Supplementary Table 1. Investigations Into the Role of Conduction System Pacing in Cardiac Resynchronization Therapy

Section A: His-Bundle-Pacing with Left-Bundle-Branch Recruitment

1st Author, Year	Design	Indication	N	Success	Follow Up *(m)*	Echocardiographic Hemodynamic	EKG/QRS-duration	Outcomes
Lustgarten, 2010[1]	Single Center, Prospective observational	HBP for CRT	10	90%	n/a	n/a	•QRS-duration 171→148ms	•DHBP resulted in a significantly narrower QRS compared with native conduction
Barba-Pinchardo, 2013[2]	Single Center, prospective observational	HBP in CRT with dilated LV, LBBB, no coronary venous access	16	56%	31	•LVEF 29→36% •LVEDD 66→60mm •LVESD 55◊51mm	•QRS-duration 166→97ms	•Improved NYHA III◊II
Lustgarten, 2015[3]	Multicenter, Prospective Cross-over of HBP vs BiV	HBP for CRT -97% LBBB	29	59%	6	•LVEF Baseline 26% HBP 32% BiV 31%	•QRS-duration Baseline 169ms NSHBP 160ms SHBP 131ms BiV 165ms	•Improved NYHA Class •Improved 6 min walk •Improved Quality of Life
Ajijola, 2017[4]	Single Center, prospective observational	HBP for CRT	21	76%	12	•LVEF 27→41% •LVEDD 54◊45mm	•QRS-duration 180→129ms	•NYHA III◊II
Sharma, 2018[5]	Multicenter, prospective observational	HBP for CRT after BiV failure or primary HBP 45% BBB 39% Paced 16% AVB	106	90%	14	•LVEF 30→44% •LVEF 25→40% (BL LVEF≤35%) •LVEDD 55→54mm	•QRS-duration 157→118ms	•NYHA 2.8→1.8 •Demonstrates HBP feasibility, safety as alternative to CRT.
Upadhyay, 2019[6]	Multicenter, prospective, randomized, cross-over trial	HBP for CRT in LBBB	41	76%	12	•LVEF 26→32%	•QRS-duration 172→144ms	•Demonstrated feasibility and safety of HBP as an alternative to CRT.
Huang, 2019[7]	Single Center, prospective observational	HBP in, LBBB, NYHA II-IV with CRT or pacing indication	74	76%	37	•LVEF 31→57% •LVESV 140→65ml	•QRS-duration Baseline 171ms HBP 113ms SHBP 173→105ms NSHBP161→140ms	•NYHA 2.8→1.0 •HBP corrected LBBB in most patients with HF and typical LBBB.
Morina-Vazquez, 2020[8]	Single Center, prospective descriptive study	P-HBP for CRT indication and LBBB	48	75%	1	•LVEF 30→51%	•QRS duration 160→132 ms	•P-HBP resulted in early LVEF improvement and electromechanical synchronization.
Arnold, 2018[9]	Acute Cross-Over Study	Acute hemodynamic study of HBP in CRT patients with LBBB	18	n/a	n/a	•Increased SBP with HBP compared to BiV	•QRS-duration Baseline 178ms BiV 158ms HBP 139ms •HBP resulted in shorter LV activation time compared to BiV	•HBP delivers superior hemodynamic response compared to BiV pacing
Vinther, 2021[10]	Single Center, prospective, randomized controlled clinical trial	HBP for CRT in patients with LBBB	50	76%	6	•BiV CRT LVEF 30→43% •HBP CRT LVEF 30→46%	•QRS duration BiV CRT 167→134 ms HBP CRT 165→131 ms	•Δ NYHA ≥ 1 BiV CRT - 40% HBP CRT - 48% •HBP provided similar clinical and physical improvement compared to BiV pacing
Wu, 2021[11]	Single Center, Prospective Observational Case control	CRT with BVP, HBP or LBBP in LVEF ≤40%, LBBB	137	48%	12	•HBP CRT ΔLVEF: 24%	•QRS duration HBP 170→101 ms BiV 140 ms	•HBP showed significantly greater improvements in NYHA class and higher improvements in BNP and CTR compared with the BVP group
Kato, 2022[12]	Single Center, prospective HBP vs BiV pacing.	HBP for CRT indication for LBBB	14	64%	12	•LVEF HBP 21→52% BiV 18→29%	•QRS duration HBP 175→144 ms BiV 175→149 ms	•HBP resulted in a greater improvement of LV relaxation and systolic function than conventional BVP
Morina-Vazquez, 2023[13]	Single Center study comparing a prospective series of P-HBP with BVP	P-HBP for CRT indication, LBBB in patients with non-ischemic cardiomyopathy	103	78%	12	•LVEF Baseline 30% P-HBP 55% BiV 40%	•QRS duration Baseline 160 ms P-HBP 110 ms BiV 140 ms	•P-HBP is superior to classic CRT in improving LVEF and QRS duration.
Section B: His-Bundle-Pacing in Right Bundle Branch Block								
Sharma, 2018[14]	Retrospective, observational multicenter study	HBP in RBBB QRSd ≥120ms NYHA class II to IV, LVEF ≤50%.	39	95%	15	•LVEF 31→39%. •LVEF 26→34% (BL LVEF≤35%) •19% super-responders	•QRS-duration 158→127ms	•NYHA 2.8→2.0 •HBP appears to be a reasonable therapy for patients with RBBB and depressed LVEF
Section C: Deep Septal Left-Bundle-Branch Pacing (LBBP)								
1st Author, Year	**Design**	**Indication**	**N**	**Success**	**Follow Up *(m)***	**Echocardiographic Hemodynamic**	**EKG/QRS-duration**	**Outcomes**

Vijayaraman, 2019[15]	Single center, prospective observational	LBBP for bradycardia or CRT (11%) if CS lead or HBP failed. LBBB 24% RBBB 25% IVCD 8% AV block 61%	100	93%	3	n/a	•QRS-duration 133→136ms •QRS-duration 162→137ms for LBBB subgroup	•LBBP feasible •Low thresholds observed
Wang, 2019[16]	Retrospective, Single Center Case–Control	LBBP after AV junctional ablation in persistent AF and HF	86	95%	31	•LVEF 35→49% •LVESV 161→96ml	•QRS duration 95ms (baseline)	•NYHA 2.6→1.7 •Lower rate of inappropriate ICD shocks, death, HF hospitalizations
Wang, 2020[17]	Single Centre, prospective LBBAP vs. BiV pacing	LBBAP/BiV pacing for CRT indication, LBBB and LVEF≤35%	40	n/a	6	•LVEF LBBAP: 27→46% BiV: 26→39% •LVEDD LBBAP 69→57 mm BiV 70→62 mm	•QRS duration LBBAP 184→123 ms BiV 175→142 ms	•NYHA 2.9→1.5 •Compared with BIVP, LBBAP improved cardiac function more effectively by reversing left ventricular remodeling
Huang, 2020[18]	Prospective Multi-Center Observational	Non-Ischemic Cardiomyopathy LBBB LVEF≤50%	63	97%	12	•LVEF 33→55% •LVESV 123→67ml	•QRS-duration Baseline 169ms LBBP 118ms	•NYHA 2.8→1.4 •LBBP may be a reasonable therapy for patients with LBBB and nonischemic cardiomyopathy
Li, 2020[19]	Multi-Centre, prospective observational	LBBP/BiV for CRT indication, LBBB and LVEF≤35%	81	81%	6	•ΔLVEF LBBAP 17% BiV 7%	•QRS duration: LBBP 124→121 ms BiV 158→158 ms	•NYHA 3→1.5
Wu, 2021[20]	Prospective, observations, case-control	CRT with BVP, HBP or LBBP in LVEF ≤40%, LBBB	137	100%	12	•ΔLVEF 24%	•QRS duration Baseline 166ms LBBP 111ms	•Echo outcomes were similar to HBP and significantly greater than BVP
Vijayaraman, 2020[21]	Retrospective Multicenter Observational	CRT/Pacing LVEF ≤50%	325	85%	6	•LVEF 33→44% •LVEDD 56→54 mm •LVESV 114→83 ml •LVEF 27 → 40% (BL LVEF≤35%) •Response 73% •Super-response 31%	•QRS-duration 152→137ms LBBB Subgroup 162→133ms	•NYHA 2.7→1.8 •LBBB (OR 3.96; p<0.01) LVEDD (OR 0.62; p<0.01) were independent predictors of response •LBBP may be a reasonable CRT alternative
Zu, 2021[22]	Single Centre, prospective observational LBBAP vs. CRT	LBBP/CRT for CRT indication, LBBB and dilated cardiomyopathy	32	100%	12	•LVEF LBBAP 31→49% CRT 29→43% •LVEDD LBBAP 66→56 mm	•QRS duration: LBBP 167→117 ms CRT 163→130 ms	•LBBAP showed stable threshold and better improvement of QRS wave duration and improved cardiac function in patients with DCM.
Hua, 2022[23]	Single Centre, prospective observational LBBAP vs. BiV pacing	LBBP for HF and LBBB	41	90%	24	•LVEF LBBAP 30→47% BiV 31→44%	•QRS duration: Baseline 178 ms LBBP 129 ms BiV 157 ms	•NYHA class: 3→1.7 •LVEDD and BNP levels were significantly lower in LBBAP group as compared to BiVP group.
Vijayaraman, 2022[24]	Multi-Centre, prospective observational	LVEF ≤35% and class I or II indications for CRT	477 (HBP 91; LBBAP 143; LOT-CRT 24)	86%	27	•LVEF CSP 26→40% BiV 26→33%	•QRS duration CSP 150→133 ms BiV 161→152 ms	•CSP was associated with a significant reduction in the composite outcome of all-cause mortality or HFH compared to traditional BVP
Wang, 2022[25]	Single Centre, prospective Randomized cross-over LBBAP vs. BiV pacing	Non-ischemic cardiomyopathy LBBB	40	90%	6	•ΔLVEF LBBAP 21% BiV 16%	•QRS duration LBBP 175→131 ms CRT 175→137 ms	•Improved NYHA class. •LBBP and BiVP might be effective for CRT in patients with NICM and LBBB.
Pujol-Lopez, 2022[26]	Single Centre, prospective randomized noninferiority	CSP/BiV for CRT indication, LBBB and LVEF≤35%	70	82%	6	•LVEF LBBAP 27→39% BiV 28→41%	•QRS duration LBBP 177→119 ms BiV 178→132 ms	•Similar degrees of cardiac resynchronization, ventricular reverse remodeling, and clinical outcomes were attained by CSP as compared to BiVP
Diaz, 2023[27]	Multicenter, observational	LBBP/BiV for CRT indication, LBBB and LVEF≤35%	371	n/a	11	•LVEF LBBAP 34% BiV 31%	•QRS duration LBBP 124 ms BiV 149 ms	•LBBAP as an initial CRT strategy resulted in a lower risk of HF-related hospitalizations compared to BiVp
Shroff, 2024[28]	Single Center, Prospective, Cohort study	CSP/BiV for CRT indication	101	100%	34	•LVEF LBBAP 29→50% BiV 29→47%	•QRS duration LBBP 161→111 ms BiV 161→137 ms	•NYHA class: 2.8→1.3 •LBBAP-CRT is a feasible and effective cardiac resynchronization therapy.

Zhu, 2024[29]	Multicenter, Prospective, observational	LBBP/BiV/LVSP for CRT indication, LBBB and LVEF<50%	259	56%	29	•ΔLVEF ≥10% LBBAP 60% BiV 36% LVSP 16%	•LBBP had a greater reduction in paced QRSd (ΔQRSd) than BiVP and LVSP (both p<0.001)	•Improved NYHA class •LBBP yielded superior long-term clinical outcomes to BiVP and LVSP.

Section D: Septal Pacing Without Targeted Conduction System Capture

1st Author, Year	Design	Indication	N	Success	Follow Up *(m)*	Echocardiographic Hemodynamic	QRS	Outcomes
Salden, 2020[30]	Multicenter Retrospective	CRT indication LBBB 89% IVCD 11%	27	100%	36	• LV septal, LV septal+RV, BiV, and HBP all increased LVdP/dtmax (al though LV septal+RV was inferior)	•QRS-duration Baseline 151ms LV septal 135ms LV septal+RV 134ms BiV 136ms HBP 110ms	•LV septal pacing resulted in electric resynchronization and hemodynamic improvement similar to BiV pacing •LV septal pacing may be a reasonable CRT alternative

Section E: Deep Septal LBBP in Right Bundle Branch Block

1st Author, Year	Design	Indication	N	Success	Follow Up *(m)*	Echocardiographic Hemodynamic	QRS	Outcomes
Vijayaraman, 2021[31]	Retrospective Multicenter Observational	CRT indication, LVEF < 50%, RBBB	121	88%		LVEF 35→43% (p<0.01)	156→150 ms (p=0.05)	LBBP is feasible, safe and provides alternative option for CRT in patients with RBBB

Section F: His-Optimized Cardiac Resynchronization Therapy

1st Author, Year	Design	Indication	N	Success	Follow Up *(m)*	Echocardiographic Hemodynamic	QRS	Outcomes
Vijayaraman, 2019[32]	Retrospective Multicenter Observational	HOT-CRT in LBBB and IVCD with QRS ≥ 140ms or AV block with LBBB type escape	27	93%	12	•LVEF 24→38% •LVEDD 65→59mm LVEDV 225→200ml LVESV 171→138ml. •Super-response 28%	•QRS-duration Baseline 183ms BiV 162ms HBP 151ms HOT-CRT 120ms	•NYHA 3.3→2.0 •Reduced HF hospitalizations •Reduced loop diuretic and aldosterone antagonist doses
Zweerink, 2021[33]	Prospective Single Center Observational	CRT indication implanted with HBP without correction of BBB combined with either BiV pacing or RV pacing in the setting RBBB	19	N/a	N/a	•Baseline LVEF 31%	•QRS-duration Baseline 142 ms HBP 142 ms BiV 154 ms HOT-CRT 126 ms	•HOT-CRT acutely improves ventricular electrical synchrony compared to BiV and HBP. •HOT-CRT reduced LV activation time by 21% compared to HBP
Deshmukh, 2021[34]	Retrospective Single Center	CRT indication in whom His pacing did not result in resynchronization	21	100%	32	•LVEF 27→41%	•QRS-duration Baseline 170ms HBP 157 ms BiV 141 ms HOT-CRT 110 ms	•NYHA 3→2 •HOT-CRT resulted in superior acute electrical synchrony in this population

Section G: Left Bundle Branch-Optimized Cardiac Resynchronization Therapy

1st Author, Year	Design	Indication	N	Success	Follow Up *(m)*	Echocardiographic Hemodynamic	QRS	Outcomes
Jastrzębski, 2021[35]	Prospective Multicenter Observational	CRT indication or non-responders to BiV CRT	112	81%	≥3	•LVEF 29→37% (p<0.0001) •LVEDD 62→59 mm •Super-response 24%	•QRS-duration Baseline 181ms LOT-CRT 144 ms LBBP 162 ms BiV 170 ms	•LOT-CRT provides significantly greater resynchronizatio n than LBBP or BiV CRT •NYHA 2.9→1.9

Abbreviation: AF= atrial fibrillation; BBB = bundle branch block; HBP = His bundle pacing; HOT-CRT = HBP optimized cardiac resynchronization therapy; HF = heart failure; ICD = implantable cardioverter-defibrillator; LBBP = left bundle branch Pacing; LOT = left bundle branch optimized; LVEDD = left ventricular end diastolic diameter; LVEF = left ventricular ejection fraction; LVESD = left ventricular end systolic diameter; LVSP = left ventricular septal pacing; NSHBP = non-selective HBP; NYHA = New York Heart Association; RBBB = right bundle branch block; SBP = systolic blood pressure; SHBP = selective HBP

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