A interval (A-A interval – TCL) at the VESs and VOP for AVNRT with a bystander NV/NF-pathway in Case-1 (A and B), -2 (B and C), and -3 (E, F, and G) are shown.

The horizontal void arrows show the order of the ventricular stimuli.

(A) In the VESs in Case-1, the consecutive 3 His-refractory VESs with CIs of 366→346ms prolonged the A-A intervals by 4 to 12ms (red dots), followed by the 4 consecutive earlier VESs with CIs of 336→306ms not affecting the A-A intervals (gray dots). The further earlier VESs with CIs of ≤296ms shortened the A-A intervals by ≥10ms (blue dots).

(B) The VOP in Case-1 with a PCL of 18ms shorter than the TCL prolonged the 6th and 7th A-A intervals by 6 and 10ms, respectively (red dots), but did not affect the 8th A-A interval (a gray dot). The 9th and 10th A-A intervals were shortened by 14 and 18ms, respectively (blue dots).

(C) In the VESs in Case-2, the A-A intervals were prolonged by 4 to 10ms at the 5 consecutive His-refractory VESs with CIs of 444→404ms (red dots), but was not affected by

the next 4 earlier VESs with CIs of 394→364ms (gray dots). The further earlier VESs with CIs of ≤354ms shortened the A-A intervals by >10ms (blue dots).

(D) In the VOP in Case-2 with a PCL of 18ms shorter than the TCL, the 5th to 7th A-A intervals were prolonged by 4 to 12ms (red dots), while the following 8th to 10th A-A intervals were shortened to the PCL (blue dots).

(E) In the VESs for SVT-1a of Case-3, the A-A intervals prolonged by 4 to 12ms at the 7 consecutive His-refractory VESs with CIs of 290→230ms (red dots). The following 6 earlier VESs with CIs of 220→170ms did not affect the A-A intervals. The further earlier VES with a CI of 160ms did not capture RV owing to the ERP (a blue arrow).

(F) In the VOP for SVT-1a of Case-3, with a PCL of 22ms shorter than the TCL, the 3rd to 5th A-A intervals were prolonged by 4 to 6ms (red dots), while the following 6th to 8th A-A intervals were not affected (gray dots). The 9th and 10th A-A intervals were shortened by 6 and 20ms, respectively (blue dots).

(G) In the VESs for SVT-1b of Case-3, the A-A intervals prolonged by 4 to 14ms at the 4 consecutive His-refractory VESs with CIs of 278→248ms, followed by termination of the AVNRT without atrial capture (a red arrow).

ERP=effective refractory period; PCL=pacing cycle length; RV=right ventricle; SVT=supraventricular tachycardia; TCL=tachycardia cycle length; VESs=ventricular extra stimuli; VOP=ventricular overdrive pacing. Other abbreviations as in Figure 1.

Figure 3. VOP in Case-1

ECGs during VOP with a PCL of 18ms shorter (430ms) than the TCL (448ms) in Case-1 are shown. The numbers in brackets show the numberings of the A-A intervals during VOP. The SVT resuming showed an A-V pattern. The PPI-TCL was $628-448=180\text{ms}$ ($>125\text{ms}$), and the corrected PPI-TCL was $180-(368-350)=162\text{ms}$ ($>110\text{ms}$), indicating that the SVT was typical SP/FP AVNRT.

The 6th and 7th A-A intervals were prolonged by 6 and 10ms, respectively, while the following 8th A-A interval was not affected, returning to the TCL of 448ms. The last two A-A intervals were shortened, finally becoming equal to the PCL of 430ms. Based on the ECG findings at the resetting of the AVNRT with delay by His-refractory VESs (Figure 4A and 4B), the 6th and 7th atrial activation during VOP was considered to be antegradely reset with delay through a NV/NF-pathway by the ventricular stimuli of one cycle earlier (S5 and S6). On the other hand, the 9th and 10th atrial activation was retrogradely reset through the RBB-His conduction immediately after S9 and S10, respectively. Thus, $\text{TPP}_{\text{NV/NF}}$ was $(448-430)\times 5=90\text{ms}$ and $\text{TPP}_{\text{RBB-His}}$ was $(448-430)\times 9=162\text{ms}$.

AVN=atrioventricular node; CS=coronary sinus; ECG=electrocardiogram; F=fused QRS morphology; FP=fast pathway; HRA=high right atrium; PPI=post pacing interval; RBB=right bundle branch; RVA=right ventricle apex; SM=stable QRS morphology; TPP=total pacing prematurity. Other abbreviations as in Figure 2.

Figure 4. VES in Case-1

Representative ECGs at VESs for AVNRT with a NV/NF-pathway in Case-1 are shown.

(A) The first resetting of the typical SP/FP AVNRT with delay by a His-refractory VES

with a CI of 366ms. The VES did not affect the atrial electrograms immediately after

stimulation, but delayed the next His and atrial electrograms by 12ms, suggesting an

anterograde reset of the AVNRT through a NV/NF-pathway connected to the SP. The

prematurity of the VES was $448-366=82\text{ms}$.

(B) The 3rd resetting with delay by a His-refractory VES with a CI of 346ms.

(C) An earlier VES with a CI of 316ms did not reset the AVNRT.

(D) A further earlier VES with a CI of 296ms advanced the atrial electrograms

immediately after stimulation through the RBB-His conduction.

Abbreviations as in Figure 1-3.

Figure 5. VOP in Case-2

The upper panel (A) shows ECGs during VOP with a PCL of 18ms shorter (484ms) than the TCL (502ms) in Case-2. The numbers in brackets show the numberings of the A-A and H-H intervals. The central part of the ECGs surrounded by the dotted line is enlarged and shown in the lower panel (B). In addition to the laddergram below the ECGs in the upper panel, further detailed diagrams are shown in Supplemental Figure 1.

The SVT resumed with an A-V pattern after VOP. The PPI-TCL was $676-502=174\text{ms}$ ($>125\text{ms}$), and the corrected PPI-TCL was $174-(376-356)=154\text{ms}$ ($>110\text{ms}$), showing that the SVT was typical AVNRT. The HA intervals during AVNRT and ventricular pacing were 80 and 48ms, respectively. Therefore, delta-HA interval was $80-48=32\text{ms}$, far longer than 15ms, suggesting the existence of a long LCP. Looking at the A-A interval, the VOP showed two-phase resetting. The 5th to 7th A-A intervals were prolonged by 4 to 12ms, while the following 8th to 10th A-A intervals were shortened to the PCL of 484ms (Upper panel A).

There were discrepancies between the A-A and H-H intervals after S6 and S7. Furthermore, the His activation was initially proximal to distal (purple arrows) but was reversed (orange arrows) after S6. Consistently, the bipolar His potentials recorded at the most distal electrodes were initially negative but was reversed after S6 (Lower panel B).

After S5, both the A-A and H-H intervals were significantly prolonged by 6ms. Based on the ECG findings at the resetting of the AVNRT with delay by His-refractory VESs (Figure 6A and 6B), the re-entry circuit were considered to be antegradely reset with delay through a NV/NF-pathway by the ventricular stimulus of one cycle earlier (S4) (Supplemental Figure 1A).

After S6, the A-A interval was maximally prolonged by 12ms, while the H-H interval

1 returned to the TCL with the reversal of His activation. Thus, the S6 retrogradely entrained the
2 His through the RBB, but could not penetrate the LCP, resulting in the continuous antegrade
3 resetting of the re-entry circuit and the atrium with delay by the ventricular stimulus of one
4 cycle earlier (S5) through the NV/NF-pathway (Supplemental Figure 1B).

5 After S7, the A-A interval was still prolonged by 4 ms, but the H-H interval was further
6 shortened to the PCL of 484ms. Because the next 8th A-A interval after S8 shortened to the PCL
7 of 484 ms, with a difference of $506 - 484 = 22$ ms, which was larger than the TCL–PCL of 18ms,
8 it was likely that the S7 penetrated the LCP and retrogradely entrained the FP and the atrium
9 (Supplemental Figure 1C).

10 The following 8th to 10th atrial activations were retrogradely reset through the RBB-His
11 conduction immediately after the ventricular stimuli (S8-S10), leading to the A-A and H-H
12 intervals equal to the PCL of 484ms. The activations through the NV/NF-pathway by the
13 ventricular stimuli of one cycle earlier were presumably blocked at the entrance of the re-entry
14 circuit owing to the slow conduction of the NV/NF-pathway associated with its decremental
15 conduction property (Supplemental Figure 1D).

16 $TPP_{NV/NF}$ was $(502 - 484) \times 4 = 72$ ms and $TPP_{RBB-His}$ was $(502 - 484) \times 7 = 126$ ms.

17
18 LCP=lower common pathway. Othe abbreviations as in Figure 1-3.

Figure 6. VES in Case-2

Representative ECGs at VESs for AVNRT with a NV/NF-pathway in Case-2 are shown.

(A) The first resetting of the typical AVNRT with delay by a His-refractory VES with a

CI of 444ms. The VES did not affect the atrial electrograms immediately after

stimulation but delayed the next His and atrial electrograms by 6ms, suggesting that

the AVNRT was antegradely reset through a NV/NF-pathway connected to the SP.

The prematurity of the VES was $522-444=78\text{ms}$.

(B) The second resetting of the AVNRT with delay by a His-refractory VES with a CI of

434ms. The VES reset the AVNRT with a maximum delay of 10ms.

(C) An earlier VES with a CI of 394ms did not affect the A-A interval. However, the

bipolar His potential recorded at the most distal electrodes was advanced and

reversed immediately after stimulation, suggesting that the VES retrogradely

entrained the His through the RBB, but did not penetrate the long LCP.

(D) A further earlier VES with a CI of 354ms advanced both the His and atrial

electrograms immediately after stimulation through the RBB-His conduction.

Abbreviations as in Figure 1-3.

Figure 7. VOP in Case-3

ECGs during VOP for SVT-1a in Case-3 are shown. The numbers in brackets show the numberings of the A-A intervals. SVT-1a was a wide-QRS, long RP tachycardia with EAAS at CS ostium in a patient with preexcitation.²

(A) VOP with a PCL of 330ms was delivered at the time when the TCL was 352ms. The SVT-1a resumed with a pseudo A-A-V pattern after VOP. The PPI-TCL was $570 - 352 = 218\text{ms}$ ($>125\text{ms}$), and the corrected PPI-TCL was $218 - (72 - 72) = 218\text{ms}$ ($>110\text{ms}$), indicating that the SVT was atypical FP/SP AVNRT with bystander preexcitation.

The 3rd to 5th A-A intervals were prolonged by 4 to 6ms, while the following 6th to 8th A-A intervals were not affected, returning to the TCL. Subsequently, the A-A interval was shortened, finally becoming nearly equal to the PCL. The initial transient resetting with delay was through a bystander NV/NF-pathway connected to the retrograde SP, and the later resetting with advance was through the RBB-His conduction. $\text{TPP}_{\text{NV/NF}}$ was $(352 - 330) \times 3 = 66\text{ms}$, and $\text{TPP}_{\text{RBB-His}}$ was $(352 - 330) \times 9 = 198\text{ms}$.

(B) VOP with a PCL of 320ms was delivered at the time when the TCL was 360ms. The 2nd and 3rd A-A intervals were prolonged by 6ms, followed by the 4th A-A interval

returning to the TCL of 360ms. Subsequently, the 5th A-A interval was shortened, followed by termination of the SVT-1a with VA block after S6. The VA conduction at S7-10 was through the posteroseptal AP, of which the ERP was 280ms. $TPP_{NV/NF}$ was $(360-336)+(360-320)=64\text{ms}$, and $TPP_{RBB-His}$ was $(360-336)+(360-320)\times 4=184\text{ms}$.

Note that the CI of S1 was not equal to the PCL.

AP=accessory pathway. Other abbreviations as in Figure 1-3.

Figure 8. VES in Case-3

Representative ECGs of the VESs for SVT-1a (A, B and C) and SVT-1b (D, E and F) in Case-3 are shown. The SVT-1a and SVT-1b were atypical FP/SP AVNRTs with and without bystander preexcitation.²

(A) The first resetting of the SVT-1a with delay by a His-refractory VES with a CI of 290ms. The VES delayed the subsequent atrial electrograms by 8ms, suggesting retrograde resetting of the SVT-1a through a bystander NV/NF-pathway connected to the SP. The prematurity of the VES was $344-290=54\text{ms}$.

(B) The third resetting of the SVT-1a with delay by a His-refractory VES with a CI of 270ms. The A-A interval was maximally prolonged by 12ms.

- 1 (C) An earlier VES with a CI of 180ms for SVT-1adid not affect the A-A interval.
- 2 (D) The first resetting of the SVT-1b with delay by a His-refractory VES with a CI of
3 278ms. The VES delayed the subsequent atrial electrograms by 4ms. The prematurity
4 of the VES was $340-278=62$ ms.
- 5 (E) The fourth resetting of the SVT-1b with delay by a His-refractory VES with a CI of
6 248ms, showing a maximum A-A prolongation of +14ms.
- 7 (F) Termination of the SVT-1b without atrial capture by a His-refractory VES with a CI
8 of 238ms.
- 9 AP=accessory pathway. Other abbreviations as in Figure 1-3.

153 patients undergoing catheter ablation for AVNRT
(February 2015-December 2022, Kyoto university hospital, Japan)

52 patients who had exclusion criteria

4 patients without available data of electrophysiological study during catheter ablation

1 patient in whom His electrograms were not obtained

15 patients in whom sustained tachycardia was not induced

15 patients who did not undergo pacing maneuvers during tachycardia

13 patients with cycle-length alternations during tachycardia

4 patients with atrioventricular block due to lower common pathway during tachycardia

101 patients with AVNRT undergoing catheter ablation and full pacing maneuvers

**98 patients with
pure AVNRT (97.0%)**

**3 patients with AVNRT and a bystander
concealed NV/NF pathway (3.0%)**

Case 1

Typical AVNRT with
bystander NV/NF-SP

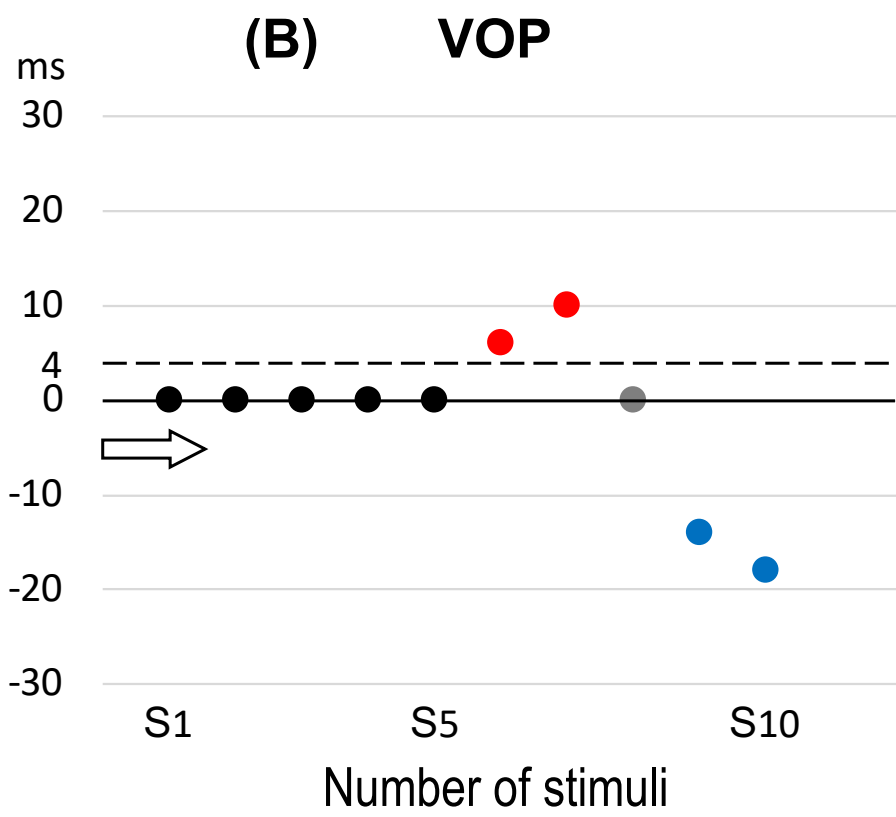
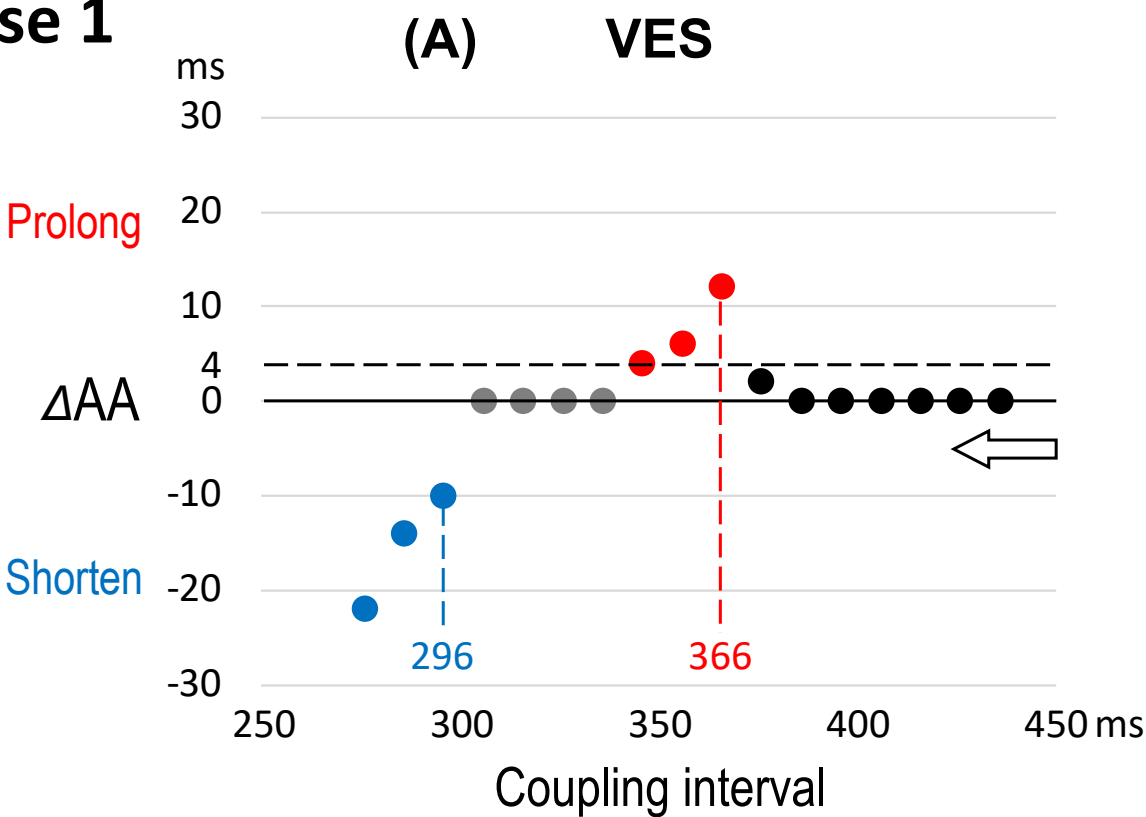
Case 2

Typical AVNRT with
bystander NV/NF-SP

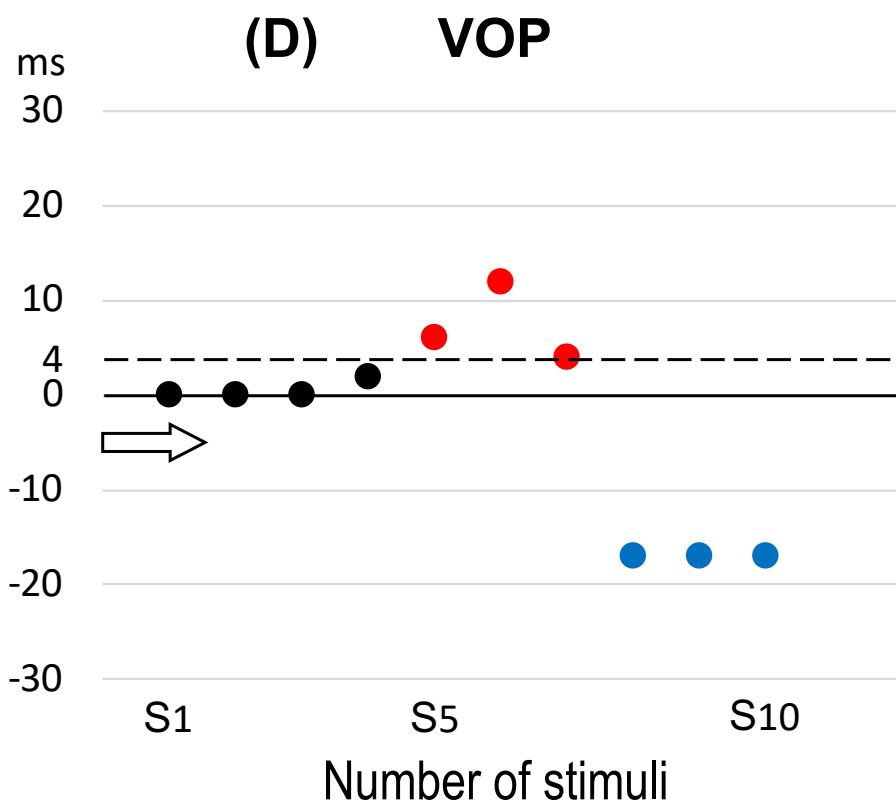
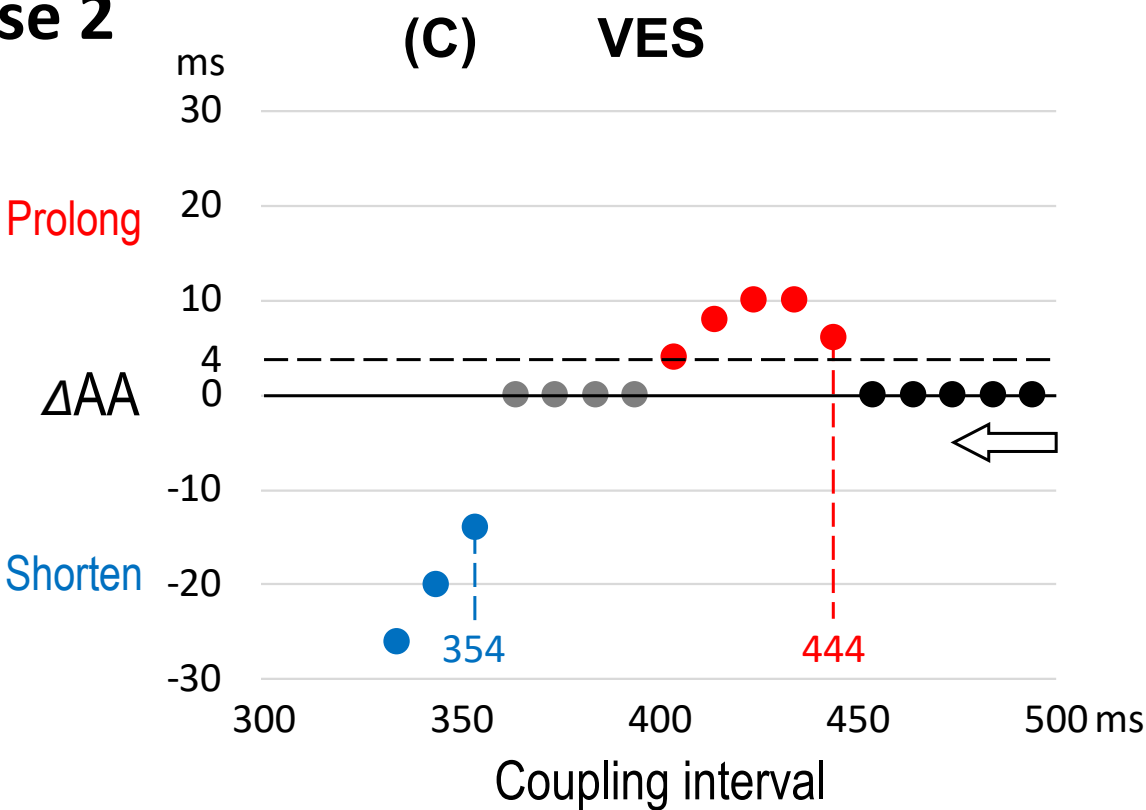
Case 3

Atypical AVNRT with
bystander NV/NF-SP and
accessory pathway

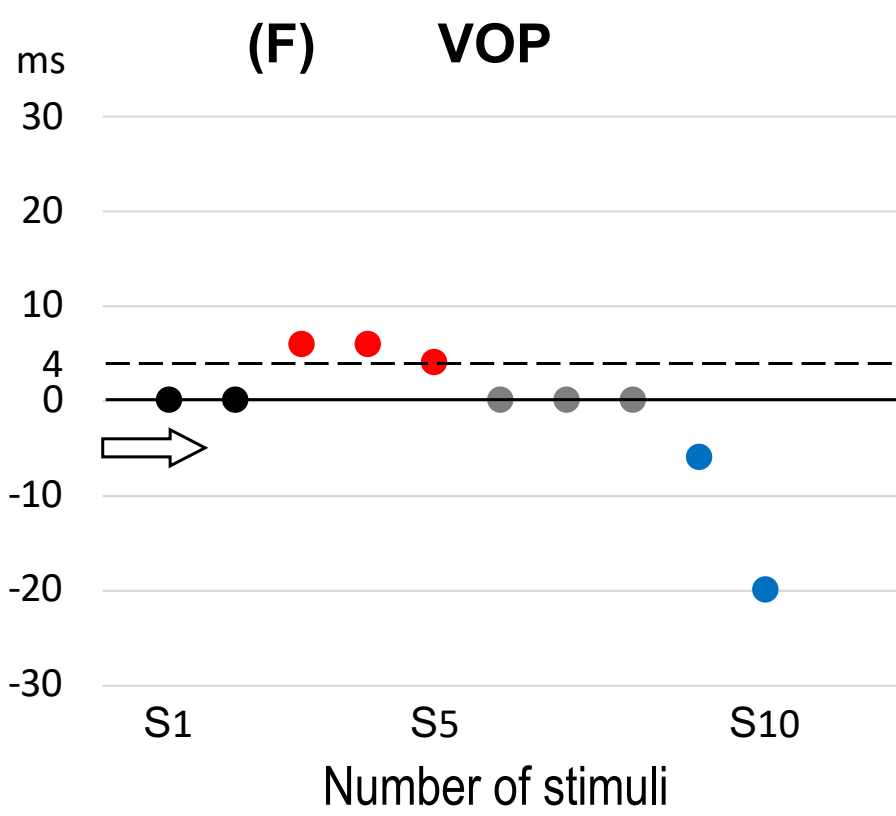
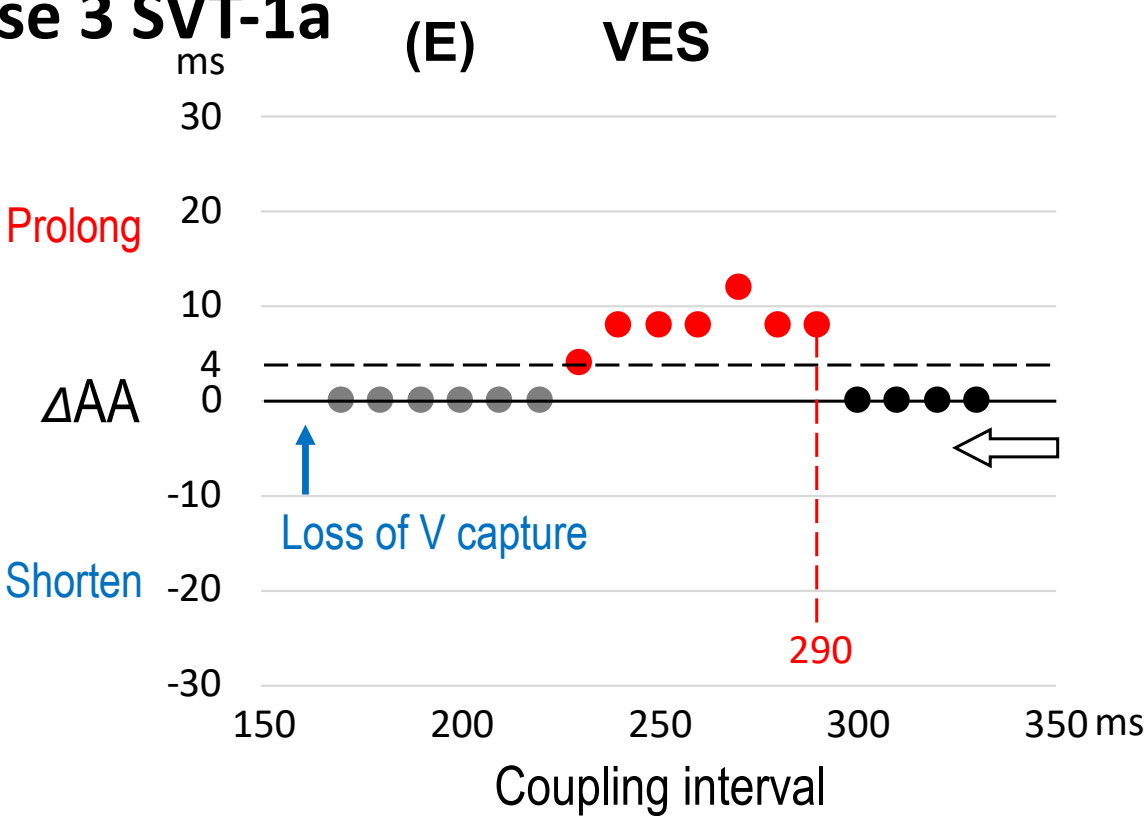
Case 1



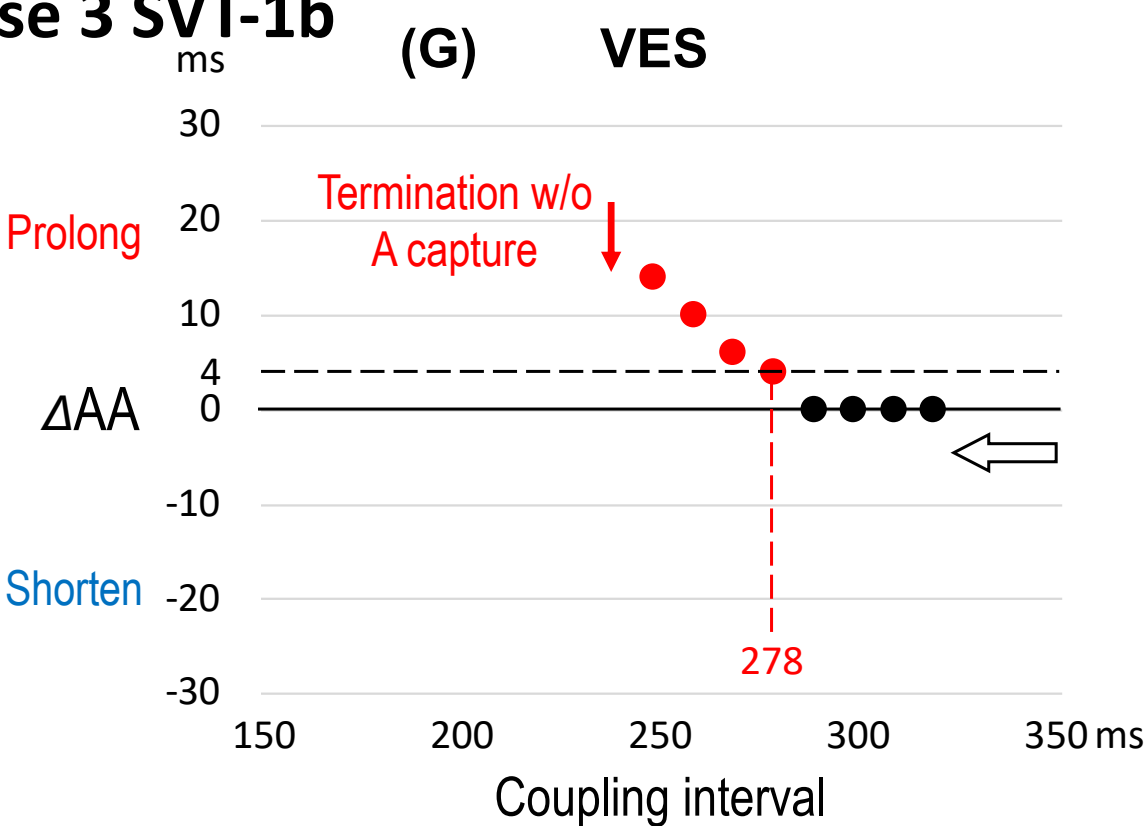
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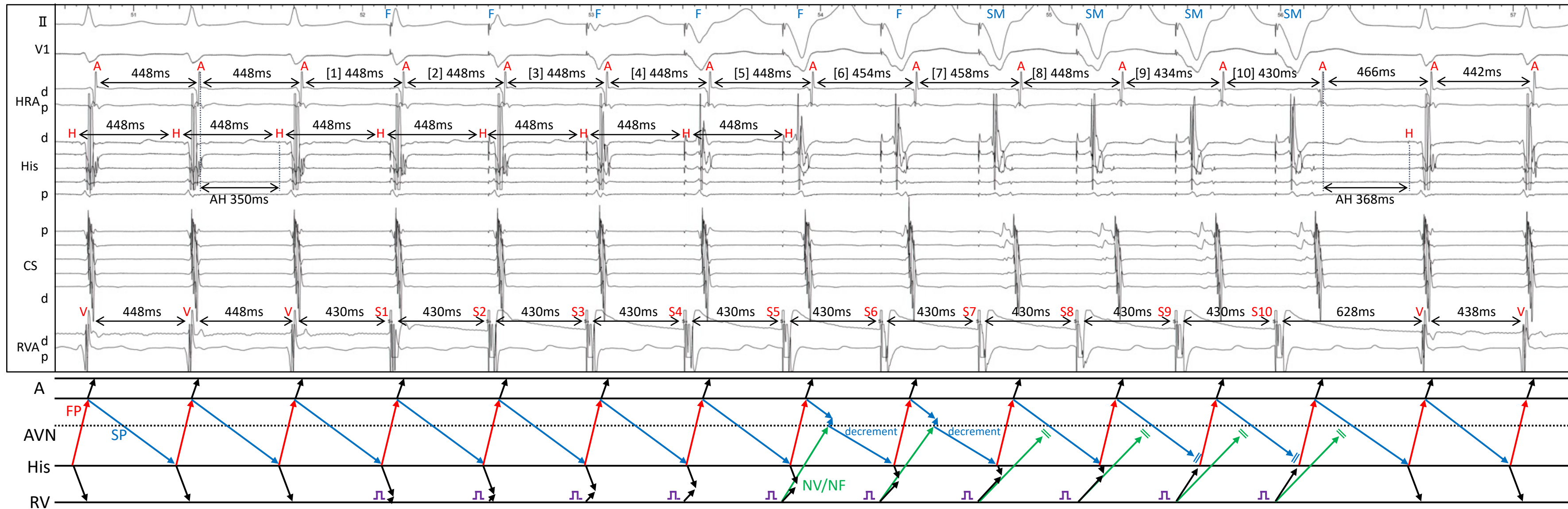
Case 3 SVT-1a



Case 3 SVT-1b



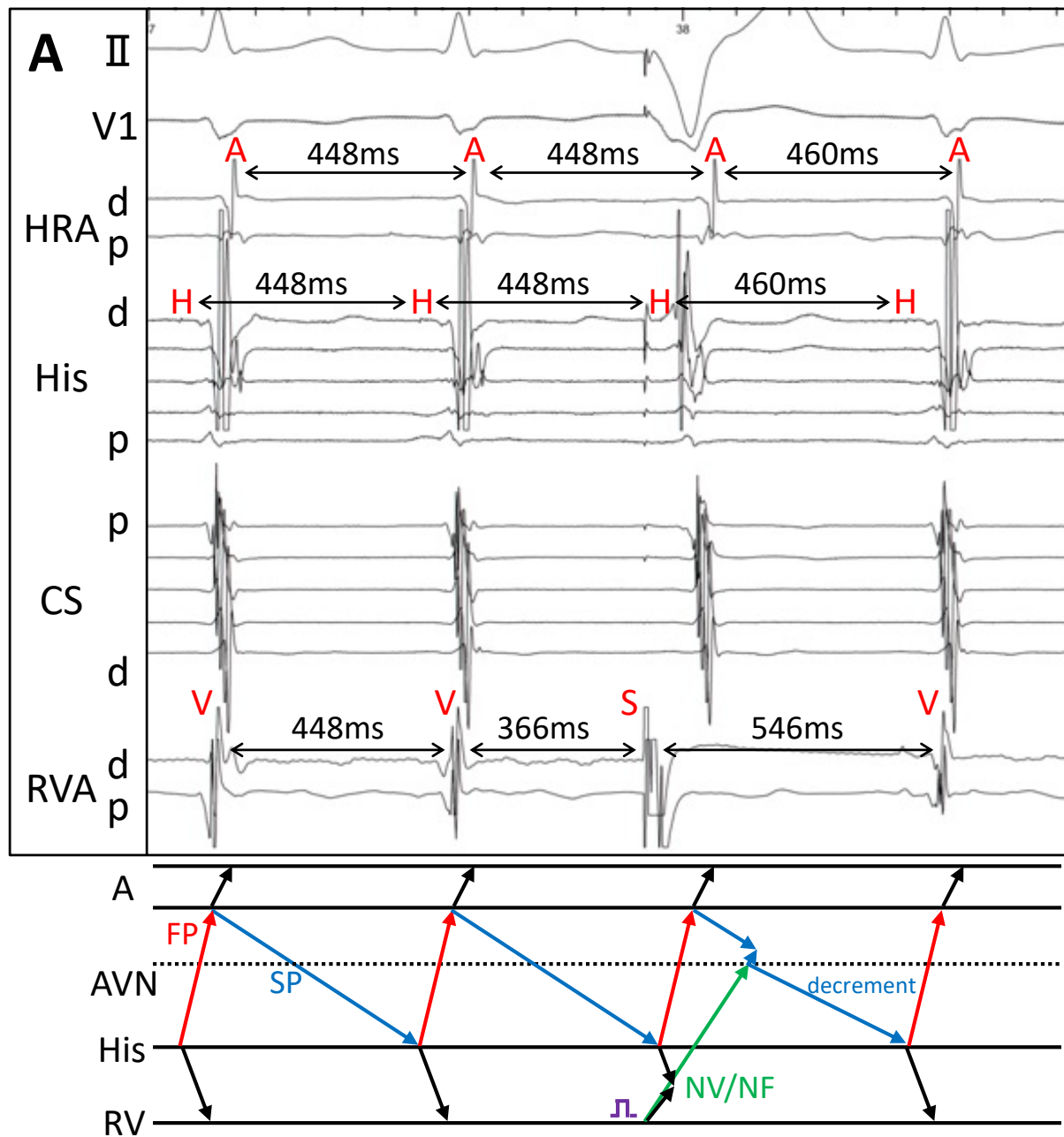
Case 1



His-refractory VES

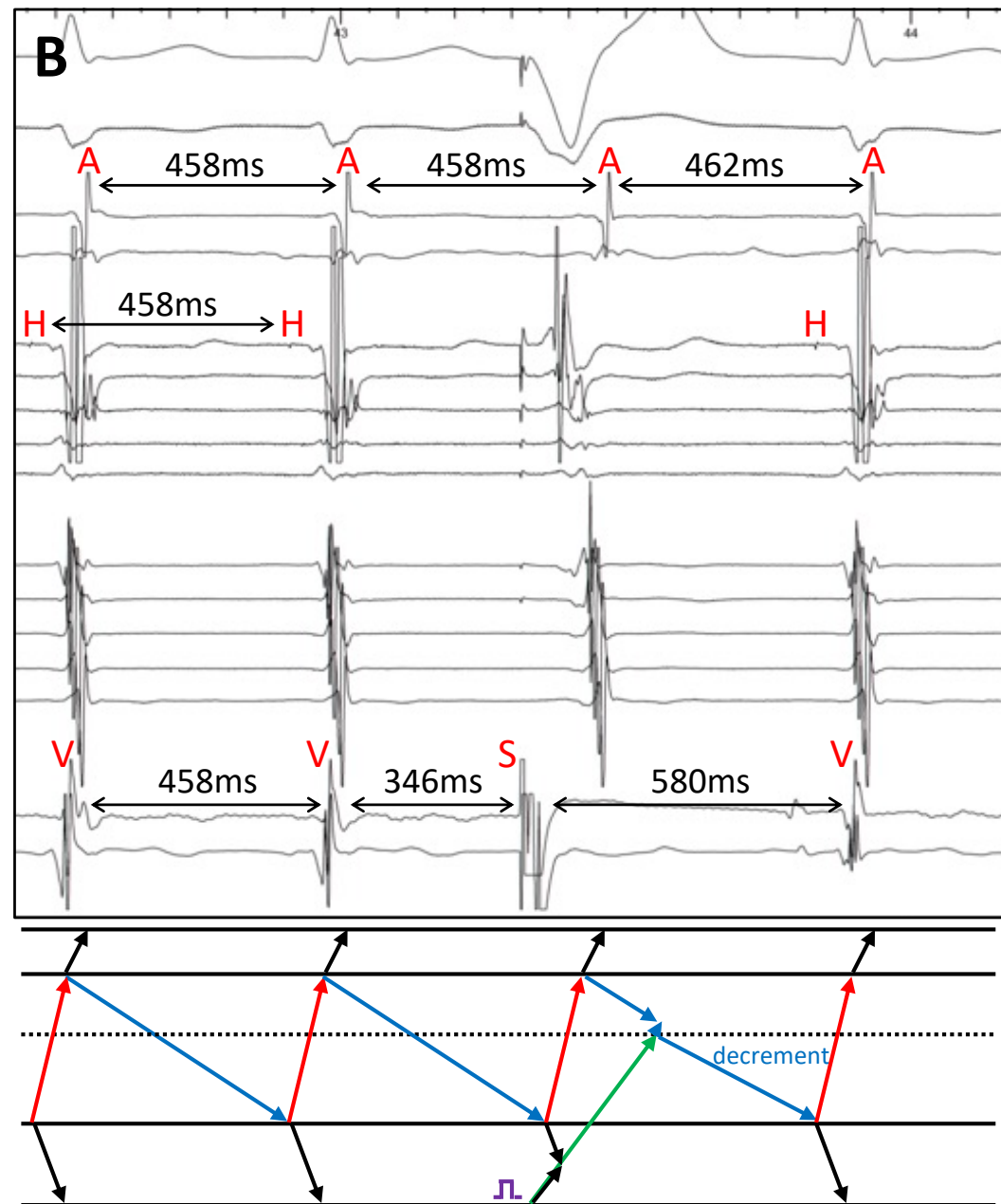
Case 1

1st reset with maximum delay



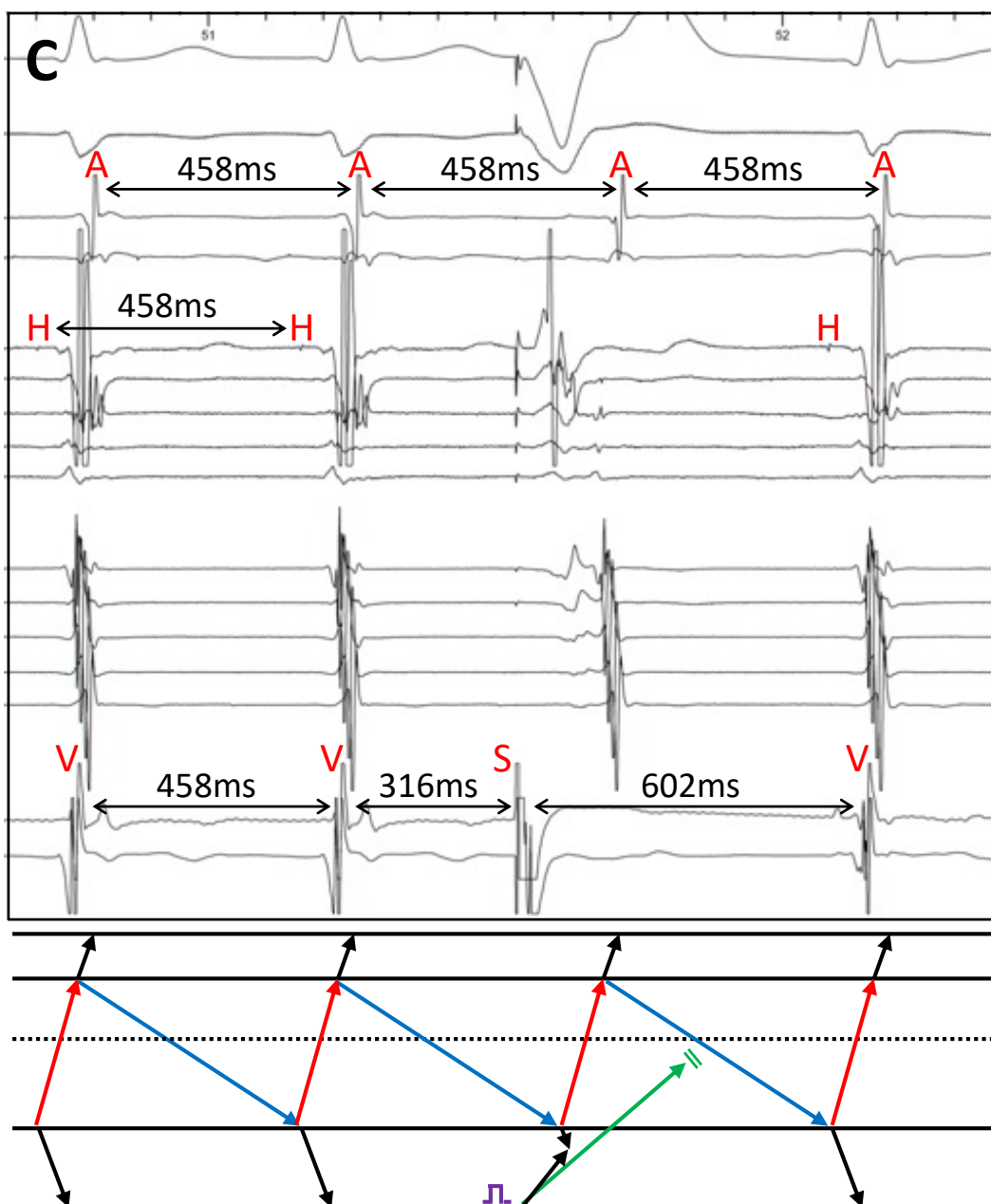
His-refractory VES

3rd reset with delay



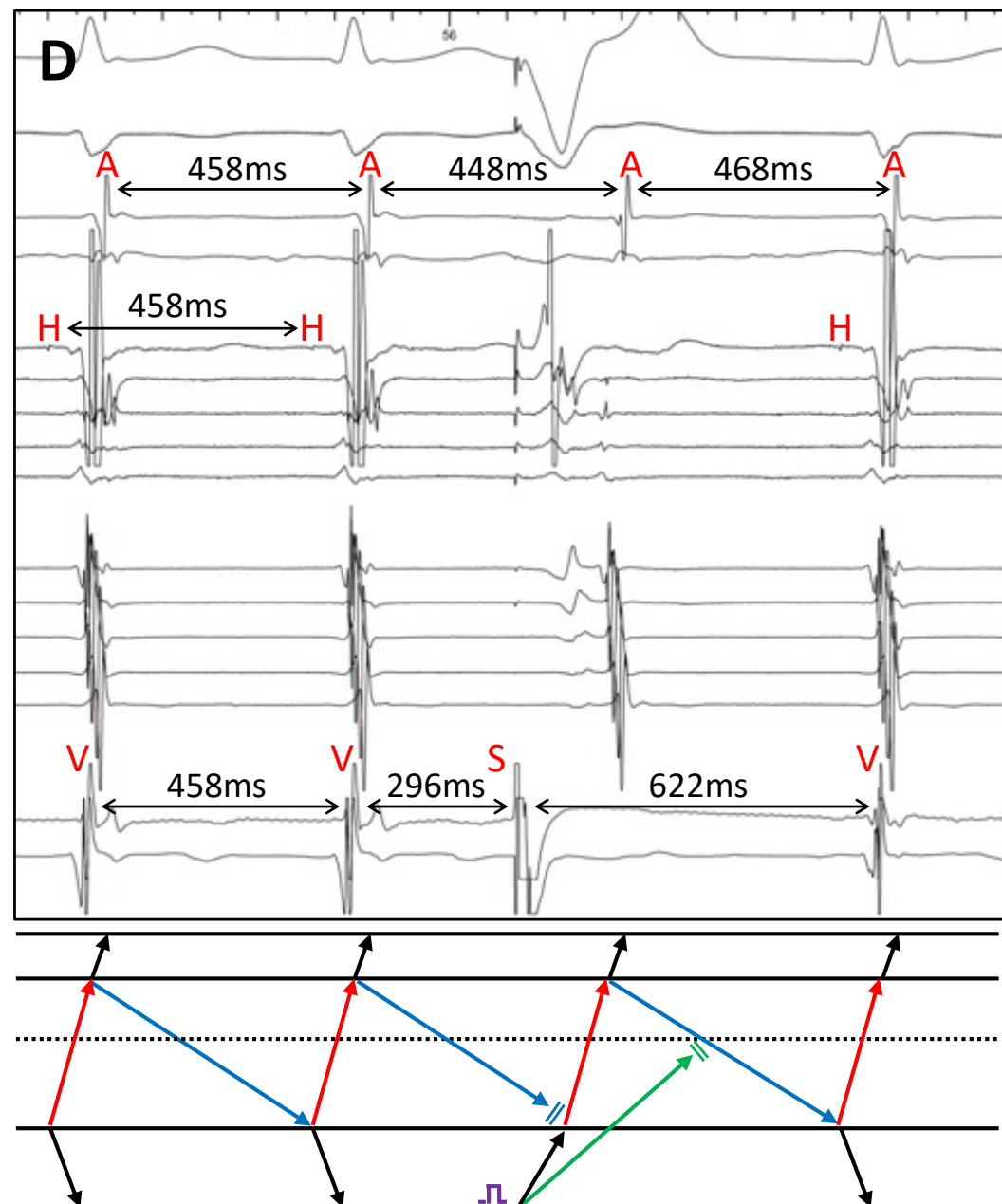
Earlier VES

3rd No reset

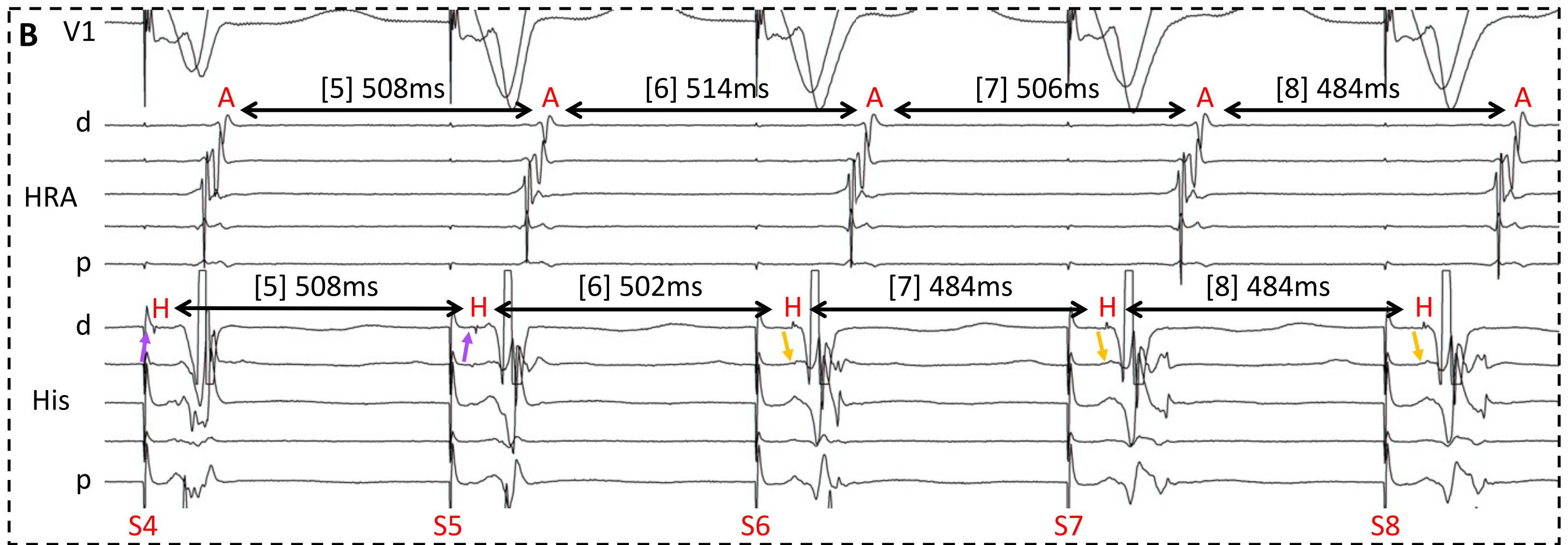
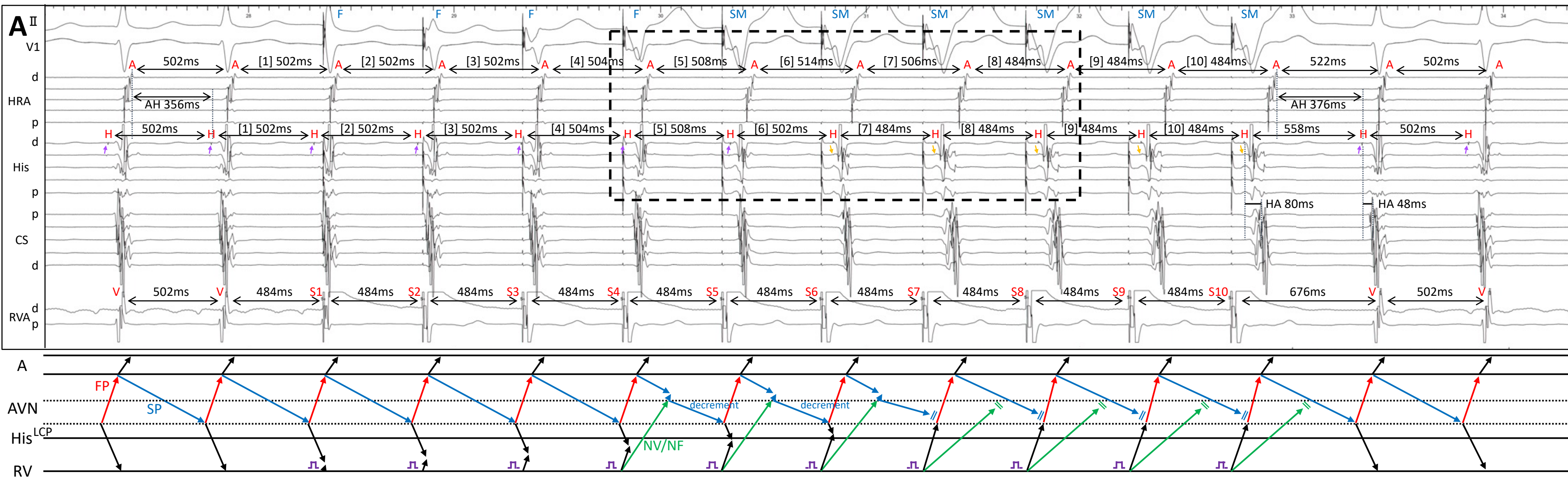


Further earlier VES

1st reset with advance



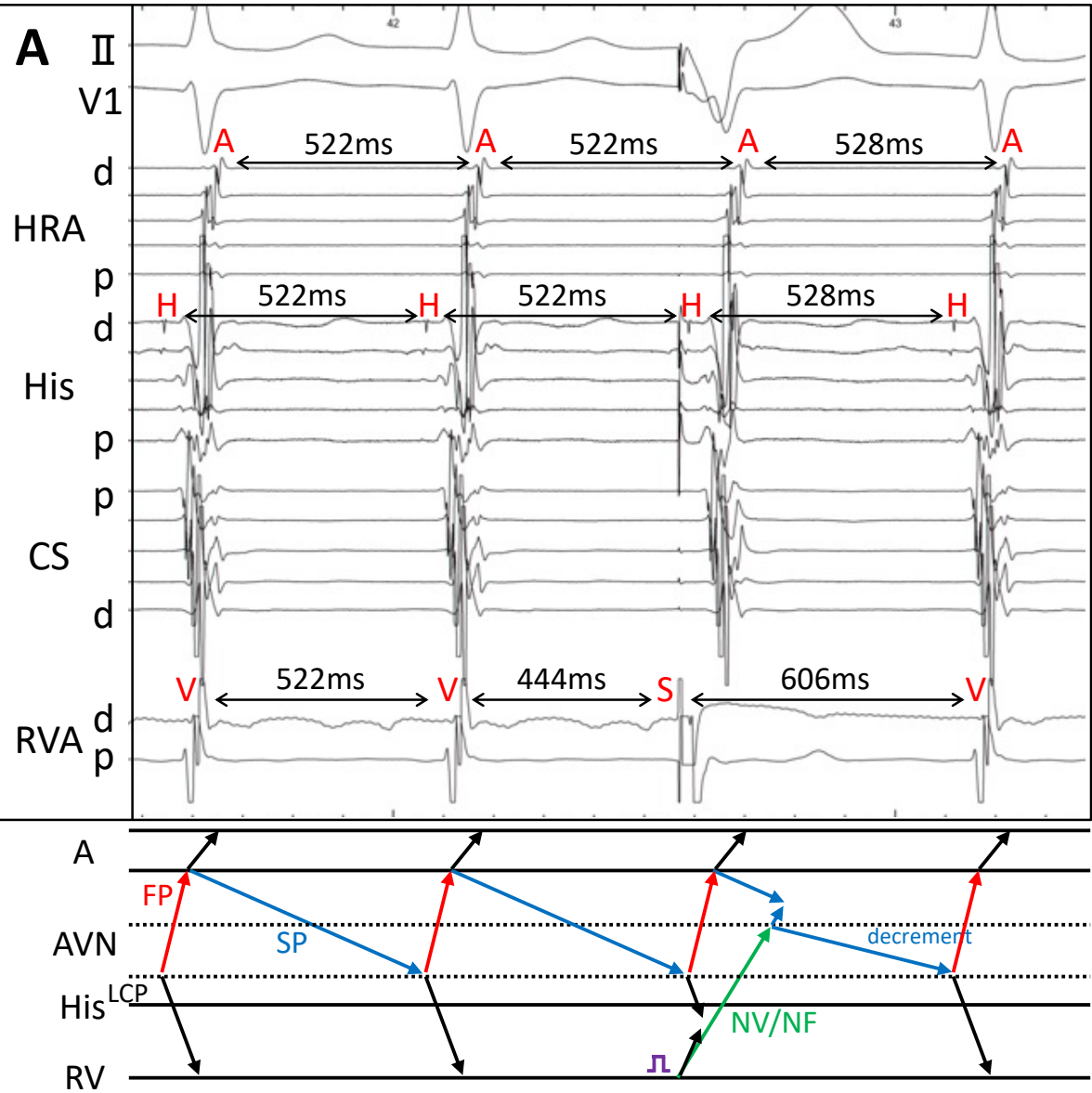
Case 2



His-refractory VES

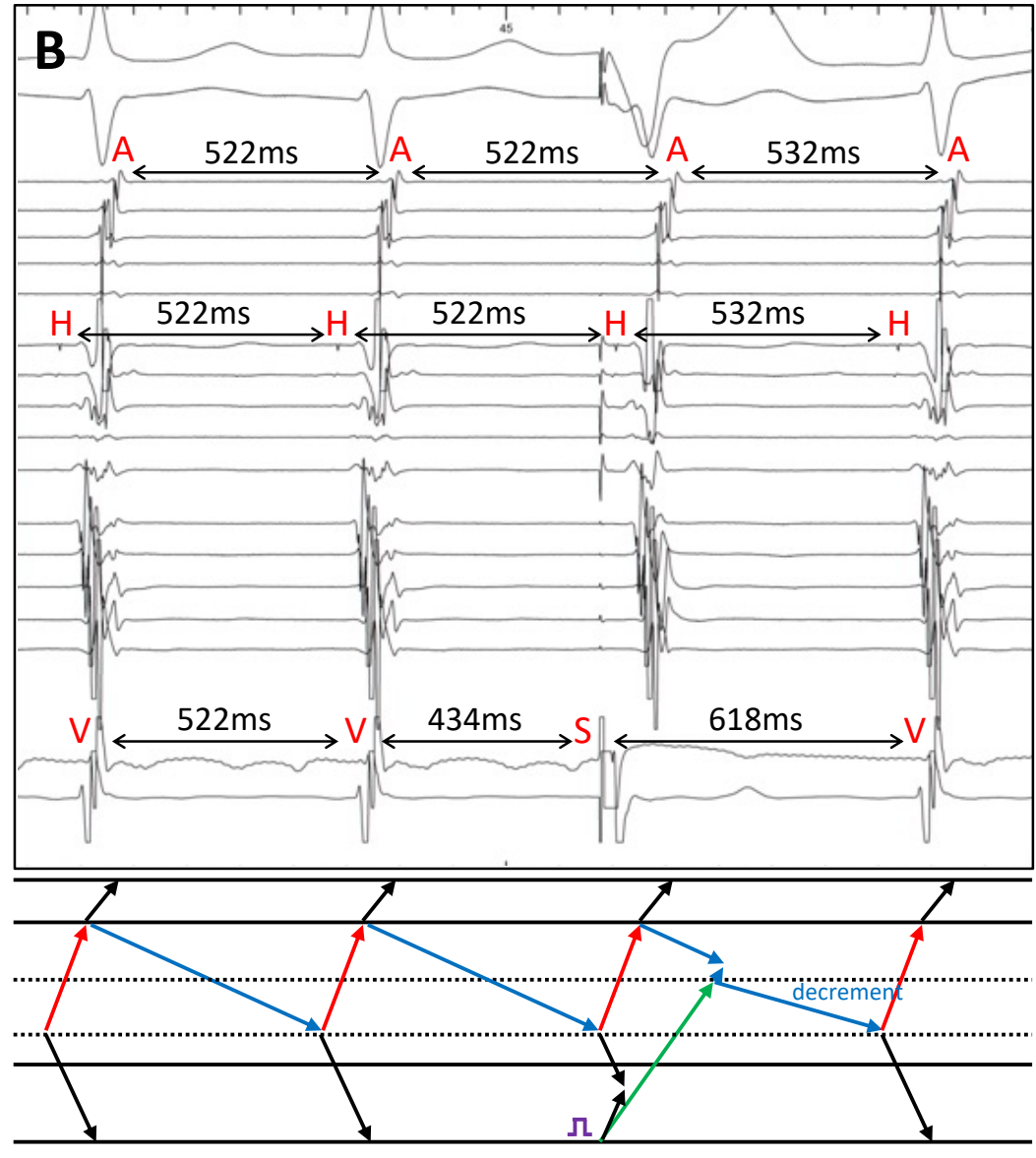
Case 2

1st reset with delay



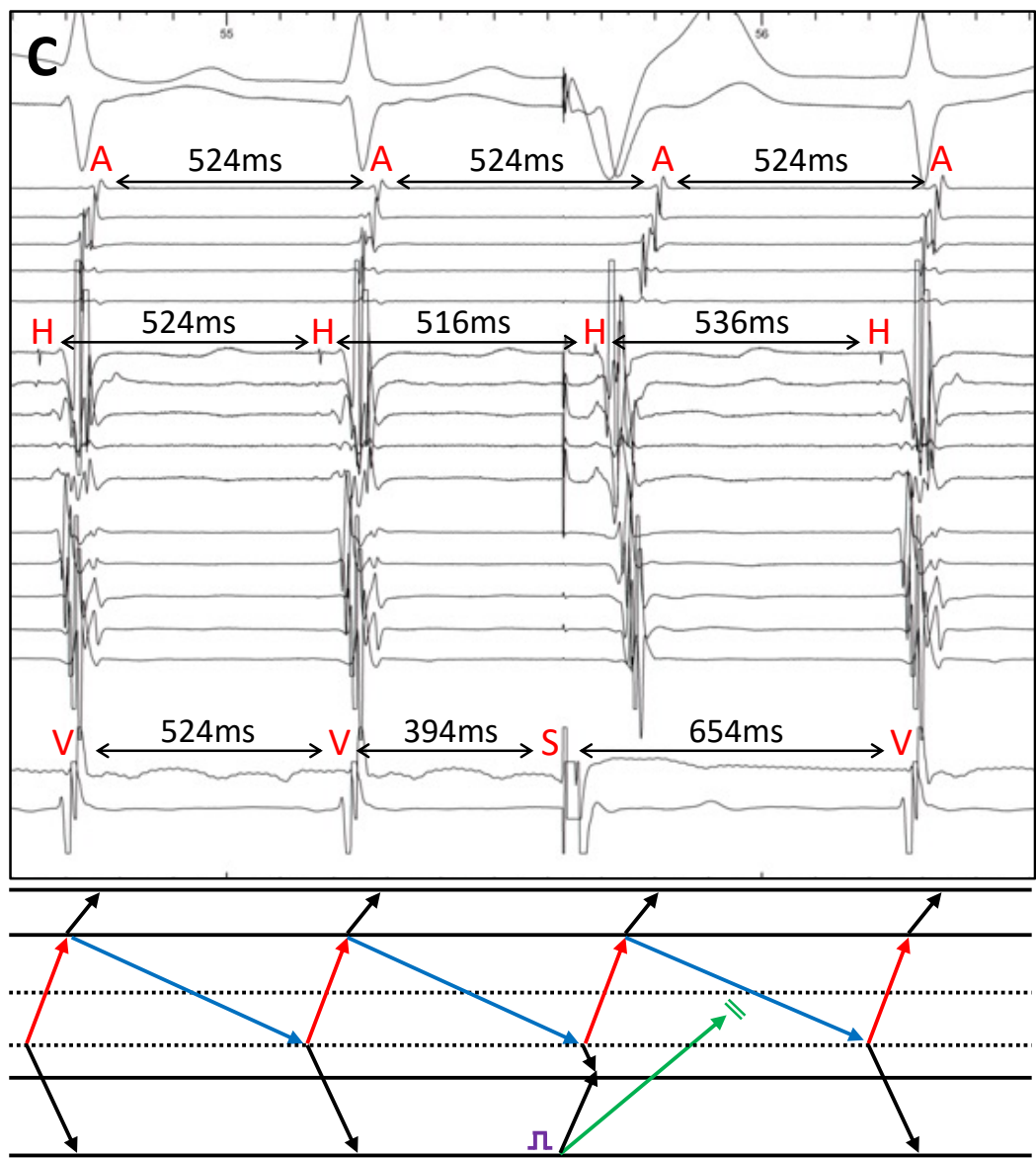
His-refractory VES

2nd reset with maximum delay



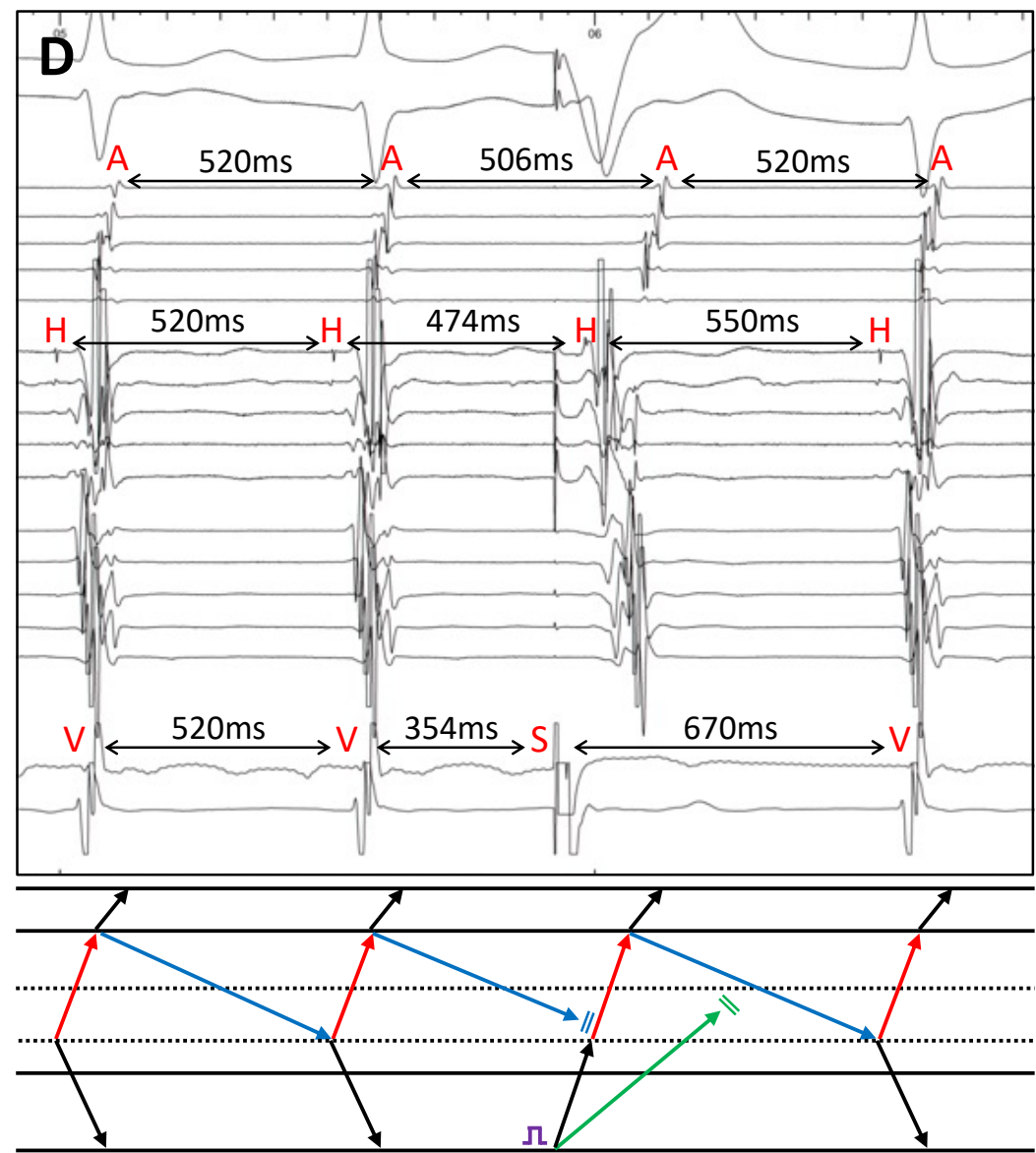
Earlier VES

1st No reset

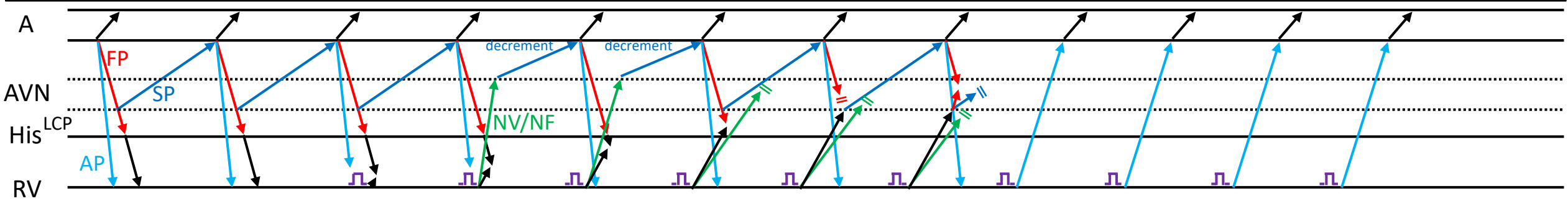
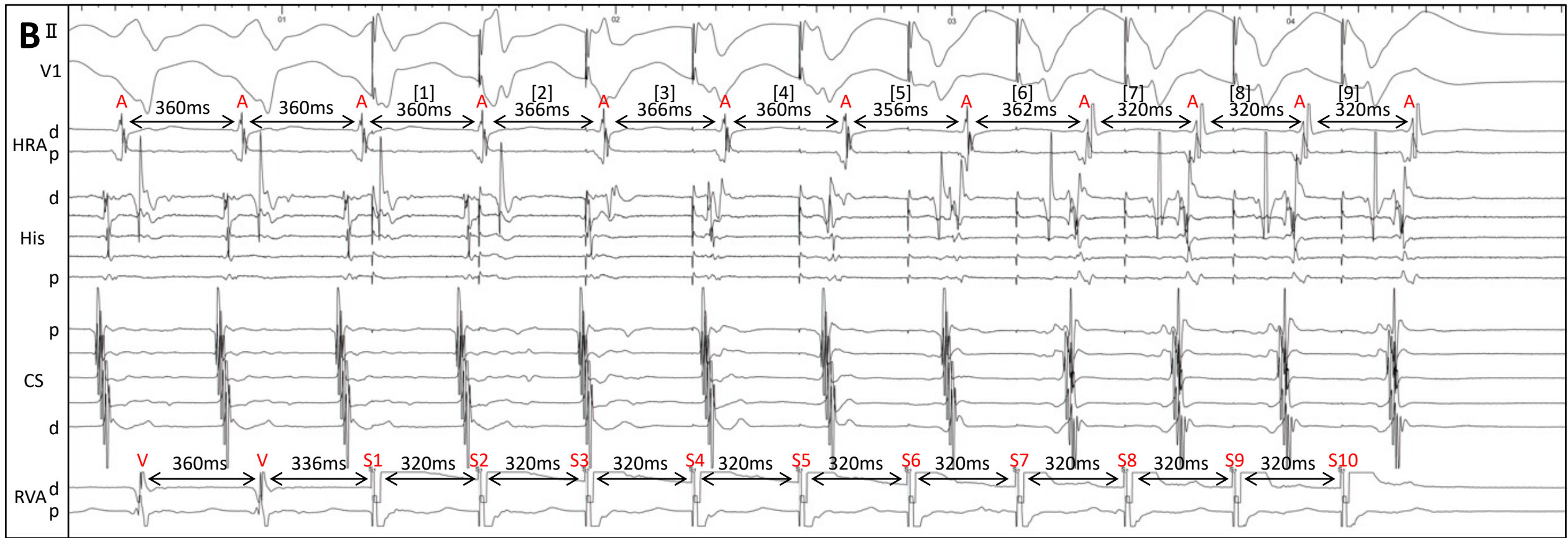
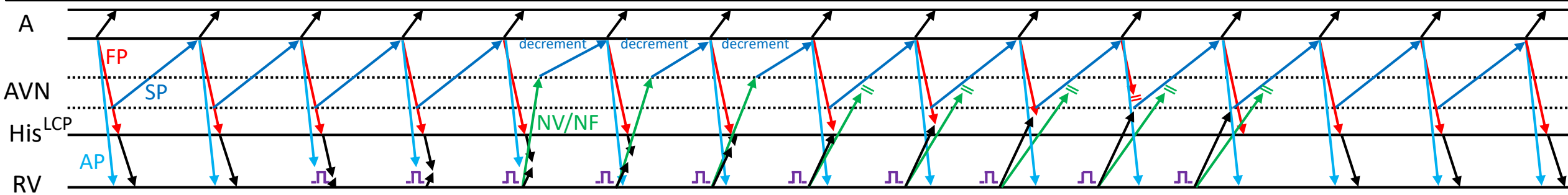
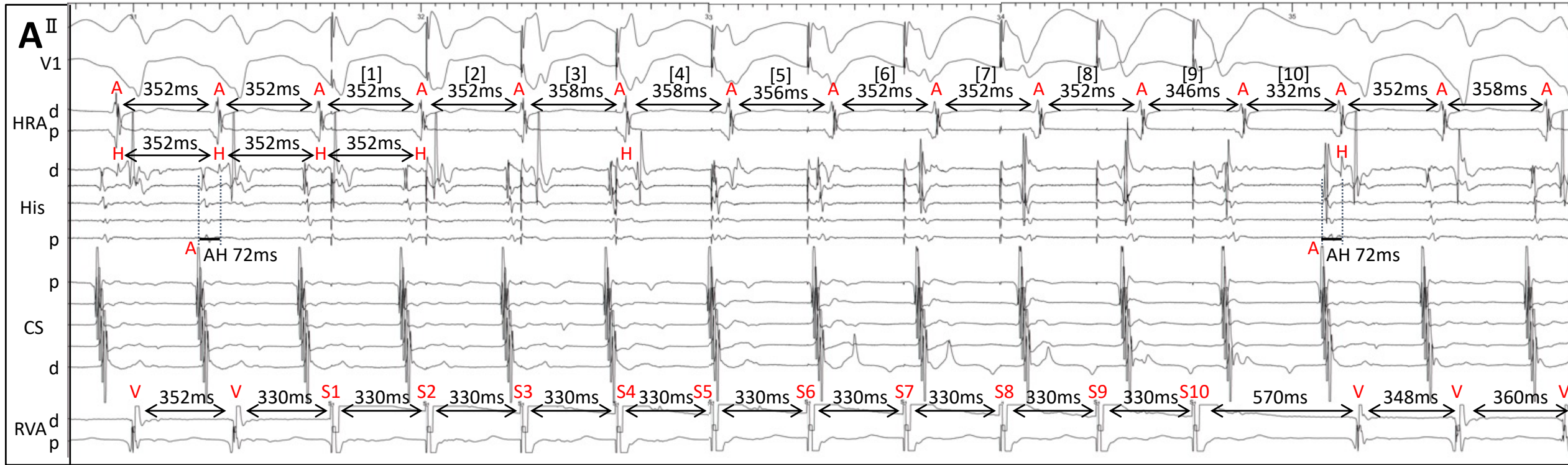


Further earlier VES

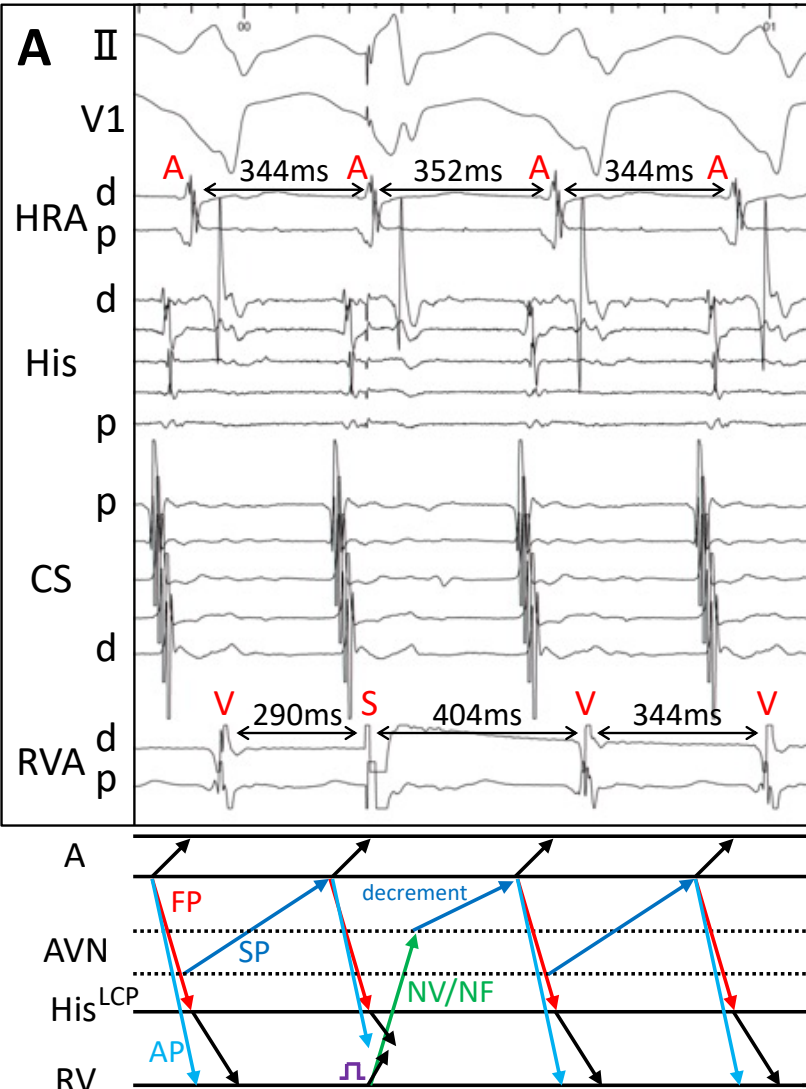
1st reset with advance



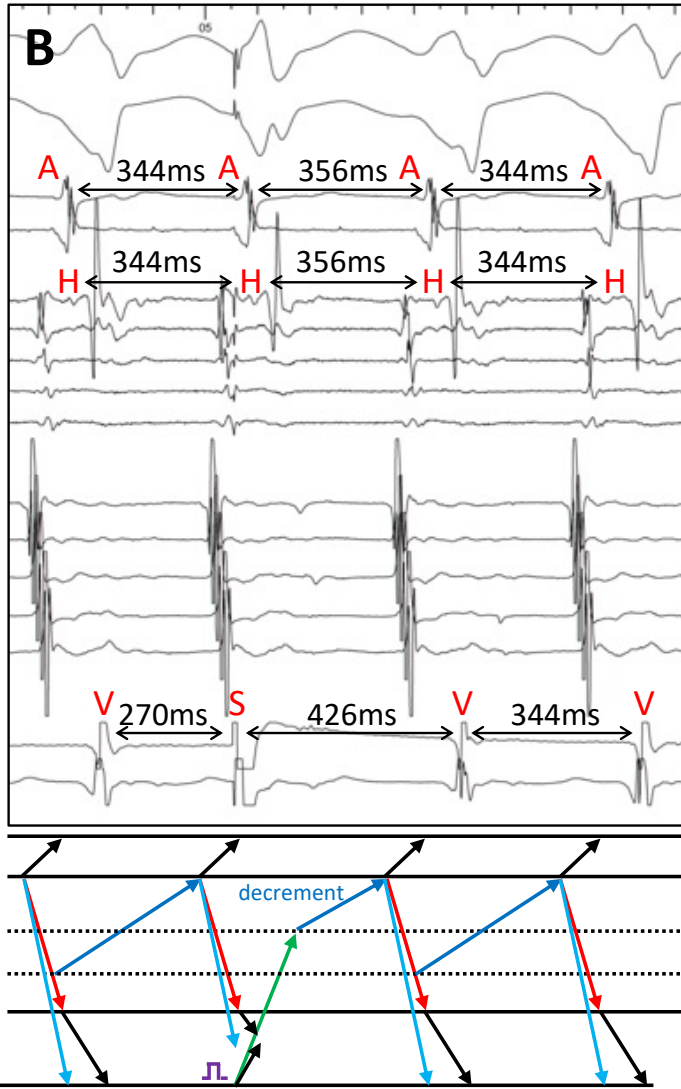
Case 3 SVT-1a



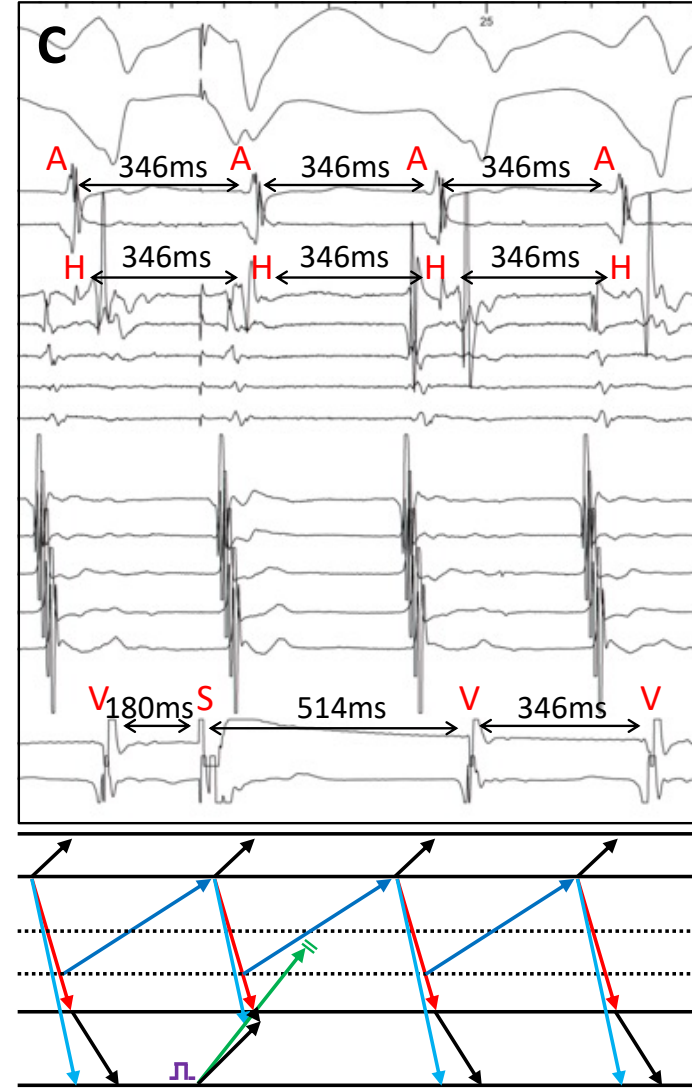
Case 3
SVT-1a **His-refractory VES**
1st reset with delay



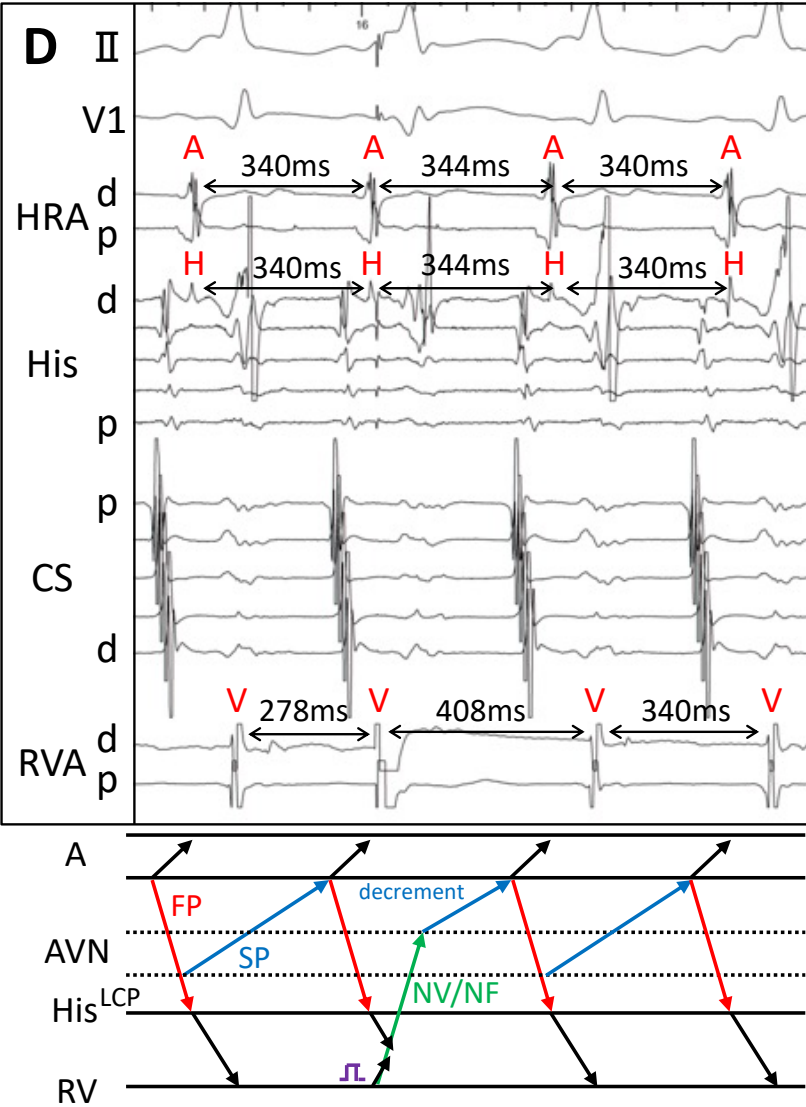
His-refractory VES
3rd reset with maximum delay



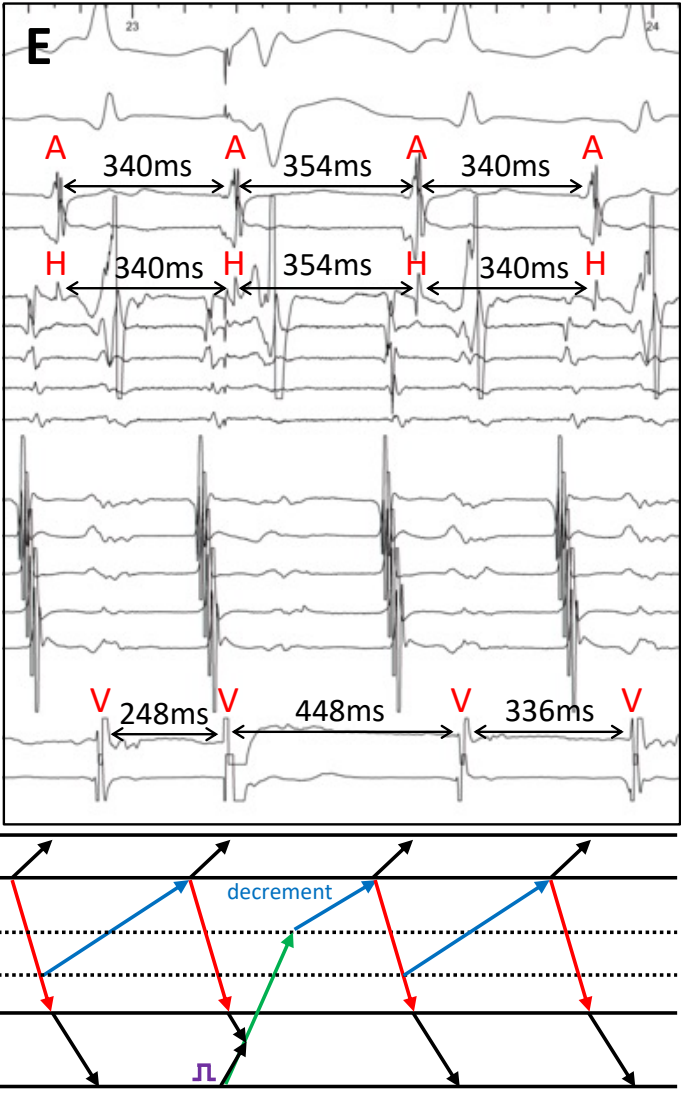
Earlier VES
5th No reset



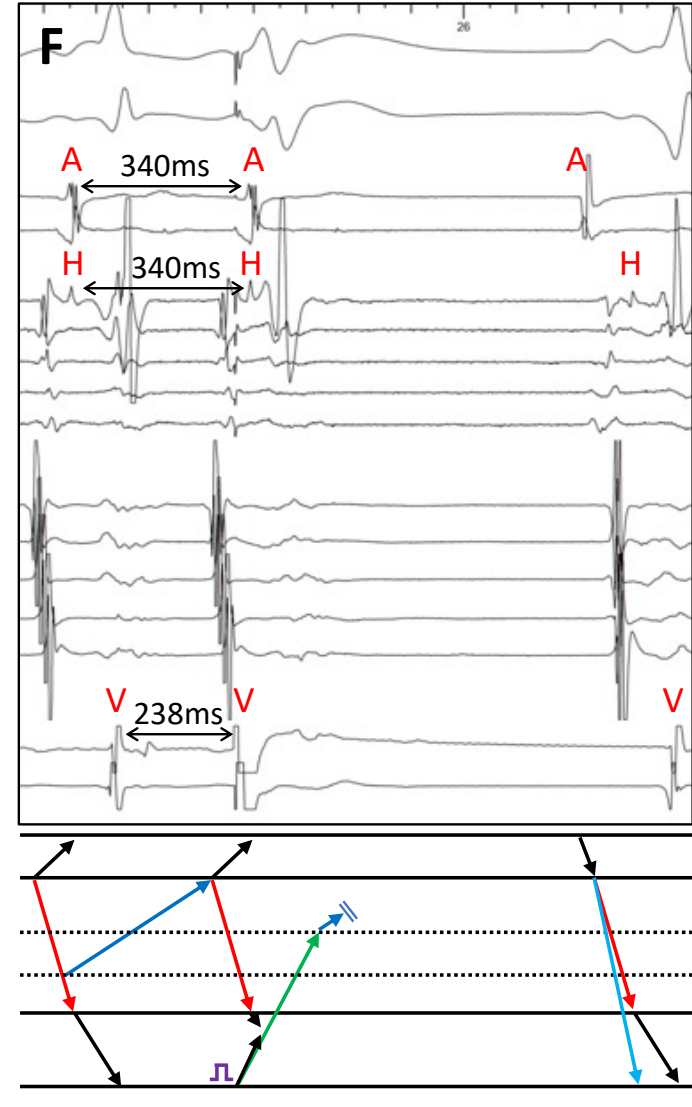
SVT-1b **His-refractory VES**
1st reset with delay



His-refractory VES
4th reset with maximum delay



His-refractory VES
Termination without A capture



Supplemental Materials

Supplemental Appendix

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Supplemental Methods

The diagnosis of atrioventricular nodal reentrant tachycardia (AVNRT) was made comprehensively based on the tachycardia features, responses to the diagnostic pacing maneuvers, and results of the catheter ablation.

Baseline electrophysiological study (EPS)

The EPS and ablation procedures were usually performed in an awake, unsedated state. All sheaths were inserted via right femoral vein. Decapolar electrode catheters were placed at His region and in coronary sinus. Quadripolar electrode catheters were placed at the high right atrium and right ventricular (RV) apex. Bipolar intracardiac and 12-lead body-surface electrocardiograms were recorded using a digital recording system (LabSystem PRO, Bard Electrophysiology, Lowell, Massachusetts, USA). Atrial and ventricular burst pacing and extra stimulation were performed to induce supraventricular tachycardia (SVT). When the SVT was not induced, isoproterenol was administered, and the stimulation maneuvers were repeated.

Definition of corrected post pacing interval (PPI)–tachycardia cycle length (TCL) and total pacing prematurity (TPP)

The corrected PPI–TCL was defined as $PPI - TCL - [post-pacing\ A-H\ interval - A-H\ interval\ during\ tachycardia]$. TPP was defined as $N \times [TCL - pacing\ cycle\ length\ (PCL)]$ (N; number of stimuli needed to reset the atrium or to terminate the tachycardia)¹ in cases of the coupling interval of S1 equal to the PCL. When the coupling interval of S1 was not equal to the PCL, then the TPP was calculated as $[TCL - coupling\ interval] + (N-1) \times [TCL - PCL]$.

Exclusion of atrial tachycardia

Atrial tachycardia was excluded based on the following criteria: 1) A-V response after ventricular overdrive pacing (VOP)² and 2) delta-VA interval of ≤ 20 ms after differential atrial overdrive pacing.³

Definition of the ventricular insertion of the nodoventricular (NV)/nodofascicular (NF)-pathway

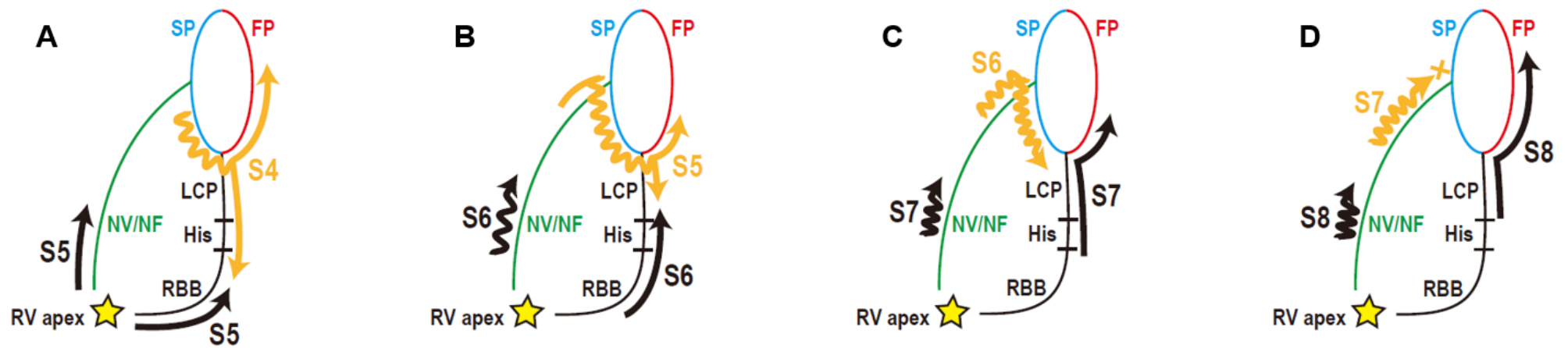
In a previous study,⁴ the ventricular insertion of a bystander NV/NF-pathway was considered RV myocardium (NV pathway) when VOP resets the AVNRT in the fused QRS zone, while it is considered right

bundle branch (RBB) (NF pathway) when VOP resets the AVNRT after stabilizing QRS morphology. However, in case of the RV pacing site being close to the ventricular insertion of a NF pathway in RBB, the VOP can reach the NF pathway earlier and reset the AVNRT in the fused QRS zone. Thus, in the present study, the ventricular insertion was considered undistinguishable (NV/NF-pathway) when VOP reset the AVNRT in the fused QRS zone and was considered RBB (NF pathway) when VOP reset the AVNRT after stabilization of the QRS.

Supplemental Figure 1.

Diagrams showing the mechanisms of the two-phase resetting and the discrepancy between the A-A and H-H intervals during VOP in Case-2

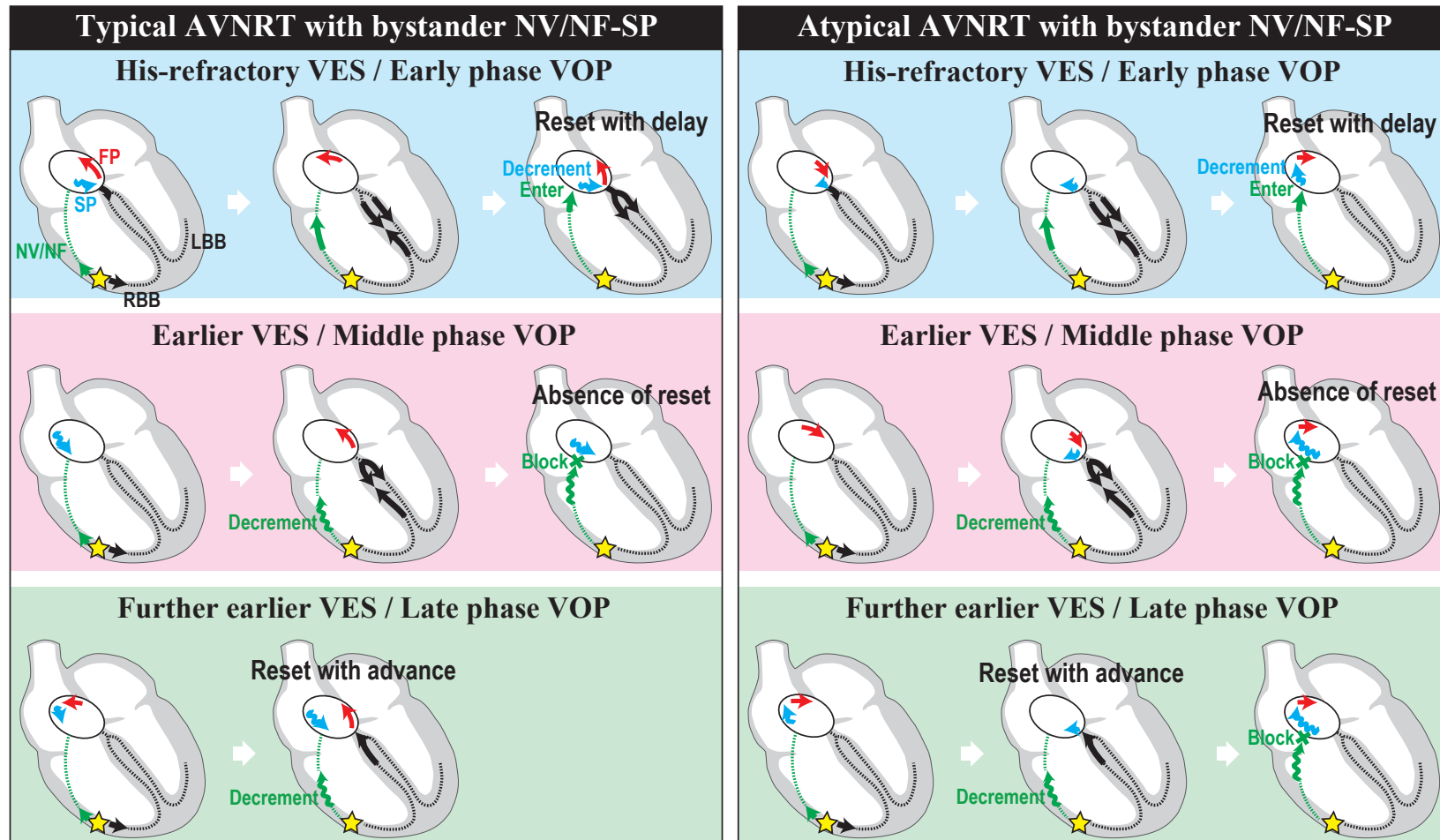
The wave lines indicate slowly conducting activations associated with the decremental conduction property.



Supplemental Figure 2.

Proposed explanation of the two-phase resetting phenomenon in AVNRT with a bystander concealed NV/NF-pathway connected to SP.

His-refractory VESs and VOP in the early phase reset the tachycardia through the bystander concealed NV/NF-pathway anterogradely in typical SP/FP AVNRT and retrogradely in atypical FP/SP AVNRT. Earlier VESs and VOP in the middle phase do not reset the tachycardia. Further earlier VESs and VOP in the late phase retrogradely reset AVNRT through the RBB-His conduction.



AVNRT, atrioventricular nodal reentrant tachycardia; ERP, effective refractory period; FP, fast pathway; LBB, left bundle branch; NF, nodofascicular; NV, nodoventricular; RBB, right bundle branch; SP, slow pathway; SVT, supraventricular tachycardia; VES, ventricular extra stimulation; VOP, ventricular overdrive pacing.

Supplemental Table 1.

Baseline and procedural characteristics and clinical outcomes comparing patients with pure AVNRT and those with AVNRT plus NV/NF-pathway.

	Pure AVNRT N=98	AVNRT with bystander concealed NV/NF-pathway N=3
Baseline characteristics		
Age, years	64 (50 – 73)	67 (37 – 69)
Female, %	56 (57)	2 (67)
Typical AVNRT, %	85 (87)	2 (67)
Clinical outcomes		
Complication* (%)	1 (1)	0 (0)
Follow-up period, days	161 (9-705)	246 (44-369)
Arrhythmia recurrence (%)	5 (5)	0 (0)

Categorical variables are presented as numbers and percentages, and continuous variables are presented as medians with interquartile ranges.

*Complete atrioventricular block requiring permanent pacemaker implantation occurred in one patient in the pure AVNRT group.

AVNRT, atrioventricular nodal reentrant tachycardia; NV, nodoventricular; NF, nodofascicular.

Supplemental Table 2. Electrophysiological characteristics of the AVNRTs and NV/NF-pathways

	Case-1	Case-2	Case-3	
			SVT-1a	SVT-1b
Type of AVNRT	Typical (SP/FP)	Typical (SP/FP)	Atypical (FP/SP)	Atypical (FP/SP)
Ventricular insertion of the NV/NF-pathway	Undistinguishable	Undistinguishable	Undistinguishable	Undistinguishable
Atrial insertion of the NV/NF-pathway	SP	SP	SP	SP
Response to VESs				
Resetting with delay by His-refractory VESs	Yes	Yes	Yes	Yes
Termination without atrial capture by His-refractory VESs	No	No	No	Yes
Prematurity at the 1st reset with delay through the NV/NF-pathway	82 ms	78 ms	54 ms	62 ms
Prematurity at the 1st reset with advance through the RBB-His	162 ms	166 ms	NA	NA
Response to VOP			*	*
Mode of SVT resuming	A-V	A-V	Pseudo A-A-V / NA	NA
Resetting with delay in the transition zone	Yes	Yes	Yes / Yes	NA
PPI – TCL	180 ms	174 ms	218 ms / NA	NA
Corrected PPI – TCL	162 ms	154 ms	218ms / NA	NA
TPP _{NV/NF}	90 ms	72 ms	66 / 64 ms	NA
TPP _{RBB-His}	162 ms	126 ms	198 / 184 ms	NA

* In Case-3, two VOP maneuvers were performed for SVT-1a, while VOP was not performed for SVT-1b.

AVNRT, atrioventricular nodal reentrant tachycardia; FP, fast pathway; NA, not available; NF, nodofascicular; NV, nodoventricular; VES, ventricular extra stimulus; TPP, total pacing prematurity; PPI, post pacing interval; SP, slow pathway; SVT, supraventricular tachycardia; TCL, tachycardia cycle length, VOP, ventricular overdrive pacing.

Supplemental Discussion

Prematurity to reset AVNRT through the NV/NF-pathways and RBB-His conduction

The $TPP_{NV/NF}$ during VOP was close to the prematurity of the His-refractory ventricular extra stimuli (VES) at the first resetting with delay in all 3 cases of the present study. Similarly, the $TPP_{RBB-His}$ was close to the prematurity of the further earlier VES at the first resetting with advance through the RBB-His conduction (Supplemental Table 2).

Catheter ablation of AVNRT with a NV/NF-pathway

Regarding the ablation strategy for AVNRT with a bystander concealed NV/NF-pathway connected to slow pathway (SP), simple SP ablation or modification without targeting the NV/NF-pathway is adequate. However, when NV/NF orthodromic reciprocating tachycardia (ORT) is induced after SP modification for AVNRT, complete SP elimination or additional ablation targeting the NV/NF-pathway should be considered. Although manifest NV/NF-pathways can be eliminated by complete SP ablation⁵ or ventricular insertion ablation targeting the earliest ventricular activation site,⁶ it is usually difficult to identify the location of the ventricular insertion of the concealed NV/NF-pathways. In recent reports,^{7,8} however, NV/NF ORTs were successfully eliminated by targeting discrete NV/NF-pathway potentials in the RV or coronary sinus. Also, in another report,⁹ the right or left high basal ventricular septum with a short PPI was ablated from the peri-hisian area including the right coronary cusp, leading to successful elimination of NV/NF-ORT.

Supplemental References

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