Experimental, Pathologic, and Clinical Findings of Radiofrequency Catheter Ablation of Para-Hisian Region From the Right Ventricle in Dogs and Humans

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Background—Ablation of para-Hisian accessory pathway (AP) poses high risks of atrioventricular block. We developed a pacing technique to differentiate the near-field (NF) from far-field His activations to avoid the complication.

Methods and Results—Three-dimensional mapping of the right ventricle was performed in 15 mongrel dogs and 23 patients with para-Hisian AP. Using different pacing outputs, the NF- and far-field His activation was identified on the ventricular aspect. Radiofrequency application was delivered at the NF His site in 8 (group 1) and the far-field His site in 7 dogs (group 2), followed by pathologic examination after 14 days. NF His activation was captured with 5 mA/1 ms in 10 and 10 mA/1 ms in 5 dogs. In group 1, radiofrequency delivery resulted in complete atrioventricular block in 3, right bundle branch block in 5 dogs, whereas no changes occurred in group 2. Pathologic examination in group-1 dogs showed complete partial necrosis of the His bundle in 4 and complete necrosis of the right bundle branch in 5 dogs. In group 2, partial necrosis in the right bundle branch was found only in 1 dog. Using this pacing technique, the APs were 5.7±1.2 mm away from the His bundle located superiorly in 20 or inferiorly in 3 patients. All APs were successfully eliminated with 1 to 3 radiofrequency applications. No complications and recurrence occurred during a follow-up of 11.8±1.4 months.

Conclusions—Differentiating the NF His from far-field His activations led to a high ablation success without atrioventricular block in para-Hisian AP patients. (Circ Arrhythm Electrophysiol. 2017;10:e005207.DOI: 10.1161/CIRCEP.116.005207.)

Key Words: arrhythmias, cardiac bundle of His catheter ablation heart ventricles tachycardia, supraventricular

The incidence of the atrioventricular conduction system (AVCS) damage during catheter ablation of para-Hisian (PH) accessory pathway (AP) had been reported to be ≥2% to 10%.1–3 Electrophysiologically, the His activation on 3-dimensional (3D) map can be found in a relatively large area on 3D mapping, which does not correlate with anatomic findings that define the His bundle (HB) as a small and long structure encased in thick fibrous tissue.4 This may be because of recordings of both near-field (NF) and far-field (FF) His activations. Therefore, the differentiation between the NF His and FF His activations is critical in clinical practice to minimize inadvertent AVCS damage in PH arrhythmias. We hypothesized that the site where a HB potential is recorded and the HB can be captured with minimal output represents NF His activation, indicating close proximity to the HB. In the first part of the study, we investigated the incidence and pathologic characteristics of AVCS injury after only a single radiofrequency application at the NF His site versus at a FF His site in dogs. In the second part of the study, we applied this technique to patients presented with ablation of a PH-AP.
WHAT IS KNOWN

- With clinical mapping catheters a His bundle electrogram that is either near-field or far-field signal can be recorded over a relatively large area.
- Catheter ablation of Para-Hisian accessory pathway has a potential risk of damage to the atrioventricular conduction system.

WHAT THE STUDY ADDS

- We developed a novel strategy using pacing from the mapping catheter to recognize near field and far-field His electrograms to select safe ablation sites.
- Observations in a series of patients suggests that this technique may help improve outcomes for ablation of arrhythmias in the para-His region.

Methods

Part 1: Electrophysiologic Study, 3D Mapping, and Radiofrequency Ablation in Dogs

Electrophysiologic Study

The experimental protocol was approved by the Institutional Animal Care and Use Committee at Guangdong General Hospital. The study included 15 adult mongrel dogs with a weight of 25 to 35 kg. All dogs were anesthetized and intubated with an endotracheal tube and ventilated mechanically with room air using an Aeon7200 respirator (Aeonmed Co Ltd, Beijing, China). Jet ventilation (200 mL; 30 breaths per minute) was used to facilitate mapping and ablation; two 5F catheters were placed into the coronary sinus and at the HB under fluoroscopic guidance via the right jugular vein and the left femoral vein, respectively. All bipolar intracardiac electrograms were filtered at 30 to 500 Hz and recorded. Baseline PR, AH, and His-to-ventricular (HV) intervals were measured during sinus rhythm (SR) before and after ablation.

3D Electroanatomic Map

The mapping (CARTO; Biosense Webster, Diamond Bar, CA) of the right ventricle (RV) was performed as previously reported.1 A 7.5F, D-curve catheter with a 3.5-mm irrigated-tip electrode (Navistar Thermo-Cool with unidirectional curve) was always advanced via a long sheath to the RV. A high-density activation map with manual annotation was achieved at the ventricular aspect of the tricuspid annulus near the HB and the right bundle branch (RBB) during SR (Figure 1A). The sites of the His potential in the RV were defined as a potential with the longest interval from the Purkinje potential to the ventricular activation and a large atrial activation and tagged on the 3D map (Figure 1A).

Pacing Protocol at the Region With His Activation

Bipolar pacing from the mapping catheter was performed. The pacing protocol consisted of different pacing current (20, 15, 10, and 5 mA) at a different pulse width (2, 1.5, 1, and 0.5 ms). Pacing with a cycle length of 350 to 400 ms was performed at the site recording a HB potential along the tricuspid annulus (Figure 1B). The QRS morphology during pacing were as follows: (1) narrow QRS complexes indicating both myocardial and His capture, (2) wide QRS complexes indicating only myocardial capture, and (3) paced QRS morphology identical to that during SR, and long stimulus to QRS morphology indicating only pure HB capture.4,5,6,7 The right-sided NF His were defined as the presence of His capture with minimal pacing output.8,9 FF His sites were defined if they required >10 mA/2 ms to capture the HB.

Radiofrequency Ablation Protocol

Radiofrequency applications using an irrigated catheter were delivered in power-control mode with a power of 25 W and a flow rate of 17 mL/min and maintained for 60 seconds at the NF His site in 8 dogs (group 1) and at the FF His site superior to the NF His site in 7 dogs (group 2). During radiofrequency delivery, the PR interval, junctional beats, and catheter movement were continuously monitored. The AH and HV intervals were repeatedly measured immediately after the procedure. If a His potential was not visualized in the RV after the ablation, the mapping catheter was subsequently advanced into the LV via 8F sheath in a femoral artery.

For those dogs with third-degree AV block, a permanent single chamber (Sigma permanent ventricular pacemaker; Medtronic, To流通az, Switzerland) was implanted under fluoroscopic guidance. An active fixation lead (5076 model; Medtronic, Villalba, PR) was inserted through the right jugular vein and positioned in the RV septum. Pacemakers were programmed to VVI mode with a rate of 100 beats per minute.

Pathologic Examination

All dogs were monitored for 14 to 17 days after euthanasia by intravenous injection of >30% potassium chloride. The heart was removed and the radiofrequency lesion size and distance to the atrioventricular junction was examined. The hearts were then fixed with a 10% neutral buffered formalin solution. Atrioventricular junction areas were resected between the coronary sinus ostia and the anterior rim of the membranous septum of the hearts, and these areas were cut into 7 to 9 blocks with a thickness of ≥3 mm perpendicular to the annulus of the tricuspid valve (Figure 2A). These tissue blocks were then dehydrated and embedded in paraffin and sectioned with a thickness of 4 mm. All tissue sections were stained with hematoxylin and eosin and Masson trichrome using routine protocols. The histologic images were visualized under an ECLIPSE 80i microscope (Nikon, Tokyo, Japan), captured with a DS-Ri1 digital camera (Nikon, Tokyo, Japan), and analyzed using Image-Pro Plus software, version 6.0 (Media Cybernetics, MD).

The ablation lesion and its related conduction tissue injury were histologically determined at the tissue section with the maximum ablation injury (Figure 2B). The diameter and depth of the ablation lesion and the distance between the ablation site and penetrating BBs were measured. The shortest distance was defined by measuring the distance between the lesion edge and the PHB or BB. Interventricular septum thickness was measured at the level of the lesion center. The HB length was defined as the distance from its penetrating point into the central fibrous body to the beginning of the site of BB. In addition, the HB length was estimated based on histologic review of serial sections of the atrioventricular junction.

Part II: 3D Mapping and Radiofrequency Ablation in PH-AP Patients

The second part of the study included 23 consecutive patients (16 men; 19.3±12.3 years of age) with PH-AP, which was ablated in 15 at Guangdong General Hospital, in 8 patients at 2 European centers between August 2015 and June 2016 (Table 1). All patients had structurally normal hearts except for 2 patients (11-month-old girl; 12-year-old boy) with LV ejection fraction of 35% and 48%, which was suspected to be because of dyssynchronized movement during maximal preexcitation during SR. All patients were refractory to a mean of 1.9±0.7 antiarrhythmic drugs before the initial ablation procedure. The experimental protocol was approved by the Institutional Animal Care and Use Committee at Guangdong General Hospital.

Electrophysiologic Study

After giving written informed consent and withdrawal of antiarrhythmic drugs for a period ≥5 half-lives, all patients underwent ablation procedure under general anesthesia in pediatric patients and under conscious sedation with midazolam and fentanyl in adults. Three diagnostic catheters were positioned into the coronary sinus, at the HB region,
Figure 1. A, Left, fluoroscopic image of left anterior oblique and posteroanterior view showing the mapping catheter in the right ventricle (RV) below the tricuspid annulus with a reverse-C curve. Middle, High-density map at the para-Hisian region in the right ventricle during sinus rhythm. Right, His activation (marked by arrow) can be recorded in a relatively large area along the tricuspid annulus. B, Activation map of RV and pace mapping with different outputs at 3 different sites with a His-bundle (HB) potential. Middle, activation map of 3 sites with a HB potential (marked with arrow at sites 1, 2, and 4). In the left panel (pace site 1), pacing at this site produced intermittent loss of HB capture (wider QRS complex), but pacing at high output led to persistent capture of the HB (narrower QRS complex). The captured HB with lower output indicates these sites with near-field His activation and closer to the anatomic HB. Top, only wider QRS is demonstrated at pace output of 20 mA at 2 ms, indicating the HB potential recorded here was far-field His. Also, all paced QRS morphologies were different. Yellow dots are sites of His activation and white dots are sites of right bundle branch potential. CS indicates coronary sinus catheter; LAO, left anterior oblique; Map, mapping catheter; PA, posteroanterior; and RVOT, right ventricular outflow tract.
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and in the RV under fluoroscopic guidance except for the 11-month-old baby, in whom a single mapping catheter was used. Programmed stimulation was performed to induce AVRT and to measure the anterograde and retrograde-effective refractory period of the AP.

Mapping the Atrial and Ventricular Insertion of PH-AP

3D mapping of the right atrium and RV was performed using a steerable 7F or 7.5F D-curve catheter (Navistar Thermo-Cool or Navistar Catheter). In patients with manifest preexcitation on the surface ECG, the site of earliest ventricular activation via AP was initially located and identified whether there is a His potential when antegrade AP conduction blocked (Figure 3A). In patients with concealed APs, the local atrial activation was manually measured (Figure 3B). A high-density 3D map at the ventricular aspect of the tricuspid annulus near the HB region was achieved using a reversed-C curve of the ablation catheter, via an 8.5F long sheath (SL1; St. Jude).

After identifying the site of earliest activation, the same pace protocol as in dogs was used. The NF and FF His activations were identified and tagged on 3D. The paced QRS duration at the targeted and the NF His sites and the distance between the successful site and the NF His site were measured. After the HB identification, the PH-AP was classified into superior or inferior PH-APs relative to the HB.

Radiofrequency Ablation

Nonirrigated radiofrequency current was delivered in temperature-controlled mode, with a temperature limit of 55°C. In patients with superior PH-APs, radiofrequency initially started at 20 W and was gradually titrated to a maximal power of 35 W. In patients with inferior PH-APs, radiofrequency was initially started at 10 W and was gradually titrated to a maximal power of 30 W as this site, which is adjacent to the compact AV node. During radiofrequency delivery, the PR interval, the presence of junctional beats, and catheter movement were continuously monitored. The radiofrequency application was maintained for 60 seconds if the AP was blocked within the first 7 seconds. Intravenous administration of adenosine was routinely performed to evaluate the AP conduction after ablation.

ECG Analysis

Detailed analysis was performed offline using either the Bard system with a recording speed of 50 to 100 mm/s, or 12-lead ECG with a recording speed of 25 to 50 mm/s in patients with manifest preexcitation. During SR, QRS morphology in surface ECG leads I, II, aVR, and aVL were assessed, as well as the following parameters: (1) R-wave amplitude in ECG leads I, II, III, aVF, V1, and V2, and the II/III R ratio and (2) the precordial R/S transitional zone. All measurements were independently adjudicated by 3 physicians.

Postablation and Follow-Up

Surface ECGs were recorded immediately and at 1 day after the ablation procedure. Echocardiography was routinely performed to
exclude pericardial effusion and LV function after ablation. Each patient returned for evaluation in the outpatient clinics at 2 weeks, 1 month, and every 3 months thereafter.

**Statistics**

Continuous variables were reported as means±SD or medians with minimum and maximum values, and comparisons between groups
were based on the Mann–Whitney U test (nonparametric). Categorical variables were summarized as counts and percentages and compared using a Fisher exact test. Significance was defined as a P<0.05.

Results

Part I: Animal Data
Baseline AH and HV intervals were not different between group-1 and group-2 dogs (group 1: AH=65.9±17.6 ms, HV=40.3±4.3 ms; group 2: AH=65.4±19.4 ms, HV=34.6±5.5 ms). Also, QRS duration before the RV map was 70.6±10.2 ms in group 1 and 68.6±9.9 mm in group 2, respectively.

3D Mapping and Pacing in the RV
An average of 120±39 points were taken for 3D map of the RV during SR. In group 1, the minimal output captured at the NF His activation was 5 mA at 1 ms in 5 dogs and 10 mA at 1 ms in 3 dogs (Figure 1B), and the duration of the His-captured QRS morphology was 79.3±11.1 ms (61 to 96 ms) in these 8 dogs. The His amplitude at these NF His sites was 0.24 mV with an atrium/ventricle ratio of 0.06 (Table 1 in the Data Supplement).

In group 2, the targeted sites were located 6.8±1.1 mm (5.2 to 8.2 mm) superior to the NF His sites. The maximal output used to pace the FF His sites was 15 mA at 2 ms in 3 dogs and 20 mA at 2 ms in 4 dogs (Figure 1B) and always produced wide QRS duration of 122.4±14.8 ms (109 to 150 ms). The His amplitude at these sites was 0.06 mV with an atrium/ventricle ratio of 0.18 (Table 1 in the Data Supplement). The amplitudes of His and ventricular potentials were clearly larger in group 1 than those in group 2 (0.24 mV [0.09 to 0.5 mV] versus 0.06 mV [0.02 to 0.36 mV]; P=0.007; 3.12 mV [0.63 to 9.71 mV] versus 1 mV [0.25 to 2.37 mV]; P=0.037).

Irrigated Radiofrequency Ablation
In group 1, complete atrioventricular block occurred in 3 dogs (Figure 4A). Radiofrequency delivery resulted in junctional rhythm and progressive change from incomplete RBB block (RBBB) to complete RBBB in 3 dogs. After ablation, a HB potential could only be found at the opposite site below the noncoronary sinus cusp–right coronary sinus cusp junction in these 3 dogs, in whom the HV interval prolonged from 36 to 56 ms in dog 2 (Figure 4B) and did not change in the other 2 dogs. In the 2 dogs without AV block or a change of QRS morphology, the HV interval did not change. The AH interval before and after ablation was 63.6±5.7 ms (54 to 69 ms) and 63.4±7.6 ms (54 to 73 ms) in the 5 dogs without AV block.

In 4 dogs with AV block or HV prolongation, the minimal output required to capture the NF His was 5 mA at 1 ms in 3 dogs and 10 mA at 1 ms in 1 dog. However, there was no significant difference between the minimal output compared with the other 4 dogs without AV block and HV prolongation from group 1.

In group 2, there was no evidence of AVCS injury, specifically AH or HV prolongation or RBBB during radiofrequency application. Junctional rhythm was observed in only 1 of 8 dogs. The His activation could not be observed at the targeted site after ablation. However, it could still be recorded at the previous NF His site in all 7 dogs.

Follow-Up
No dog died suddenly or developed new atrioventricular block and RBBB during the follow-up period. In group 1, complete atrioventricular block or RBBB persisted after ablation in these 6 dogs.

Pathologic Findings
Pathologic examination was achieved in 7 of 8 dogs in group 1 and in 6 of 7 dogs in group 2. Detailed information of lesion formation is shown in Table 2. In group 1, the radiofrequency-induced lesions occurred in the RV below the tricuspid valve in 6 of 7 dogs; in group 2, radiofrequency lesions were seen in both atrial and ventricular muscle in 4 of 6 dogs.

In group 1, in the 3 dogs with complete AV block, complete coagulative necrosis occurred at the PHB, which extended into the compact AV node and resulted in the partial damage of the compact AV node in dog 1 (5A), and extended anteriorly into the RBB and resulted in the complete necrosis of proximal RBB in dogs 4 and 7 (Figure 5B). In 3 dogs with RBBB, PHB was shown to have undergone partial coagulative necrosis, which was continuously extended into the proximal RBB and resulted in complete damage of the RBB in dog 2 with prolonged HV interval (Figure 5C); the PHB was intact with complete coagulative necrosis of the RBB in the dogs 3 and 6 (Figure 5D). In dog 5 without a change of QRS morphology, the AVCS, including the compact the AV node, PHB, and RBB, were intact without any coagulative necrosis.

In group 2, all radiofrequency-induced lesions were located superiorly to the PHB in all 6 dogs. No coagulative necrosis was shown at the compact AV node, PHB, or proximal RBB in all dogs (Figure 5E) except in dog 13, in which coagulative necrosis close to the PHB led to partial damage of the proximal RBB (Figure 5F) but without ECG changes. Table 2 showed detailed lesion formation and relation with the HB. The lesion edge was closer to the PHB in group 1 (0 mm [0 to 0.4 mm] versus 1.45 mm [0 to 5 mm], P<0.001). No difference was found in HB length (5.7±1.32 mm versus 6.67±2.29 mm) and ablation lesion width (8.24±1.99 mm versus 6.10±0.58 mm) between the groups. However, the lesions in group 1 were markedly deeper than that in group 2 (4.07±0.60 mm versus 2.35±0.58 mm; P<0.001), which may be because of the thicker tissue at ablation sites in group 1 than in group 2.

Part II: PH-AP
Patient characteristics are shown in Table 1. Catheter ablation had previously been attempted in 8 of the 23 patients (35%). No preexcitation was documented in 3 patients. In another 2 patients, preexcitation had disappeared after previous ablation, but these 2 patients still experienced AVRT. In addition, complete RBBB was documented after previous ablation attempt in 2 patients.

Electrophysiologic Characteristics and Mapping
The electrophysiologic and mapping characteristics are shown in Table 3. Only retrograde conduction over the PH-AP was seen in 5 patients, including the 2 patients who lost their preexcitation after the initial ablation attempts. In 2 patients, AP conduction disappeared transiently after mechanical bump. Clinical AVRT with a cycle length of 322±32 ms was
Figure 4. A single ablation at the near-field (NF) His activation in 2 dogs. A. Right shows surface ECG, electrogams recording from a catheter in the right ventricle, a catheter within the coronary sinus, and a map catheter at the NF His site before ablation in dog 1. Note that a large His activation with stable atrium/ventricle ratio, surface ECG II, aVF, and an intracardiac recording from a catheter in the right ventricle with continuous recording (A through C) during radiofrequency ablation in the same dog. Note that (1) junctional rhythm immediately occurs after ablation (A), and 3:2 and 2:1 atrioventricular block (AVB) follows 7 s after ablation (B) and (2) finally complete AVB occurs at 10.8 s after ablation (C). B. The His-to-ventricular (HV) interval before and after the single ablation at the near-field His activation in dog 3. Note that (1) there is a HV interval of 36 ms and a large His activation recorded at the targeted site during sinus rhythm before ablation in the right and (2) there are right bundle branch blocks on V1 from surface ECG, prolonged HV interval of 56 ms, and a tiny His activation recorded below the noncoronary sinus cusp–right coronary sinus cusp junction after the single ablation. AV indicates atrioventricular; CS, coronary sinus; Map, mapping catheter; RF, radiofrequency; and RV, right ventricle.
Para-Hisian Ablation

reproducibly induced in all patients except in the 2 patients with mechanical bump by a diagnostic catheter and the 2 patients with LV dysfunction and without retrograde conduction.

In the 16 patients with manifest preexcitation, the earliest ventricular activation preceded the onset of the QRS complexes by 25.5±4.1 ms and demonstrated a QRS morphology in unipolar recording at the ventricular insertion in all 16 patients (Figure 3A). In 2 of these 16 patients, the His potential could not be found during programmed atrial stimulation. In 5 patients with concealed AP, mapping the earliest atrial activation was performed along the tricuspid annulus by programmed ventricular pacing with an extrasystole (Figure 3B).

In summary, there was always a discrete His potential with an amplitude of 0.08±0.05 mV at the successful ablation site in 21 patients, including 5 concealed APs and 16 manifest APs. The amplitude of His activation at the successful site was 0.09±0.06 mV and 0.06±0.01 mV in patients without and with previous ablation attempts, respectively (P=0.034). The mapping catheter with a reverse-C curve position was successfully achieved to localize the ventricular insertion of the PH-AP in 20 patients. In the 2 patients who had loss of AP conduction after mechanical bump by the diagnostic catheter, pace mapping with minimal output was performed to identify the ventricular insertion. The site with the best QRS match during pacing mapping was 4.2 and 5 mm away from the His-captured site.

Identification of HB by Pacing Techniques
Pace mapping at different outputs was performed at the region of interest to identify the NF His activation (Figure 6A and 6B) in all patients. The minimal pacing output at the site with a narrow QRS of 96.5±9.6 ms (80 to 118 ms) was 5 mA at 1 ms in 13, 10 mA at 1 ms in 7, and 10 mA at 2 ms in 3 patients, whereas the pacing output at the ventricular site of either earliest atrium or ventricle activation always demonstrated a wide QRS morphology of 122.9±9.3 ms (106 to 142 ms) and was 20 mA at 2 ms in 19 and 10 mA at 2 ms in 2 patients, in whom the pacing output at the tagged HB was 5 mA at 1 ms. The difference between the paced QRS durations at the NF His and targeted sites was 26.8±4.2 ms (22–36 ms). Also, pacing at the NF His and targeted sites demonstrated a narrow and wide QRS morphology even in 4 with RBBB and other 2 patients with AP-ERP<AVCS-ERP (Figure 6A and 6B).

Using this technique, the AP was located superior to the HB in 20 (group 3) and inferior to the HB in 3 patients (group 4). The distance between the AP ventricular insertion and the HB was 5.9±1.2 mm (4 to 8.5 mm) in group 3 and 4.4±0.7 mm (3.7 to 5.5 mm) in group 4.

Nonirrigated Radiofrequency Ablation
In patients with a superior location, the APs were successfully ablated with 1 radiofrequency ablation in 9 (Figure 7A), 2 radiofrequency ablations in 7, and 3 radiofrequency ablations in 4 patients. In patients with manifest APs, the AP was blocked within the first 4.1±1.5 seconds. In patients with concealed APs, radiofrequency ablation was initially performed during SR. VA dissociation was observed during transient RV pacing 7 seconds after ablation in all 5 patients. During radiofrequency ablation, a junctional beat was seen because of slight dislodgment of mapping catheter only in one 7-year-old man.

### Table 2. Lesion Location, Diameter, and Potential AVCS Injury

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AMS indicates anterior membranous septum; APSL, anterior part of septal leaflet; AVCS, atrioventricular conduction system; AVN, atrioventricular node; BB, bundle branches; HB, His bundle; IVS, intraventricular septum; NA, not applicable; NL, no lesion; PB, penetrating bundle of His; PMS, posterior membranous septum; PPSL, posterior part of septal leaflet; and SMS, septal membraneous septum.

*Incomplete lesion.
Figure 5. Representative histopathologic images and their schematics of different locations of ablation lesions and related injuries on atrioventricular conduction system in dog hearts 2 wk after radiofrequency delivering procedure. A, Completed necrosis of penetrating His bundle (PHB) and partial involvement of compact AVN induced by a transvalvular ablation at the posterior part of septal valve in the dog 1; B, Completed necrosis of PHB and proximal right bundle branch (RBB) induced by an ablation at the middle part of septal valve in the dog 4; C, Partial necrosis of PHB (alive left part of PHB indicated with an asterisk) and completed RBB injury induced by an ablation in the dog 2 with a site similar to the dog 4 (B); D, Completed RBB necrosis without PHB involvement by a transvalvular ablation at the anterior part of septal valve in the dog 3; E, No damage of PHB and RBB when an ablation above the inferior rim of septal membrane in the dog 9; F, Uncompleted damage of RBB (remnant-conducting fibers indicated by black arrow) without PHB involvement in a supra-valvular ablation at the anterior part of septal valve in the dog 13. All ablation lesions are indicated by white arrows in histologic images, whereas completed necrosis and partial or uncompleted damage of atrioventricular conduction tissue are labeled by red patch and red dots, respectively, in schematic pictures. All histologic images stained with Masson trichrome and the bar represented a length of 1 mm.

A indicates atrium; AV, aortic valve; AVN, atrioventricular node; BB, bundle branches or proximal part of right bundle branch; CFB, central fibrous body; CL, cycle length IAS, interatrial septum; IVS, interventricular septum; LBB, left bundle branch; MV, mitral valve; PHB, penetrating His bundle; RBB, right bundle branch; S, sectioning level of histologic image; and TV, tricuspid valve.
Table 3. Electrophysiologic Study, Mapping, and Ablation Data

<table>
<thead>
<tr>
<th>Electrophysiologic, Mapping, and Ablation Characteristics</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>AP manifest</td>
<td>18</td>
</tr>
<tr>
<td>AP antegrade ERP, ms</td>
<td>278±19 (240–320)</td>
</tr>
<tr>
<td>AP retrograde ERP, ms</td>
<td>260±31 (230–360)</td>
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<tr>
<td>Tachycardia cycle length, ms</td>
<td>322±32 (270–390)</td>
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<td>Mechanical block</td>
<td>8/23 (34.8%)</td>
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<tr>
<td>Persistent block</td>
<td>2/23 (8.7%)</td>
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<tr>
<td>Intermittent block</td>
<td>6/23 (26.1%)</td>
</tr>
<tr>
<td>Anatomic location of the AP</td>
<td></td>
</tr>
<tr>
<td>Posterosuperior to the HB</td>
<td>20/23 (87%)</td>
</tr>
<tr>
<td>Anteroinferior to the HB</td>
<td>3/23 (13%)</td>
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<td>AP-His distance, mm</td>
<td>5.7±1.2 (3.7–8.5)</td>
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<td>Preceding timing at the successful site, ms</td>
<td>25.5±4.1 (20–37)</td>
</tr>
<tr>
<td>AV ratio at the successful site</td>
<td>0.36±0.23 (0.1–1)</td>
</tr>
<tr>
<td>His amplitude at the successful site, mV</td>
<td>0.08±0.05 (0.03–0.20)</td>
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<tr>
<td>RF applications per patient, n</td>
<td>1.9±0.8 (1–3)</td>
</tr>
<tr>
<td>Patients requiring single RF application, n</td>
<td>10</td>
</tr>
<tr>
<td>Patients requiring 2 RF applications, n</td>
<td>8</td>
</tr>
<tr>
<td>Patients requiring 3 RF applications, n</td>
<td>4</td>
</tr>
<tr>
<td>Patients having junctional beats during RF, n</td>
<td>3</td>
</tr>
<tr>
<td>Procedural duration, min</td>
<td>95±39 (60–200)</td>
</tr>
<tr>
<td>Fluoroscopic time, min</td>
<td>4.8±1.4 (1.5–7)</td>
</tr>
</tbody>
</table>

AP indicates accessory pathway; AV, indicates atrium/ventricle; ERP, effective refractory period; HB, His bundle; and RF, radiofrequency.

In patients with AP inferior to the HB, the AP was successfully blocked with 1 radiofrequency application in 1. In the remaining 2 patients, the first radiofrequency ablation resulted in conduction block over the AP, then followed immediately by an accelerated junctional rhythm, which aborted further energy delivery. A second radiofrequency delivery was performed with radiofrequency energy titration from 10 to 20 W during atrial pacing at cycle length of 400 ms in a 48-year-old man (Figure 7B). No further ablation attempt was performed because of high risk in a 9-year-old boy.

None of the patients developed complete heart block or impairment of AV conduction. RBBB after successful ablation was shown in 4 patients, which was caused by prior ablation in 3 of 4 patients.

**Electrocardiographic Characteristics of PH-APs**

Before ablation procedure, 17 of 23 patients with PH-APs had persistent ventricular preexcitation, 3 of 23 had intermittent, and 3 of 23 had no ventricular preexcitation. All 20 patients with ventricular preexcitation showed a typical R wave in leads I, II, and aVF (Figure 8). In lead III, a large R wave was noted in 17 patients (100% from group 3) and an rS wave in 3 patients (100% from group 4; Figure 8). The II/III R ratio in groups 3 and 4 was 2.07±0.70 (1.03 to 3.67) and 6.23±3.12 (3.03 to 9.29). Precordial transition was always at or after V3 in group 3, in V2 in 1 and V3 in 2 patients from group 4.

Additional, different APs were found in 3 of 23 patients and successfully ablated without complications. At the end of procedure, VA dissociation was shown during intravenous administration of adenosine in the 22 patients with successful ablation. The total procedure time and fluoroscopic time was 95±39 minutes and 4.8±1.4 minutes, respectively.

**Follow-Up**

In all 23 patients, surface ECG after ablation showed RBBB in 4 patients because of previous ablation in 3 patients and catheter dislodgement producing incomplete RBBB in 1 patient with junction beat during ablation. The LV function returned to normal after ablation in both patients with LV dysfunction. All 22 patients with successful ablation were free of all antiarrhythmic drugs during a follow-up period of 11.8±1.4 months.

**Discussion**

**Main Findings**

We developed a novel ablation strategy to select the target and minimize AV conduction injury by pacing the potential ablation sites. We hypothesized that if high output pacing at a specific site fails to produce a narrower QRS complex by capturing the HB, the HB potential is deemed to be a FF His. In contrast, if low pacing output can capture the HB, it indicates NF His, and ablation there should be avoided. Our working hypothesis was first corroborated by animal studies. When this approach was applied to PH-AP patients, it produced good success without AV node injury.

**Identification of NF and FF His Activation by Pacing Techniques**

The HB passes through the central fibrous body until it reaches the lower edge of the membranous septum, where it continues into the PHB that bifurcates into the left and RBBs. Given the thin HB, the HB potential should not be recorded in a large area as frequently shown in 3D mapping (Figures 1 and 2). Poor electrode–tissue contact often artificially diminishes the amplitude of the HB potential, making it inaccurate to differentiate FF His from NF His. In our study, the anatomic HB location was easily identified in all 15 dogs and in 23 patients with PH-AP. The minimal output to capture the NF His activations was 5 mA/1 ms in 10 of 15 dogs and 10 mA/1 ms in 5 dogs, and 5 mA at 1 ms in 13, 10 mA at 1 ms in 7, and 10 mA at 2 ms in 3 patients. Several issues were different from PH: the paced QRS duration seemed narrower and (2) a larger atrial electrogram was found at the paced site, and narrow QRS was still achieved in 4 patients with complete RBBB, which support that the NF His activation was captured in our study. Furthermore, a single, irrigated radiofrequency ablation with power mode of 25 W and 60 seconds resulted in severe damage of the AVCS in 6 of 8 dogs in group 1 and no AVCS damage in all 7 group-2 dogs at a FF His site.

**Clinical–Pathologic Findings in Ablating NF and FF His Activation**

In our study, where with a single irrigated radiofrequency ablation with 25 W histologic study 2 weeks after ablation
Figure 6. Pace at the near-field His and the targeted sites on 3-dimensional (3D) map of the right ventricle in a patient with a concealed para-Hisian accessory pathway (PH-AP) and mechanically-induced right bundle branch block (A), and in a 33-y-old patient with a manifest PH-AP, in whom the AP-ERP<AVCS-ERP (B). A, Middle, 3D is shown a relative large area of a His activation (with different color tags) during sinus rhythm in the posteroanterior and left lateral view. A large His activation is shown at the targeted and captured NF His sites with a distance of 5.4 mm between both sites. Left, pacing with 5 mA at 1 ms at the site (marked blue, His amplitude of 0.14 mV) demonstrates narrower morphology of QRS duration of 100 ms (Left), whereas pacing with 10 mA at 2 ms at the targeted site (marked with red dot, His amplitude of 0.18 mV) shows wider morphology of QRS duration of 124 ms, indicating no captured His activation in the right. B, Pacing with output of 5 mA at 1 ms at the site (posterior yellow dot) shows a narrower morphology of QRS duration of 96 ms (left), whereas pacing with output of 10 mA at 2 ms at the targeted site (superior light blue dot) shows a wider morphology of QRS duration of 128 ms (right). Middle, note that the local ventricular activation (mapping catheter [Map] 1–2, Map 3–4, and Map Uni) at the targeted site is 7 ms earlier than the activation at the His-captured site (narrower QRS during pacing) relative to the Peak of QRS in lead II. The distance between the 2 sites was 5 mm. Map indicates mapping catheter; RV, right ventricle; and RVOT, right ventricular outflow tract.
Figure 7. A, Radiofrequency delivery in 1 patient with the accessory pathway (AP) superior to the His bundle (HB). ECG and a mapping catheter (Map) before ablation (left) and 30 s after ablation (right). Note that a clear His activation is recorded from the Map after ablation. Bottom, the AP is blocked within 4.3 s during the first radiofrequency (RF) application with a power of 20 W. B, Surface ECG, 3-dimensional (3D) Map, fluoroscopic image, and ablation in a 48-yr-old man with para-Hisian accessory pathway located inferior to HB. Left shows an rS wave in lead III during preexcitation. In upper right, 3D mapping shows the sites of captured His activation and right bundle branch (yellow dot) and the targeted site of earliest ventricular activation (red dot), located inferior to the HB. The distance between the targeted site and the HB is 5.5 mm. A reverse-C curve of Map is achieved to reach the targeted site. Lower right, a discrete His activation from Map is shown immediately after conduction block over the AP at RF energy of 10 W during second applications. CS indicates coronary sinus; RF, radiofrequency; RV, right ventricle; RVA, right ventricular apex; and RVOT, right ventricular outflow tract.
showed a clear coagulative necrosis with a diameter of 6 to 8 mm, which was consistent with previous animal studies. In the 7 dogs from group 1, radiofrequency-induced coagulative necrosis of the PHB resulted in total AV block in 3 dogs and HV prolongation in 1 dog. On the other contrary, no lesion in PHB in 3 dogs can be explained by (1) radiofrequency lesion depth with a limited energy of 25 W and 60 seconds might have created the lesion depth not enough to penetrate the PHB encased in the central fibrous body and (2) the range of bipolar recording and pacing may be too large, which may differ from unipolar pacing. Furthermore, the mechanism of coagulative necrosis of RBB may be complex and associated with direct thermal effect or lesion expansion, which can lead to delayed PHB–RBB damage. Additionally, the edge of the coagulative necrosis was in close proximity to the PHB even in the dog without PHB/RBB injury. This pathologic finding corroborated that ablation at the NF His site is associated with a high risk of AV block, and ablation at the FF His site superior to the HB is relatively safe with limited energy.

Anatomy of the Right-Sided PH-AP
PH-APs are usually defined as the site with earliest ventricular activation and a discrete His potential, which indicates that the AP can be anatomically located either superior or inferior to the HB. Clinically, it can be difficult to identify which His potential is a NF or FF His activation in patients with antegrade PH-AP. Using our pacing technique, the PH-AP was located superior to the HB in 20 of 23 patients and inferior to the HB in 3 of 23 patients. The ECG lead III during manifest preexcitation showed R wave in superior PH-AP in 17 of 17 patients and an rS in inferior PH-AP in 3 of 3 patients. These results were consistent with previous studies of anteroseptal and midseptal AP. Furthermore, this anatomic distance of 5.9±1.2 mm in superior PH-AP and 4.4±0.7 mm in inferior PH-AP provides important information for catheter ablation and energy settings.

Mapping and Ablation of PH-AP
Previous studies have demonstrated that PH-APs could be interrupted, without any impairment to AVCS, via the superior approach at the ventricular aspect of the tricuspid annulus or using titrated radiofrequency energy. Successful ablation of these APs using radiofrequency energy is associated with a risk of 2% to 10% of permanent AV block in reported large series. Therefore, cryoenergy was suggested as an alternative energy in ablating PH-AP, especially in pediatric patients. However, the high rate of recurrence is a limitation in clinical practice. In our study, 18 of 20 patients with PH-AP superior to the HB, mapping with the ablation catheter in reverse-C curve was stably achieved in 18 patients. The APs were
rapidly blocked with power of 20 W at the beginning and was achieved after single radiofrequency application in 9 patients, 2 radiofrequency applications in 7 patients, and 3 radiofrequency applications in 4 patients. The number of radiofrequency applications was much less than that of previous publications. Importantly, only 1 junctional beat occurred without any change in PR interval in a 7-year-old man. In contrast, in 3 patients with a PH-AP inferior to the HB, accelerated junctional rhythm was observed in 2 patients even with up traction of radiofrequency energy from 10 to 20 W. This rapid junctional rhythm resulted in the subsequent performance of radiofrequency delivery during fast pacing in 1 and ablation interruption because of high risk of AVCS block in the 9-year-old boy. This important information strongly indicates that anatomic differentiation of the PH-AP superior and inferior to the HB is crucial for choosing ablation strategy to minimize potential injury of the AVCS. Furthermore, our study is unique in that RBBB occurred only in 1 patient because of catheter dislodgement during ablation, which was much less than in the previous publications. The low incidence of RBBB can be explained by the use of a reverse-C curve of the ablation catheter to achieve a more stable position in the majority of patients and pacing method to avoid inadvertent ablation of NF His and RBB. In addition, the antegrade conduction over the PH-AP can dyssynchronize LV contraction and result in LV deterioration in 2 of 23 patients. The LV function normalized in both patients after ablation. Early ablation should be performed in these patients because of low risk of AV block using the pacing technique we proposed.

Limitations
There were several limitations in our study: (1) invasive recording of AH and HV intervals were not measured before sacrifice, (2) Anatomic location of these PH-APs was only based on the ventricular insertion on 3D mapping, it was unknown about the atrial insertion of these PH-Aps, and (3) in the present study, bipolar pace with 2-mm interelectrode distance was only performed. Theoretically, unipolar pacing is more precise than bipolar pacing. Therefore, it needs further investigation whether identification of HB will be facilitated using unipolar pacing.

Conclusions
The NF His activation in the RV can be identified using our pacing techniques. A single radiofrequency application with limited energy at the NF His site in the RV can result in a high risk of AV block, which was consistent with coagulative necrosis of the PHB or RBB on pathologic examination. By avoiding the NF His sites and targeting the FF His sites, successful ablation without AV node injury can be achieved. This method may improve outcomes for ablation of APs that are in close proximity to the HB.

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Disclosures
None.

References
Experimental, Pathologic, and Clinical Findings of Radiofrequency Catheter Ablation of Para-Hisian Region From the Right Ventricle in Dogs and Humans


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SUPPLEMENTAL MATERIAL
**Table 1 Local electrograms at the targeted sites and ablation data**

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<th>Dog</th>
<th>Atrial (mV)</th>
<th>Ventricular (mV)</th>
<th>A/V ratio</th>
<th>His (mV)</th>
<th>Junctional rhythm</th>
<th>AV block</th>
<th>RBBB</th>
<th>HV prolongation</th>
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<tr>
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LEG: local electrograms; mV = microvoltage; HBBB = right bundle branch block;