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ScienceDirect

Journal of Electrocardiology 49 (2016) 644 – 648

JOURNAL OF Electrocardiology

www.jecgonline.com

Review

# Physiological mechanisms of QRS narrowing in bundle branch block patients undergoing permanent His bundle pacing☆

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**Abstract** His bundle pacing is increasingly used to avoid chronic right ventricular pacing, and electrically resynchronize ventricular activation by narrowing or normalizing the QRS interval in left and right bundle branch block. The mechanisms by which this occurs remain poorly understood. In this review, the proposed mechanisms and evidence supporting them are discussed. Also discussed are aspects of mechanisms that are not completely supported by the evidence. We also review the differences and physiological bases for direct vs. indirect His bundle capture, and the physiological mechanisms for QRS narrowing vs. normalization following His bundle pacing.


*Keywords:* His bundle; His bundle pacing; left bundle branch block; cardiac resynchronization

## Introduction

It is recognized that chronic right ventricular pacing (RVP) has deleterious effects on cardiac function, including decreased global left ventricular (LV) function and worsening functional status [1,2]. This is a result of abnormal myocardial activation due to slow muscle-to-muscle conduction, compared to the rapid conduction of the His–Purkinje system (HPS) [3]. Similarly, left bundle branch block (LBBB) results in dyssynchronous contraction, with delayed electrical activation of the lateral wall of the left ventricle relative to the interventricular septum.

Cardiac resynchronization therapy (CRT) addresses the dyssynchronous activation created by RVP as well as LBBB, with earlier activation of the LV by a lead placed via the coronary venous system. CRT has been shown to improve mortality and non-fatal heart failure events [4–6]. His bundle pacing (HBP) has emerged as a means of restoring normal myocardial activation through the native conduction system in those with proximal HPS disease. Early studies have supported HBP as non-inferior to traditional CRT, and better than RVP when it comes to clinical outcomes [7,8].

Although the idea of utilizing the native conduction system and its clinical benefits are intuitive, the mechanisms behind HBP are still not well understood. Traditionally, the success of HBP has been posited on the theory of longitudinal dissociation, that fibers within the His Bundle (HB) are pre-destined for their respective bundles. Therefore a block that occurred within the HB could be bypassed by pacing distal to the block but proximal to the bifurcation of the bundles [9]. However, more recent studies have shown success in patients that may not be expected to have a block within the proximal HB, suggesting that there may be alternative, and likely complementary mechanisms underlying HBP [10].

Further details of the history, technique, criteria, and benefits of HBP are described elsewhere in this symposium on HBP. In this section, we will focus on the potential mechanisms underlying QRS narrowing with HBP, including the classic understanding of longitudinal dissociation and possible alternative mechanisms, including penetration of the proximal HPS, output dependence, and virtual electrode polarization effect. Furthermore, we describe how these mechanisms may translate to non-selective versus selective HBP and result in narrowing versus normalization of the QRS interval.

## Longitudinal dissociation

Longitudinal dissociation is the theory that bundle branch block may originate within the proximal HB when block occurs in the fibers predestined for the left or right bundle branches (Fig. 1). This concept dates back to the early 1900s when Kaufman and Rothberger, and later Condorelli (1930s), and Sciacca & Sangiorgi (1950s) demonstrated that traumatic HB lesions could result in bundle branch block patterns [11,12]. Further evaluation of the anatomy and electrophysiological properties of the HPS as evaluated in

☆ Disclosures: None.

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http://dx.doi.org/10.1016/j.jelectrocard.2016.07.013
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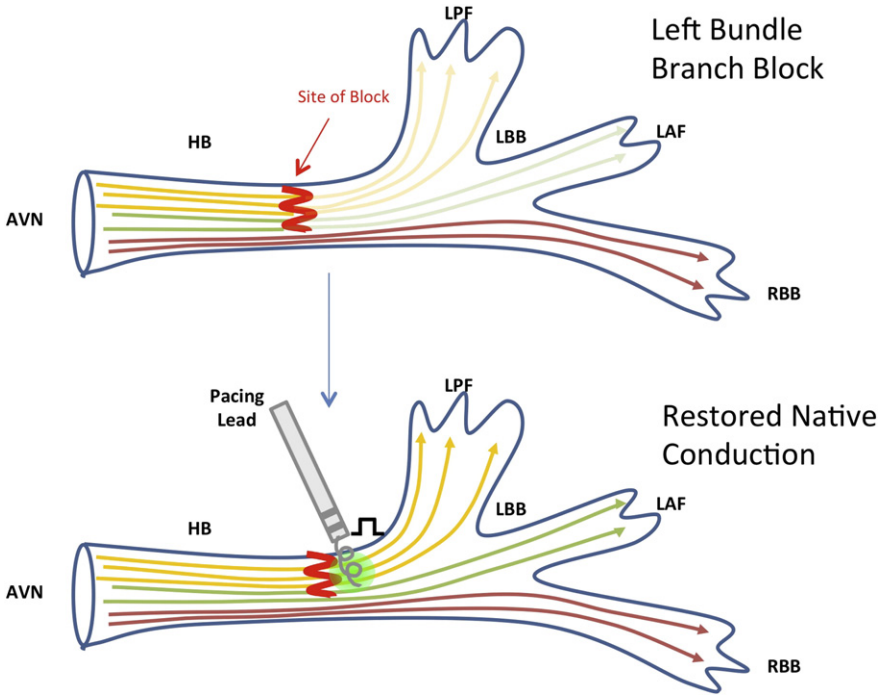


Fig. 1. Restoration of normal conduction in left bundle branch block due to longitudinal dissociation. Simplified construct of fibers coursing through the AVN surrounded by parallel sheaths that extend into the bundle branches, making each fiber "pre-destined." Pacing beyond the level of the block restores conduction through the His–Purkinje system [25].

human and canine hearts in the 1970s by James and Sherf identified fibers separated by collagen sheaths longitudinally directly into the bundle branches [13]. Based on this, El-Sherif et al. suggested that block could occur more proximally, within the HB, but still manifest as a bundle branch block pattern. This theory was demonstrated in canine experiments, where conduction delay within the HB identified by split HB potential was associated with the appearance of a bundle branch block pattern following anterior septal artery ligation [14].

This theory was supported by Narula, who demonstrated that advancing a catheter more distally within the HB could restore the native QRS, suggesting a block within the HB could be bypassed [9]. Barba-Pichardo et al. explored the feasibility of permanent HBP and concluded that the success of HBP in normalizing the QRS was determined by how proximal the block was, making the block bypassable [15]. As depicted in Fig. 1, pacing from a catheter distal to this site of block restores normal conduction via the HPS.

Although it is likely that location of the block and the ability to bypass it play a role in the mechanism behind HBP, Teng et al. recently studied the relationship between QRS axis and QRS narrowing with HBP. It was hypothesized that a left axis deviation in the setting of strictly defined complete LBBB signifies escape of left posterior fascicular fibers prior to the level of the block, therefore representing a more distal block that would not be bypassed. However, there was no correlation between absolute QRS narrowing and QRS axis using this paradigm. Further, 83% of the 29 patients studied exhibited narrowing [10]. Similar success rates have been found in other recent studies [7,8]. While it is possible that a high percentage of LBBBs may be within the proximal HB, or that HB lead placement is actually extending beyond the HB and has the ability to capture and bypass more distal blocks than traditionally considered, it is more likely that there are complementary mechanisms at play. Lazzara et al. studied the effects of incisions within the HB followed by intracellular stimulation. Restoration of native conduction via intracellular stimulation suggested that transverse connections exist and allow for signal to travel across fibers, challenging the theory of longitudinal dissociation. However, the authors concluded that perhaps these concepts could be reconciled by recognizing that under certain circumstances transverse interconnections do not function [16]. Still the question remains that if transverse connections do coexist with longitudinal tracts, then it should follow that native conduction would be able to circumnavigate around a block, negating the need for an external pacing stimulus. These questions highlight the limitations of these theories and suggest that additional mechanisms must exist.

## Output dependence

It has been observed that slight increases in stimulus strength during distal HBP can result in normalization of bundle branch block. While the focus remained on the theory of longitudinal dissociation and the need for high pacing outputs to penetrate the HB sheath or to overcome a physical structural block (for example scar), it is possible that applying increasing stimulus strength could recruit fibers closely bordering the abnormal myocardium causing functional block, and mimic native conduction through the HPS [9].

Thus perhaps, HBP pacing relies not only on bypassing a structural block, but may also depend on overcoming a block in local propagation by applying a high effective output to a region of the block. In general, HBP requires higher pacing