REVIEW ARTICLES

Direct His Bundle and Parahisian Cardiac Pacing

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The success rate of direct His bundle pacing (DHBP) and parahisian pacing has improved remarkably in the last 3–5 years with the advent of dedicated fixation systems that have reduced procedural duration, dislodgement rate, and fluoroscopy time. The methodology of DBHP remains still more complex than parahisian pacing and is associated with high-pacing thresholds. Thus, DHBP entails greater battery current drain and reduced device longevity. A shift toward parahisian pacing (which is fusion pacing of myocardium and His bundle) has occurred because its implementation is easier and the electrical parameters are superior to those of DBHP. Currently, an additional safety lead is inserted at the RV apex or outflow tract to prevent asystole, especially in patients with pure DHBP. It is often possible to avoid a safety lead with parahisian pacing because ventricular pacing is virtually assured on a long-term basis via myocardial capture. DBHP and parahisian pacing can be achieved in a substantial proportion of patients with varying grades of narrow QRS AV block or after AV junctional ablation and in some patients with the ECG manifestation of bundle branch block caused by an intraHisian lesion. Preliminary observations suggest that DHBP may be useful in some patients requiring cardiac resynchronization if it produces a narrow QRS complex because the site of an intraHisian lesion responsible for left bundle branch block is above the site of DHBP.

Ann Noninvasive Electrocardiol 2012;17(2):70–78

cardiac pacing; His bundle pacing; parahisian pacing; cardiac resynchronization

Over the last 10 years the site of antibradycardia ventricular pacing has gradually moved away from the right ventricular (RV) apex to the RV outflow tract and septum on the belief that closer proximity to the His-Purkinje system may prevent or minimize the long-term detrimental consequences of RV pacing. These consist of mechanical left ventricular (LV) dyssynchrony secondary to electrical dyssynchrony and myocardial perfusion disorders associated with RV apical pacing. Both direct His bundle pacing and parahisian pacing that preserve a near-to-normal electrical activation of the left ventricle (LV) have gained prominence in the last 5–7 years. These pacing techniques represent the last step of the progressive shift of the preferred pacing to sites closer to the conduction system involving the His bundle and its surroundings. Surprisingly, as an added benefit, direct His bundle pacing was even found to correct a number of conduction disturbances previously considered to be infraHisian.

Direct His bundle pacing (DHBP) was first described in 1967 by Scherlag et al.¹ who used plunge electrodes in the intact dog heart. The following year, Scherlag et al.² demonstrated direct His bundle pacing in the dog by an endocardial approach. In 1970, Narula et al.³ showed how to perform temporary His bundle pacing in man using the endocardial technique for His bundle recordings. The first report of permanent DHBP was published in 2000 by Deshmukh et al.⁴ who documented that the procedure was feasible, fairly reliable, and effective in many patients. In 2004, the same authors expanded their experience to 54 patients suffering from dilated cardiomyopathy, poor LV ejection fraction of $23 \pm 11\%$, persistent atrial fibrillation, and QRS < 120 ms.⁵ Permanent DHBP was achieved in 36/54 patients (66%). Follow-up showed improvement in LV function. Deshmukh et al.^{4,5} established many of the current criteria used to assess successful DHBP: (1) His-Purkinje-mediated cardiac activation and repolarization, as

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evidenced by ECG concordance of QRS and T-wave complexes. Paced QRS morphology and duration equal to the intrinsic QRS in the 12-lead ECG; (2) the pace-ventricular interval being almost identical to the His-ventricular interval, and (3) His bundle capture in an all-or-none fashion, as demonstrated by the absence of QRS widening at a lower pacing output.

In complete AV block with a narrow QRS complex caused by a central His bundle block, pure DHBP can control the heart rate on a 1:1 basis and induce a QRS complex with a morphology and repolarization identical to the native ECG.^{4,5} This can only occur if stimulation captures the His bundle at a site distal to the blocked region where it can initiate an impulse that is conducted along the His-Purkinje axis. During "pure" His bundle capture, the latency interval (from the stimulus to the onset of the QRS complex) represents the conduction time from capture of the His bundle region to the beginning of ventricular depolarization. The latency interval is basically equal to the HV interval. If the native ECG shows right bundle branch block or left bundle branch block (LBBB), these patterns will be preserved with successful DHBP if the bundle branch blocks are peripheral and not central or intraHisian. Pacing near but not directly over the His bundle as occurs in paraHisian capture induces capture of both the His bundle and the adjacent myocardium creating two activation fronts with fusion: one contribution from the natural conduction system and the other via right antero-septal myocardium.⁶ In this setting, pacing does not normalize the QRS complex but produces fusion QRS complexes with a LBBB configuration without latency.⁶⁻⁸ Pure and fused captures can often be observed in the same ECG, depending on output voltage and lead contact with the His bundle area. Many workers now believe that fused captures (as in paraHisian pacing) can be accepted as a satisfactory outcome of His bundle pacing because "fused" capture depolarizes the LV via the Purkinje system promoting synchronous activation of the ventricles and avoiding potentially harmful LV dyssynchrony.⁷

Longitudinal His Bundle Dissociation

In the case of bundle branch block (BBB) with a wide QRS complex, DHBP may correct BBB and produce a normal QRS complex. This response is explained by the concept of longitudinal dissociation

of the His bundle.⁹⁻¹⁴ Studies in dogs suggest that certain fibers of the His bundle are organized longitudinally and predestined to activate only one fascicle or bundle branch. The fibers destined for the left and right bundle branches are histologically differentiated and isolated in the His bundle trunk. Injury or disease to the His bundle trunk may damage these fibers, resulting in asynchronous His bundle activation and an ECG of bundle branch block, fascicular block or complete AV block. That this sequence of QRS normalization can occur in humans is supported by the observations that LBBB or left anterior fascicular block can occasionally be normalized during His bundle stimulation of predestined areas distal to a site of central block. Thus, complete BBB conventionally considered to be "infraHisian" may now be classified according to the site as either central (His bundle) or peripheral (branches or Purkinje system), depending on whether or not the BBB disappears with DHBP. Pacing close but not directly over the His bundle may cause a fusion complex.^{6,7} Fusion occurs from capture of both the His bundle and the adjacent myocardium (right ventricular preexcitation). Pacing at the same site yields preexcitation of the RV via myocardial capture and engenders a paced fused QRS complex with an LBBB pattern and no latency. Therefore, normalization of either RBBB or LBBB ECG cannot occur. Thus, starting with RBBB, fusion pacing near the His bundle site produces an LBBB pattern with loss of RBBB regardless of its original central or peripheral site. Starting with LBBB, pacing at the same site as above will induce fusion between the His-bundle axis and myocardial capture. The paced ECG assumes a LBBB pattern but the LV activation occurs mostly via the His-Purkinje axis.

Criteria for His Bundle Pacing

In 2006, Cantù et al.⁶ described the criteria for selective His pacing (SHBP) as follows: SHBP was defined according to the following criteria: (1) His-Purkinje-mediated cardiac activation and repolarization, as evidenced by ECG concordance of QRS and T-wave complexes; (2) The paced ventricular interval (Vp-V) is almost identical to the His-ventricular interval (H-V); (3) Output criteria: at low-pacing output, the HB is captured, while on increasing the output both the HB and ventricular fibers are captured thereby widening the QRS at high output). ParaHisian pacing (PHP) was defined

according to the following criteria: (1) Pacing output criteria: On increasing the output step by step, at a low output only myocardial fibers are captured, resulting in a wide QRS (i.e., interventricular septal stimulation), while at high output both myocardial fibers and the HB are captured causing a shortening of the QRS (shortening of QRS at high output). (2) The interval from the pacing stimulus to the onset of ventricular activation (pace-ventricular interval) is significantly shorter than the His-ventricular interval, with value close to zero. A large QRS complex at each output level is considered to represent antero-septal ventricular capture stimulation that captured only myocardial fibers without a contribution from His bundle activation.

We tried to simplify the definitions from a functional and morphologic point of view. Based on our experience we propose the following criteria :

A. Pure HIS Pacing:

- (1) Isoelectric interval between pacemaker spike and QRS complex (corresponding to the HV interval)
- (2) QRS identical to native one
- (3) Pacing output maneuver useful but not mandatory. In our experience with testing at the maximum output of 10 V at 1.5 ms pure His pacing widens the QRS at high output in about two-thirds of cases while in one-third the QRS does not change at maximum output

B. Pure paraHisian Pacing

- (1) Isoelectric interval between spike and QRS is never observed
- (2) Maximal output: Narrowing of QRS proving the existence of fusion

C. Pseudo (or false) paraHisian Pacing (position close to the His bundle where permanent pacing is not recommended) Rx position very close to His area

- (1) A small His potential may be recorded
- (2) Maximum output maneuver produces a wide QRS complex with LBBB morphology and normal (right inferior) frontal plane axis. No narrowing of QRS with any pacing output

In summary, four different ECGs patterns may be derived from the above criteria

Figure 1. ECG showing the first two beats are pure His bundle pacing, the third is an atrial extrasystole with a normal QRS and the following two beats are normal intrinsic beats.

- (1) Narrow QRS (pure His)(Fig 1).
- (2) Slight enlargement of QRS (pure His with pre-excitation of right ventricle) (Fig 2).
- (3) Slight enlargement of QRS (paraHisian with fusion between His bundle and myocardial activation) (Fig 3).
- (4) Wide QRS LBBB morphology with frontal plane axis in the same quadrant as the normal QRS complex (paraHisian with loss of His capture or pseudo-paraHisian at all pacing outputs) (Fig 4).

ParaHISIAN PACING

Laske et al.¹⁵ demonstrated that paraHisian pacing could achieve physiologic left ventricular activation closely resembling that originating from conducted sinus rhythm. They assessed LV activation in isolated pig hearts during pacing from various zones of the interventricular septum. Even during pacing from the paraHisian region, the activation originated from the high septum and was

Figure 2. ECG showing His bundle activation with two morphologies of the QRS complex. The first QRS complex originates from an intrinsic beat. The following six beats are fusion beats between His bundle activation and slight myocardial preexcitation. The last eight beats show pure His bundle pacing.

essentially the same as the intrinsic activation. Laske et al.¹⁵ also found good pacing and sensing performance at the paraHisian site and concluded that stimulation of the tissue below the point at which the HB penetrates the central fibrous body could provide optimal LV activation.

Occhetta et al.^{7,16} from Italy pioneered paraHisian pacing and reported their large experience with 135 patients who underwent permanent RV pacing in the Hisian/para-Hisian region (85 males, 50 females; 74 ± 8 years aged) from the year 2000 to 2009. In 92 patients a conventional screw-in lead was used, and in 43 patients the screw-in lead was a special 4 French lead (Select Secure 3830, Medtronic Inc. Minneapolis, MN, USA).

Occhetta et al.^{7,16} advanced the correct criteria for the performance of paraHisian pacing as follows: (1) the distal pole of the catheter (screw-in)

must be positioned as much as possible next to the mapping dipole of the electrophysiological catheter of reference (within 1 cm in the right and left oblique projections), (2) the duration of the paced QRS can be larger than the spontaneous QRS, but the duration must be at least 50 ms shorter than the QRS obtained with RV apical pacing and, in any case, not more than 120–130 ms, (3) the electrical axis of the paced QRS must be concordant with the electrical axis of the spontaneous QRS (discrepancy $20\text{--}30^\circ$), (4) the interval between the spike and start of the paced QRS is less than the HV interval of the original rhythm, and (5) the pacing threshold must be less than 1 V because the muscular portion of the interventricular septum provides a far better stimulation site in terms of the pacing threshold than DHBP with relatively higher values. The reason is anatomical because the His bundle

Figure 3. ECG showing paraHisian pacing. The first QRS complex originates from an intrinsic beat. The following 10 beats show a wide QRS complex entirely due to myocardial activation. The narrower beats on the right represent fusion between septal myocardial activation and His bundle activation.

penetrates deep in the membranous septum where the pacing thresholds are much higher than those of direct RV pacing. Partial preexcitation of the superior portion of the interventricular septum leads to a fusion beat from simultaneous activation of the two ventricles. In this respect, we believe that the criteria used by Occhetta et al.^{7,16} are valid but somewhat imprecise and may create confusion because the His bundle ECG pattern does not specify whether there is fusion or not.

In the series of Occhetta et al.¹⁷ the pacing threshold was always < 1 V for paraHisian pacing (performed in 115/135 patients: 85%). The mean follow-up was 27 months. At that time, the QRS duration was the same as that recorded at pacemaker implantation, the pacing threshold did not exhibit any significant variations and remained within acceptable safety margins. In a previous report of 54 patients with paraHisian pacing Occhetta et al.¹⁶ found that a stable lead position could not be achieved at implantation in three patients (two of these patients had a mechanical valvular prosthesis

that probably altered the AV junction). This represents about 5% of the paraHisian group of patients. This failure rate may reflect old lead technology used in the early part of the group's experience. The average duration of the basal QRS in these 54 patients was 97.9 ± 12.4 ms, and the induced QRS by paraHisian pacing was 123.9 ± 10.6 ms.

Direct His bundle versus ParaHisian Pacing. The Italian Experience

The Italian School dominates the field of DHBP and paraHisian pacing. In 2006 Zanon et al.¹⁸ reported a study showing how DHBP could be obtained in a reliable way by using a new system consisting of a steerable catheter and a new 4.1 F screw in lead (Select Secure 3830, Medtronic Inc.,) applied at the pacing site through a steerable introducer (Select Site, Medtronic Inc.,). Stable DHBP was obtained in 24 of 26 patients (92%). The mean time for lead positioning was 19 ± 17 minutes, and the mean fluoroscopy time

Figure 4. ECG showing pseudopacing of the His bundle. The first two beats originate from intrinsic activation. The following beats show a left bundle branch morphology with a wide QRS complex and a right inferior frontal plane axis.

was 11 ± 8 minutes (2 to 60 minutes). The acute pacing threshold was 2.3 ± 1 V (0.5 ms) and the endocardial detected potential was 2.9 ± 2 mV. At a 3-month follow-up examination, the same QRS duration and morphology as recorded at implantation were observed in all patients. The pacing threshold was 2.8 ± 1.4 V, and sensed potentials were 2.5 ± 1.8 mV; the sensing configuration was changed from bipolar to unipolar in six patients to resolve issues with ventricular undersensing. No major complications were observed.

Zanon et al.⁸ recently reported the outcome of 574 patients in whom selective site pacing was performed. There were only four implantation failures at unspecified sites. There were 307 patients who underwent pacing in the His bundle area with a follow-up of 20 ± 10 months. The Medtronic Select Secure system was used in all the patients. There

were 87 patients who underwent DHBP and 220 patients underwent parahisian pacing. Assuming that the four implantation failures in the large study involved only the DHBP group, the worst case scenario would yield an implantation failure rate of 4.5% which is remarkably less than the 30–40% implantation failure reported in the literature. The mean fluoroscopic times in the two groups were comparable. A backup RV apical lead was used in 126 patients (41%). The electrical parameters remained stable in both groups during follow-up. Full data in the DHBP group were available in 63 patients. The implantation pacing threshold was 2.5 ± 2.3 V (0.5 ms) and 3.2 ± 2.9 V (0.5 ms) at 24 months while the R wave was 3.4 ± 1.0 mV at implantation and 5.8 ± 3.0 mV at 24 months. Full data in the parahisian group were available in 150 patients. At implantation the pacing threshold was

1.3 ± 1.1 V (0.5 ms), and 1.6 ± 1.5 V (0.5 ms) at 24 months while the R wave at implantation was 11.3 ± 5.2 mV and 11.1 ± 5.8 mV at 24 months. Twelve events occurred in the entire group. The DHBP group developed five events (5.7%) all due to a high-pacing threshold (>5 V). The lead was replaced in two patients and the other three were corrected by reprogramming to a higher output culminating in rapid premature battery depletion in one of these patient. There were seven events in the paraHisian pacing group. Two events were related to lead dislodgment and five were due high-threshold problems. The threshold problems were resolved in two cases by programming but the other three were switched to RV-apical pacing.

HEMODYNAMICS

Catanzariti et al.¹⁹ evaluated acute hemodynamic data in 17 patients with DBHP and six with paraHisian pacing and compared the findings with right ventricular apical pacing. DHBP and paraHisian pacing showed a reduction of indices of LV dyssynchrony and mitral regurgitation together with improved LV function. In the above study, there was no statistical difference of the findings when DHBP was compared with paraHisian pacing. Kronborg et al.²⁰ also studied 11 patients with high-grade AV block and a narrow QRS and documented that paraHisian pacing was associated with a statistically significant less LV dyssynchrony compared to RV septal pacing. In a study involving three months of DHBP followed by three months of RV apical pacing, Zanon et al.²¹ found DHBP superior to RV apical pacing in preserving the physiologic distribution of myocardial blood flow and reducing mitral regurgitation and attenuating LV dyssynchrony.

Cardiac Resynchronization

DHBP was implemented temporarily in 10 patients at the time of implantation of a permanent CRT system.²² Native conduction, DHBP, and biventricular (BIV) QRS duration were compared. In 7 of 10 patients, DHBP narrowed the QRS significantly compared with native conduction and BIV (mean QRS duration: native 171 ± 13 ms, DHBP 148 ± 11 ms, BIV 158 ± 21 , $P < 0.0001$). Twenty-one QRS narrowing with DHBP was specifically attributable to capture of latent His-Purkinje tis-

sue. DHBP lead implantation time (16 minutes) was shorter than standard LV lead implantation time (42 minutes). The authors concluded on the basis of their acute study that in some patients, DHBP might offer a physiologic alternative to BIV for cardiac resynchronization therapy.

Barba-Pichardo et al.²³ attempted to implant a DHBP system in 91 patients with a success rate of 65%. This series included four patients in whom cardiac resynchronization therapy (CRT) could not be achieved by conventional techniques because of inability to cannulate the coronary sinus. No further details about the CRT patients were reported. Dabrowski et al.²⁴ reported long-term DHBP in a patient with congestive heart failure and LBBB who was referred for cardiac resynchronization therapy. Instead of implanting an LV lead in the coronary venous system, DHBP was achieved with a narrow QRS complex. During 27 months of observation, the patient improved dramatically from NYHA class IV to I. Echo parameters improved significantly the LV diameter from 75/50 to 60/40 mm, LV ejection fraction increased from 28 to 50%, and mitral regurgitation was reduced from ++++ to ++. Manovel et al.²⁵ reported a similar case involving a 62-year-old man with a dilated cardiomyopathy and NYHA class III heart failure (LV ejection fraction 30%) and complete LBBB (150 ms). DHBP was performed and the LBBB disappeared. At the 3-month follow-up, the LV ejection fraction was 57%, BNP was normal and the NHHA class was I–II. Reehwinkel et al.²⁶ also reported DHBP-induced resynchronization in a young woman with congenital complete AV block and severe RV induced cardiomyopathy. Follow-up at 9 months showed normalization of the LV ejection fraction and elimination of symptoms.

OVERVIEW

The success rate of DBHP had been substantially less than 100% (as low as 65%)^{3,4,23,27,28} until recently when the Italian School reported a much greater success rate.⁸ DHBP and paraHisian pacing can be used only in patients with an intact distal conduction system with the understanding that it carries the risk of an unpredictable gradual progression of conduction disturbances distal to the pacing site. DBHP and paraHisian pacing can be achieved in a substantial proportion of patients with varying grades of AV block^{28,29} (some after AV junctional ablation^{7,16,30,31}) and a narrow QRS

complex and in some patients with bundle branch block caused by an intraHisian lesion. However, paraHisian pacing is generally preferred in patients with AV block because it is easier to achieve. At present in this group of patients DBHP technique may seem tedious and time-consuming in some patients because multiple attempts may be necessary. This can increase the rate of complications (particularly, infection of the system), which is why some workers limit the time dedicated to the His bundle lead implantation to no more than 20 minutes of fluoroscopy time. New leads specifically designed for DHBP or paraHisian pacing with dedicated fixation systems have helped reduce procedure duration, dislodgement rate, and fluoroscopy time. However, the methodology of DBHP is still more complex than paraHisian pacing and is associated with high-pacing thresholds and occasional unreliable ventricular sensing. Thus, DHBP entails greater battery current drain and reduced device longevity. A shift toward paraHisian pacing has occurred because its implementation seems easier and the electrical parameters are superior to those of DHBP. Currently, an additional safety lead is inserted at the RV apex or outflow tract to prevent asystole, especially in patients with pure DHBP as was the practice in the recent report by the Italian group.⁸ For antibradycardia DHBP or CRT, a dedicated CRT device can be used with the His channel in the LV port and the "safety" RV lead in the RV port. DHBP lengthens the procedure time and results in a higher cost. In the case of fused capture, it is often possible to avoid a safety lead because ventricular pacing is virtually assured on a long-term basis via myocardial capture. It seems likely that paraHisian pacing will continue to be more popular than DHBP because it is simpler, more reliable, and more secure. Only long-term follow-up will determine whether DHBP and paraHisian are reliable and effective methods to prevent the desynchronizing and negative effects of RV apical pacing. The future of DHBP is bright in view of preliminary observations that cardiac resynchronization can be achieved by this approach in selected patients with cardiomyopathy and complete LBBB.

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