- 1 **Running title**: Purkinje arrhythmia origin "made easy"
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1 Tachycardia originating from the fascicles or His-Purkinje system includes a wide 2 spectrum of arrhythmias such as ventricular fibrillation (VF) and ventricular tachycardia (VT) 3 which could be monomorphic or polymorphic with various substrates, locations and 4 mechanisms.<sup>1</sup> The most common type of reentrant fascicular tachycardia is left posterior 5 fascicular VT (LPF-VT) which was recognized as an electrocardiographic entity by Zipes et al.<sup>2</sup> 6 who defined its diagnostic triad as following: (1) induction with atrial pacing, (2) right bundle 7 branch block (RBBB) and a left-axis configuration, and (3) manifestation in patients without 8 structural heart disease. In 1981, Belhassen et al.<sup>3</sup> reported verapamil sensitivity, as a fourth 9 identifying feature of this tachycardia.

10 To ablate LPF-VT, there are two different successful sites defined by two different strategies (Figure 1). The first strategy was reported by Nakagawa et al.<sup>4</sup> who targeted the 11 12 earliest presystolic Purkinje potentials that can be recorded at the apical-inferior septum of 13 the left ventricle during VT. The second strategy was reported by Tsuchiya et al.<sup>5</sup> who 14 emphasized the significance of a late diastolic potential at the basal septal region close to 15 the main trunk of the left bundle branch (LBB). To delineate the reentry circuit, we 16 performed left ventricular septal mapping using an octapolar electrode catheter in 20 17 patients with LPF-VT.<sup>6</sup> In 15 of 20 patients, 2 distinct sequences of potentials other than LV 18 muscular potential were recorded during VT (Figure 1). We named these potentials P1, a 19 mid-diastolic potential recorded earlier from proximal rather than distal electrodes, and P2, 20 the fused presystolic Purkinje potential recorded earlier from distal electrodes. Because the 21 diastolic potential (P1) has been proven to be a critical potential in the VT circuit, this 22 potential can be targeted to cure the tachycardia. Any P1 in the VT circuit can be targeted 23 for catheter ablation. We usually target the apical third of the septum, to avoid the creation 24 of left bundle branch block (LBBB) or atrioventricular block.

1 In the current issue of Circulation: Arrhythmia and Electrophysiology, Ma and 2 coworkers<sup>7</sup> interestingly describe the relationship between 12-lead ECG morphology and 3 the location of the exit of LPF-VT in addition to the H-V interval during tachycardia. They 4 retrospectively analyzed the electrocardiographic and electrophysiological characteristics of 5 41 patients who underwent successful catheter ablation of LPF-VT. Patients were divided 6 into 3 subgroups: proximal, mid, and distal left posterior fascicular groups according to the 7 12-lead ECG morphology, QRS duration and H-V interval during VT. Quick prediction of 8 tachycardia exit and successful ablation sites in LPF-VT is practically useful to guide the 9 direction of further mapping. However, the study results would be practical and made easy 10 when Purkinje fibers are constructed in homogenous 2-D orientation with equal conduction 11 velocity in all parts of the heart. In animal models, conduction velocity of the His-Purkinje 12 system is heterogenous at various parts of the heart and local changes in bundle branch 13 architecture is the most likely cause of significant conduction velocity reduction in the 14 midseptum in addition to presence of regional differences in expression pattern and distribution of gap junction proteins.<sup>8</sup> Furthermore, there is intense branching of bundle 15 16 branch fibers in the midseptum resulting in load mismatch or increased path length. In 17 canine hearts, conduction velocity is faster in proximal bundle branch areas versus that in 18 the distal network areas and these variations in delay and conduction velocity may serve as 19 the physiologic substrate for fascicular VT.<sup>9</sup>

This complexity of both functional and anatomical aspects of His-Purkinje system results in complex tachycardia circuits and difficulties in predicting its exact origin. The investigators used the H-V interval during LPF-VT as a guide to identify LPF-VT origin (proximal, mid and distal LPF origin).<sup>7</sup> Theoretically, the upper turn around point of LPF-VT is undetermined while long H-V interval during LPF-VT may indicate the lower turn around

point is located basally, conversely; short the H-V interval during LPF-VT indicates that the
 lower turn-around point is more apical far from His bundle.

3 It is important to consider that, the relative duration of the H-V interval recorded 4 during VT as compared to sinus rhythm would depend on 2 factors: (a) the balance between 5 antegrade and retrograde conduction times from the upper turnaround point of the reentry 6 circuit; and (b) the site of His bundle recording relative to the upper turnaround point.<sup>10</sup> 7 Conduction delay in the antegrade limb of the circuit would tend to prolong H-V interval 8 during VT, while retrograde conduction delay to the His bundle recording site as well as the 9 use of relatively proximal His bundle recording site (far from the turnaround point) would 10 tend to shorten it. These facts represent a major study limitation. Another important 11 consideration is due to the fact that there may be arborization of Purkinje fibers beyond the 12 region of reentry, there may be several early myocardial sites with relatively late sites in 13 between. In conclusion, the study conducted by Ma et al. provides excellent pre-operative information to guide mapping and ablation of LPF-VT, however; potential limitations of H-V 14 15 interval value during tachycardia and surface ECG morphology should be taken into 16 consideration when predicting the origin of LPF-VT.

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### 1 Figure legends

2 **Figure 1.** 

3 Schematic representation of our hypothetical circuit of reentrant LPF-VT. During VT, 4 diastolic potential (P1) is propagated antegradely. In the distal third of the septum, the 5 antegrade wavefront penetrates the posterior fascicle of the left bundle branch system at 6 the so-called *lower turn around point*. This creates diverging wavefronts traveling to the 7 myocardial exit site as well as activating the posterior fascicle in a retrograde fashion, 8 represented by presystolic potential (P2), until the wavefront reaches the basal septum and 9 exits the fascicle close to the main left bundle then the His bundle. Then propagation 10 wavefront re-enters the zone of slow conduction via so called upper turn around point. The 11 dotted lines indicate the speculated upper turnaround and its connection to the His-Purkinje 12 system. Successful ablation can be achieved by targeting the earliest P2 or any P1 in the 13 circuit, preferably in the apical third of the septum to avoid the creation of left bundle 14 branch block (LBBB) or atrioventricular block. 15

