# His Corrective Pacing or Biventricular Pacing for Cardiac Resynchronization in Heart Failure

Gaurav A. Upadhyay MD[a], Pugazhendi Vijayaraman MD[b], Hemal M. Nayak MD[a], Nishant Verma MD[c], Gopi Dandamudi MD [d], Parikshit S. Sharma MD[e], Moeen Saleem MD [f], John Mandrola MD[g], Davide Genovese MD[a], Roderick Tung MD[a] on behalf of the His-SYNC Investigators

[a]The University of Chicago Medicine, Center for Arrhythmia Care, Pritzker School of Medicine, Department of Medicine, Section of Cardiology, Chicago, IL (Study Coordinating Site)
[b]Geisinger Heart Institute, Wilkes Barre, PA
[c]Northwestern University, Feinberg School of Medicine, Department of Medicine, Section of Cardiology, Chicago, IL
[d]Indiana University School of Medicine, Department of Medicine, Section of Cardiology, Indianapolis, IN
[e]Rush University Medical Center, Department of Medicine, Section of Cardiology, Chicago, IL
[f]Advocate Heart Institute, Chicago, IL [g]Baptist Health Louisville, Louisville, KY

**Funding**: None
**Disclosures**: Dr. Gaurav Upadhyay has been a speaker for Biotronik and Medtronic, and has been a consultant to Abbott, Biotronik, and Medtronic. Dr. Pugazhendi Vijayaraman has been consultant to Abbott, Biotronik, Boston Scientific, and Medtronic; he also has a patent pending for a His delivery tool. Dr. Hemal Nayak has been a speaker for Medtronic, Biotronik, and Boston Scientific. Dr. Nishant Verma has been a speaker for Biotronik and Medtronic. Dr. Gopi Dandamudi has been a speaker and consultant for Medtronic and serves on the advisory board for Biotronik. Dr. Parikshit Sharma has been a speaker for Medtronic and has been a consultant for Abbott and Biotronik. Dr. Moeen Saleem has been a consultant for Medtronic, Boston Scientific, and Abbott. Dr. Roderick Tung has been on the advisory board for Abbott and Boston Scientific. Dr. John Mandrola and Dr. Davide Genovese report no relevant disclosures. Northwestern University receives institutional support for the training of fellows from Abbott, Biosense Webster, Biotronik, Boston Scientific, and Medtronic. The University of Chicago Medicine receives institutional support for the training of fellows from Abbott, Biotronik, Boston Scientific, and Medtronic.
**Acknowledgements:** The authors thank Dalise Shatz, BA, and Stephanie Besser, MSAS, for data management and statistical support.

**Correspondence:**
Roderick Tung, MD
The University of Chicago Medicine
Center for Arrhythmia Care
Pritzker School of Medicine
5841 S. Maryland Ave. MC 6080
Chicago, IL 60637
Telephone: 773-834-0455
Fax: 773-702-1025
E-mail: rodericktung@uchicago.edu

---

Biventricular pacing (BiV) is established as the primary modality to achieve cardiac resynchronization therapy (CRT), although non-response rates approach 30-40% (1). His bundle pacing has emerged as a viable option for CRT with physiological restoration of electrical synchrony by circumventing proximal conduction disease (2-4). The frequency in which His bundle pacing can correct left bundle branch block patterns (LBBB) in an unselected heart failure population is not known, and no prospective trials comparing BiV-CRT versus His bundle pacing in lieu of an LV lead for CRT (His-CRT) have been performed to date. The His Bundle Pacing versus Coronary Sinus Pacing for Cardiac Resynchronization Therapy (His-SYNC) pilot trial was an investigator-initiated, prospective, randomized controlled trial that aimed to assess the feasibility and efficacy of His-CRT as a first-line strategy compared to BiV-CRT.

The study was conducted between May 2016 and June 2018 at 7 centers, and the University of Chicago served as the Study Coordinating Site (~~NCT0270045~~NCT02700425). Approval by the local institutional review board was obtained at each center, and patients were blinded to treatment allocation. Eligible patients aged >18 years meeting guideline indications for CRT were considered for inclusion. Patients were centrally randomized to His-CRT or coronary sinus lead for BiV-CRT with routine implantation techniques (1).

As the trial sought to compare two strategies for CRT, crossover was mandated in patients assigned to His-CRT who did not achieve QRS narrowing by >20%, QRS width of ≤130 ms, or who demonstrated high correction thresholds (>5V@1 ms). Crossover was permitted in patients randomized to BiV-CRT in whom an LV lead could not be placed. LV lead delivery into the anterior interventricular or middle cardiac veins was discouraged. The primary outcomes of the trial were change in QRS duration, improvement in LVEF at 6 months, and time to cardiovascular hospitalization or death at 12 months.

Among 41 patients enrolled (64±13 yrs, 38% female, LVEF 28%, 65% with coronary artery disease, QRS width 168±18 ms [LBBB pattern=35, RBBB=2, paced=3]), 21 were randomized to His-CRT and 20 to BiV-CRT. One patient withdrew prior to implant in the BiV-CRT group. Baseline characteristics revealed no differences except that LVEF was significantly lower among His-CRT (median 26.3% [21.3-28.3%] compared to BiV-CRT (30.5% [27.1-33.9%], *p*=0.011). Crossover occurred in 48% of His-CRT and 26% of BiV-CRT. The most common reasons for crossover from His-CRT was inability to correct QRS (n=5) and suboptimal venous anatomy (n=4) in BiV-CRT.

By intention-to-treat (ITT) analysis, significant reduction in QRS duration was observed with His-CRT (172±16 ms to 144±30 ms; p=0.002), but not BiV-CRT (165±18 ms to 152±30 ms; p=0.11), although between-group differences were not significant (p=0.42). At a median follow-up of 6.2 months, improvements in LVEF relative to baseline were seen in both His-CRT (26.3% to 31.9%, *p*<0.001) and BiV-CRT patients (30.5% to 34.0%, *p*<0.001). His-CRT was not superior to BiV-CRT with regard to LVEF improvement (median +9.1% [5.0-14.4%] vs. +5.2 [1.5-11.3%], *p*=0.33) or rate of echocardiographic response ≥5% (76% vs. 53%, p=0.13). Overall event rates were low (6 cardiovascular hospitalizations, 2 deaths), with no differences observed between groups (**Figure**). No His or LV lead dislodgements were observed during study follow-up.

QLV was reported in 20 of 24 patients receiving BiV across both arms (mean 131±29 ms; mean QLV ratio 0.80±0.19). Compared to those randomized to BiV-CRT, patients assigned to His-CRT had higher pacing thresholds (median 1.7 V versus 0.9 V, *p*=0.046), but not pulse width (median 1 ms versus 0.5 ms, *p*=0.45). His corrective capture thresholds remained stable in up to 12 months of follow-up.

In this first randomized pilot trial, His-CRT did not demonstrate significant improvements in electrocardiographic or echocardiographic parameters as compared to BiV-CRT. This study was underpowered to detect differences less than 10% between groups and a type II error cannot be excluded. Importantly, ITT analysis in the presence of high crossover rates cannot directly assess treatment efficacy. Longer helices, deflectable sheaths with septal orientation, and intra-septal fixation are likely to improve His correction rates and stability of thresholds. In patients that required crossover from His-CRT, one-half of patients exhibited nonspecific intraventricular conduction delay (IVCD), which is unlikely to be corrected by His-CRT (4). Improved patient selection may decrease crossover rates and larger prospective studies may be useful to assess for smaller differences in effect size between CRT modalities.

**References**

1. Daubert C, Behar N, Martins RP, Mabo P, Leclercq C. Avoiding non-responders to cardiac resynchronization therapy: a practical guide. Eur Heart J 2017;38:1463-1472.
2. Lustgarten DL, Crespo EM, Arkhipova-Jenkins I et al. His-bundle pacing versus biventricular pacing in cardiac resynchronization therapy patients: A crossover design comparison. Heart Rhythm 2015;12:1548-57.
3. Sharma PS, Dandamudi G, Herweg B et al. Permanent His-bundle pacing as an alternative to biventricular pacing for cardiac resynchronization therapy: A multicenter experience. Heart Rhythm 2018;15:413-420.
4. Upadhyay GA, Cherian T, Shatz DY et al. Intracardiac Delineation of Septal Conduction in Left Bundle-Branch Block Patterns. Circulation 2019;139:1876-1888.

**Figure Legend**

**Figure.** Reduction in QRS duration and echocardiographic response by intention-to-treat analysis of patients randomized to BiV-CRT versus His-CRT.