based on prevalence in reported cases and their low frequency in the population database gnomAD. Suspected-benign variants (n=25) were selected which were present at least 15 times in gnomAD but absent from published cases. We created stable HEK293T lines expressing these variants, validated their *SCN5A* expression by flow cytometry, and studied them with automated patch clamping. For each variant, 6 parameters were measured, including peak and late current, inactivation time, and recovery from inactivation, in at least 20 cells.
Results: 10/23 in-frame indel variants had partial or complete loss of function (LoF, <50% peak current), 6 of which have previously been found in at least 1 case of BrS. 4/23 indel variants had at least one gain of function (GoF) feature, including elevated peak or late current, slower inactivation time and faster recovery from inactivation; all 4 have been found in at least 1 case of LQT3. 22/64 suspected LQT3-associated missense variants had at least one GoF feature. In contrast, only 2/25 suspected benign variants had GoF features. This result indicates that GoF features are readily captured by automated patch-clamp and are specific for LQT3-associated variants. Using the missense and indel data, 33 variants were reclassified from VUS to likely pathogenic.
Conclusion: High-throughput patch clamp can identify loss and gain of function variants in *SCN5A*. In-frame indels are a substantial contributor to *SCN5A*-mediated arrhythmia risk. Missense variants in *SCN5A* associated with LQT3 can display multiple electrophysiological defects.

ABSTRACT B-AB14:
Physiologic Pacing: Where Do We Stand Now?

Thursday, July 29, 2021
3:00 pm - 4:00 pm

B-AB14-01

LEFT VENTRICULAR ACTIVATION TIME AND PATTERN ARE PRESERVED BY BOTH SELECTIVE AND NON-SELECTIVE HIS BUNDLE PACING

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Background: His bundle pacing (HBP) can be achieved selectively (S-HBP), where the His bundle is captured alone, and non-selectively (NS-HBP), where local myocardium is also captured resulting in a pre-excited QRS appearance.
Objective: To compare the effects of selective and non-selective HBP on left and right ventricular activation time (LVAT and RVAT) and pattern.
Methods: We performed non-invasive epicardial mapping in patients who displayed both selective and non-selective HBP.
Results: In the primary analysis (n=20, all patients), NS-HBP did not prolong LVAT compared to S-HBP by the pre-specified non-inferiority margin of 10ms (LVAT prolongation: -5.5ms, 95% confidence interval (CI): -0.6 to -10.4, non-inferiority p<0.0001). NS-HBP did not prolong right ventricular activation time (4.3ms, 95%CI: -4.0 to 12.8, p=0.296) but did prolong QRS duration (22.1ms, 95%CI: 11.8 to 32.4, p = 0.0003). In patients with narrow intrinsic QRS (n=6), NS-HBP preserved left ventricular activation time (-2.9ms, 95%CI: -9.7 to 4.0, p=0.331) but prolonged QRS duration (31.4ms, 95%CI: 22.0 to 40.7, p=0.0003) and mean right ventricular activation time (16.8ms, 95%CI: -5.3 to 38.9, p=0.108) compared to S-HBP. Activation pattern of the left ventricular epicardium was unchanged between S-HBP and NS-HBP.
Conclusion: Compared to S-HBP, local myocardial capture with NS-HBP pre-excites the right ventricle, prolonging QRS duration. However, NS-HBP preserves the left ventricular activation time and pattern of S-HBP. When choosing between selective and non-selective His bundle pacing, left ventricular dyssynchrony is not an important factor.

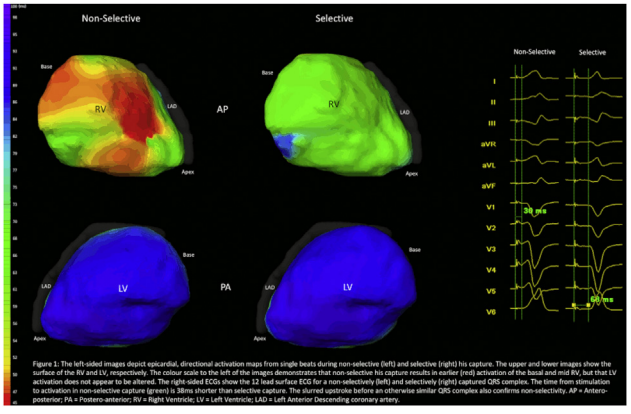


Figure 1: The left-sided images depict epicardial, directional activation maps from single beats during non-selective (left) and selective (right) his capture. The upper and lower images show the surface of the RV and LV, respectively. The colour scale to the left of the images demonstrates that non-selective his capture results in earlier (red) activation of the basal and mid RV, but that LV activation does not appear to be altered. The right-sided ECGs show the 12 lead surface ECG for a non-selectively (left) and selectively (right) captured QRS complex. The time from stimulation to activation in non-selective capture (green) is 38ms shorter than selective capture. The slurred upstroke before an otherwise similar QRS complex also confirms non-selectivity. AP = Antero-posterior; PA = Postero-anterior; RV = Right Ventricle; LV = Left Ventricle; LAD = Left Anterior Descending coronary artery.

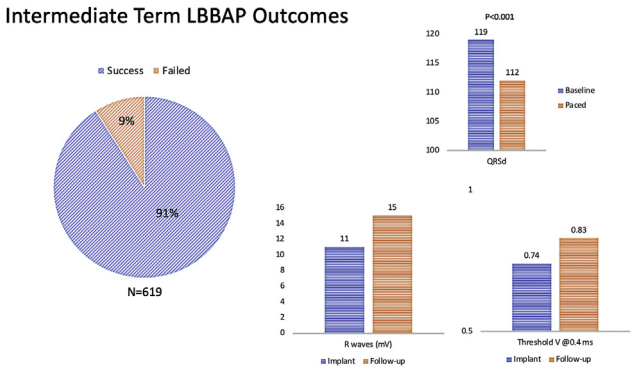
B-AB14-02

INTERMEDIATE TERM PERFORMANCE AND SAFETY OF LEFT BUNDLE BRANCH AREA CONDUCTION SYSTEM PACING LEADS: A MULTICENTER PROSPECTIVE STUDY

Santosh K. Padala MBBS, Jeffrey Kolominsky MD, Enes E. Gul PA, Ajay Pillai MD, Paula Sanchez Somonte, Jordana Kron MD, FHRS, Richard K. Shepard MD, Gautham Kalahasty MD, Bernice Tsang MD, Yaariv Khaykin MD, FHRS, Alfredo A. Pantano MD, Jayanthi N. Koneru MBBS, Kenneth A. Ellenbogen MD, FHRS and Atul Verma MD, FHRS

Background: Left bundle branch area pacing (LBBAP) has shown to be a reliable alternative to His bundle pacing (HBP) for physiologic pacing. There are limited data on the intermediate term performance of LBBAP leads.
Objective: To evaluate the intermediate term performance and safety of LBBAP.
Methods: Patients referred for pacemaker implantation at two academic centers between 02/2019 - 1/2021 were considered for LBBAP. LBBAP was performed by implanting the 3830 lumenless lead using the C315 fixed curve or C304 His deflectable sheath

(Medtronic, MN). Implant success rates, complications and electrophysiological parameters were assessed.
Results: LBBAP was successful in 566/619 patients (91%). Mean age was 73±12 yrs, 46% were women. 37% had QRSd >130 ms, 25% RBBB, 11% LBBB, 4% IVCD. Pacing indications include sinus node dysfunction in 27%, AV block 56%, CRT 7% and refractory AF 10%. Mean procedural duration was 73±32 mins (median 70 mins) and fluoroscopic time was 10±7 mins (median 8 mins). Baseline QRSd was 119±31ms vs paced QRSd was 113±12ms ($p<0.001$). Mean LV activation time was 73±12ms at high output and 76±12ms at low output. LBB potentials were noted in 175 (31%) patients. Transition from non-selective to selective LBBA or septal pacing was noted in 393 (74%). Pacing threshold and R waves were 0.74±0.3V@0.4ms and 11±5mV at implant and 0.83±0.2V@0.4ms and 15± 5mV at a mean follow-up of 167±172 days (range 25-662 days) (Fig). The only complication was LBBAP lead dislodgement in 6 (1%) patients occurring within 24-72 hours.
Conclusion: LBBA pacing is safe and feasible with high success rates and low complication rates during intermediate term follow-up.

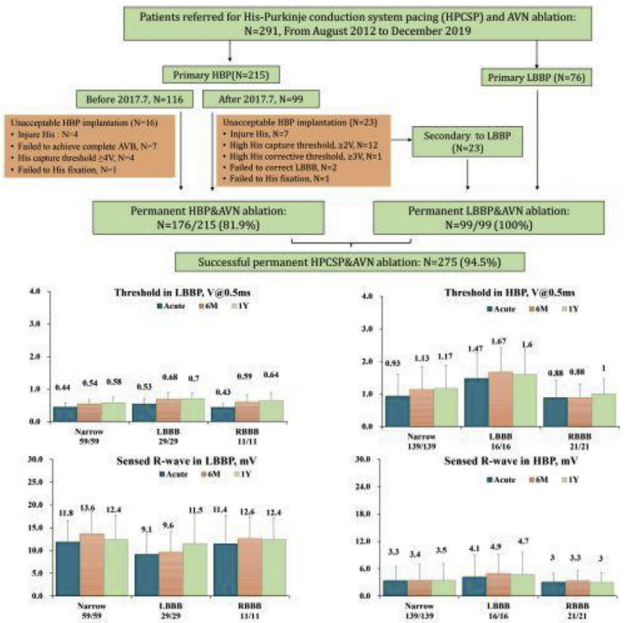


B-AB14-03

LEFT BUNDLE BRANCH PACING IN ATRIAL FIBRILLATION WITH ATRIOVENTRICULAR NODE ABLATION: A FEASIBILITY AND SAFETY ANALYSIS

Weijian Huang MD, FHRS, Mengxing Cai, Shengjie Wu, Lan Su MD, FHRS and Songjie Wang

Background: Recently, left bundle branch pacing (LBBP) has been proven effective in patients with atrial fibrillation (AF) underwent atrioventricular node (AVN) ablation, which could provide more space for AVN ablation and lower threshold compared to His bundle pacing (HBP). However, the data on the success rate and pacing parameters of LBBP in patients underwent AVN ablation for AF remains limited.
Objective: This study aimed to compare the pacing parameters and success rate between LBBP and HBP in patients with AF underwent AVN ablation.
Methods: From June 2017 to December 2019, consecutive patients with AF and HF who underwent AVN ablation and LBBP/HBP were enrolled. Pacing parameters were assessed at implant and during follow-up.
Results: A total of 291 patients were enrolled with 215 primary HBP and 76 primary LBBP. 23 had unacceptable HBP and transferred to LBBP. The success rate of permanent LBBP was higher than that of HBP (100% vs 81.5%, Figure 1). During LBBP, the acute threshold was 0.47±0.15V@0.5ms and the acute R-waves was 10.9±4.9 mv (N=99). During HBP, the acute threshold was 0.92±0.66V@0.5ms and the acute R-waves was 3.4±3.2 mv (N=176). In subgroup analysis, LBBP group with different QRS morphology all have lower thresholds and higher sensed R-waves compared to HBP group. None of the patients that underwent LBBP has increased threshold after ablation (>0.5V@0.5ms). During follow-up, 10 (5.7%) patients occurred increased threshold (>1V@0.5ms) in HBP group while 1 (1%) patient in LBBP group.
Conclusion: LBBP combined AVN ablation have well pacing parameter in patients with AF and HF and is emerging as a necessary bailout technique for unacceptable HBP following AVN ablation.



B-AB14-04

INTERMEDIATE-TERM PERFORMANCE OF MEDTRONIC 3830 LEAD FOR PHYSIOLOGIC (CONDUCTION SYSTEM) PACING: A SINGLE-CENTER EXPERIENCE

Abdullah Sarkar, Jose R. Sleiman MD, Yelenis Seijo De Armas MD, Antonio Lewis MD, Mileydis Alonso DO, John N. Bibawy MD, Marcelo E. Helguera MD, FHRS, CEPS-A, Sergio L. Pinski MD, FHRS, CCDS, CEPS-A and Jose L. Baez-Escudero MD, FHRS

Background: The short and intermediate-term performance of the Lumenless SelectSecure 3830 lead (Medtronic Inc., Minneapolis, MN) for His bundle pacing has been reported; however, its intermediate-term performance when used for left bundle branch-area pacing remains unclear.
Objective: The purpose of this study was to examine the intermediate-term performance of the Lumenless SelectSecure 3830 lead when used for His-bundle pacing (HBP), and Left-Bundle pacing (LBP) / deep septal pacing (DSP).
Methods: All consecutive patients implanted with Medtronic SelectSecure 3830-69 cm leads at Cleveland Clinic Florida between May 2016 and October 2020 were retrospectively analyzed.