**S-LBCT03**

**Late-Breaking Clinical Trials**

**Session III: Late Breaking Science**

**Friday, May 10, 2019**
4:30 - 6:00 PM

**CHAIRS:**

John D. Day, MD, FHRS. Intermountain Heart Rhythm Specialists, Park City, UT

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**S-LBCT03-01**

**PROSPECTIVE EVALUATION OF FEASIBILITY, ELECTROPHYSIOLOGICAL AND ECHOCARDIOGRAPHIC CHARACTERISTICS OF LEFT BUNDLE BRANCH AREA PACING**

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**Introduction:** His bundle pacing (HBP) can be associated with high thresholds and lower success in patients with His-Purkinje conduction disease. Recently, case reports have described transvenous left bundle branch area pacing (LBBAP). We aimed to prospectively evaluate the feasibility, and assess the electrophysiological and echocardiographic characteristics of LBBAP.

**Methods:** Patients requiring pacing for bradycardia or heart failure (failed LV lead) were prospectively enrolled. His region was mapped with 3830 lead/C315His sheath. The lead was moved 1-2 cm ventricular and posterior to the distal His and advanced deep into the septum while monitoring unipolar pacing impedance and QRS morphology and peak LV activation time (stim-peak R in V5-6). Lead depth in the septum was confirmed by contrast injection. Presence of LBB potential, paced QRS morphology/duration, threshold, impedance and R wave was assessed. Post-procedural echocardiography was performed to assess the lead distance from tricuspid annulus, lead depth in the septum and impact on tricuspid valve function.

**Applications:** LBBAP was successful in 79 of 85 (93%) pts. Age 76±11 yrs, Men 67%, HTN 76% DM 40% CAD 47% AF 48%. Indications-AV block 47, SND 21, AVN ablation 5, CRT 9, HBP lead failure 3. LBBB 34, RBBB 19, IVCD 7. Baseline QRSd 124±34 ms. Paced QRSd 131±17 ms. LBB potentials were observed in 52 patients with LB-V intervals of 25±6 ms. Stimulus to Peak R wave was 75±16 ms. Paced QRS of RBBB morphology was obtained in 73 pts and normalized QRS in 3 pts. Pacing threshold at implant was 0.62±0.3V@0.5 ms and R waves were 10±6 mV. Fluoroscopy times for LBBAP lead was 10±7 min. Lead performance, Echocardiographic analysis of lead depth and valve function will be presented.

**Next Steps/Future:** LBBAP is feasible, safe and provides an alternative in patients with challenging HBP implants, high His thresholds or conduction disease not corrected by HBP especially LBBB. LBBAP may provide stable and low conduction system capture thresholds. HBP and LBBAP may significantly increase the overall success of physiologic pacing. HBP and LBBAP may finally pave the way forward to randomized controlled trials in bradycardia and CRT population.

**S-LBCT03-02**

**IS NONSELECTIVE HIS BUNDLE PACING GOOD ENOUGH? LONG-TERM OUTCOMES FROM THE GEISINGER- RUSH HBP REGISTRY**

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**Introduction:** His bundle pacing (HBP) is the most physiologic form of pacing and was recently adopted into the guidelines to be considered in lieu of right ventricular pac-
ing. Nonselective (ns) HBP results in varying degrees of RV septal pre-excitation due to fusion myocardial capture in addition to His bundle capture compared to selective (s) HBP wherein there is no direct myocardial capture. Currently there is no evidence to suggest that nsHBP adversely affects outcomes compared to sHBP. We aim to determine whether sHBP is superior to nsHBP.

Methods: Consecutive pts undergoing HBP between January 2011 and December 2017 from the Geisinger and Rush University HBP registries were included in this study. Patients were categorized into sHBP or nsHBP based on HBP thresholds and QRS morphology at the final programmed output at 3-month follow-up. The primary outcome was a combined endpoint of all-cause mortality or heart failure hospitalization (HFH). Analysis was completed using 2-sample t-test, chi-square test, and uni- and multivariate regression analysis as appropriate.

Applications: 640 patients who underwent HBP in the Geisinger-Rush HBP registry were screened. 350 patients with an initial implant device and ≥ 20% ventricular HBP burden at 3 months (sHBP, n=118; nsHBP, n=232) were analyzed for clinical outcomes. The mean follow up duration was 1022 ± 674 days. The clinical demographics were similar but for a higher incidence of ICM (24 vs 14%, p<0.03) smoking (53 vs 37%, p<0.01), CAD (36 vs 25%, p<0.04), and HLD (74 vs 49%, p<0.01) in the nsHBP group. The native QRS durations was equivalent in the s and nsHBP groups (108 ± 30 vs 111 ± 26 ms respectively, p=0.24) while the paced QRS duration was significantly shorter in the sHBP group (103 ± 18 vs 139 ± 21 ms, p<0.01). The primary endpoint of mortality or HFH was 84 of 232 (36%) in the sHBP group (103 ± 18 vs 139 ± 21 ms, p<0.01). The primary endpoint of mortality or HFH was 84 of 232 (36%) in the sHBP group (103 ± 18 vs 139 ± 21 ms, p<0.01).

Time to Death or Heart Failure Hospitalization

Next Steps/Future: In this largest clinical study on HBP to date, with long-term follow up, nsHBP was not associated with increased adverse outcomes compared with sHBP. Multicenter risk matched clinical studies are needed to confirm these findings.

S-LBCT03-03

PREVENTIVE ABLATION OF VENTRICULAR TACHYCARDIA IN PATIENTS WITH MYOCARDIAL INFARCTION: THE BERLIN-VT TRIAL

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Introduction: Catheter ablation has shown to effectively reduce the burden of ventricular tachycardia (VT) in patients with implanted cardioverter-defibrillator (ICD). However, in patients with ICD implantation for secondary prevention of VT, the appropriate time point of catheter ablation and its effect on mortality and heart failure (HF) progression remain a matter of debate.

Methods: The BERLIN-VT trial prospectively and randomly assigned patients with stable ischemic cardiomyopathy, a left ventricular ejection fraction (LVEF) of 30-50%, and documented VT to undergo (preventive) VT ablation at the time of ICD implantation or after the third appropriate ICD shock for VT (deferred ablation). Primary endpoint was the composite of all-cause mortality and unplanned hospitalization for symptomatic VT/VF or worsening HF. Due to the group-sequential study design, three interim analyses were planned after 21, 42 and 63 (out of 85 expected) primary endpoints, with pre-specified criteria for premature study termination. After the second interim analysis in July 2018, the Data Safety Monitoring Board recommended to terminate the study early for futility.

Applications: At 26 clinical centers, 163 patients were randomized to preventive ablation (n=77) or to the control group (n=86). Four patients terminated the study prior to any procedure and were excluded from the analysis population. The remaining 159 patients (66 ± 10 years, 87% males) had a mean LVEF of 41 ± 6%, and NYHA class I (27%), II (51%), or III (22%) symptoms of HF. There were no significant between-group differences in baseline patient characteristics. Most patients (67%) received a single-chamber ICD, 26% received a dual-chamber ICD, and 7% a biventricular ICD. In the preventive ablation group, 69 (90.1%) of 76 patients underwent VT ablation at a median of 2 (interquartile range, 1-3) days after enrollment. During a median follow-up of 469 (interquartile range, 228-753) days, 25 patients (32.9%) in the preventive ablation group and 23 patients (27.7%) in the control group reached the primary endpoint. According to the time-to-first-event analysis (intention-to-treat), preventive ablation did not improve the primary endpoint compared to deferred treatment (hazard ratio for preventive ablation, 1.09 [95% CI, 0.61-1.92], Cox regression P=0.77).

Next Steps/Future: Preventive catheter ablation of VT at the time of ICD implantation was not associated with improved all-cause mortality and hospitalization for VT/VF or HF when compared to deferred ablation after the third appropriate shock for VT in patients with a secondary ICD in-
S-LBCT03-04

FIVE-YEAR OUTCOMES IN CARDIAC SURGERY PATIENTS WITH ATRIAL FIBRILLATION UNDERGOING CONCOMITANT SURGICAL ABLATION VERSUS NO ABLATION. THE LONG-TERM FOLLOW-UP OF THE PRAGUE-12 STUDY

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Introduction: Previous randomized trials have shown the efficacy of the MAZE procedure in terms of maintaining sinus rhythm, but without an effect on clinical outcomes. However, most of these studies were small with short follow-ups, generally not exceeding 1 year. The aim of this study was to assess clinical outcomes of the MAZE procedure after 5 years of follow-up.

Methods: The PRAGUE-12 study was a prospective, randomized multicenter clinical trial assessing cardiac surgery with left atrial ablation for AF vs. cardiac surgery alone. Patients with AF who were also indicated for cardiac surgery (coronary artery disease (CAD), valve surgery) were enrolled and randomized to group SA (surgical ablation) or Co (control, no ablation). All patients were followed for 5 years. The primary endpoint was a composite of cardiovascular (CV) death, stroke, hospitalization for heart failure (HFH) or severe bleeding. Secondary endpoints included all parts of the primary endpoint and recurrence of AF.

Applications: Originally, 224 patients were enrolled, with 207 patients ultimately analyzed (group SA=108, group Co=99 patients). Both groups were similar relative to important clinical characteristics except for CAD, which was more common in the Co group (SA: 55 pts. (50.9%) vs. Co 64 pts. (64.6%), p<0.05). Kaplan-Meier survival curves showed a higher incidence of the primary endpoint in the Co group (p=0.02, Figure). However, in the Cox regression model and after adjusting for all covariables, the difference between groups was not significant (hazard ratio (HR) 0.69, [0.46-1.02], p=0.063). The incidence of CV death, bleeding or HFH was nonsignificantly reduced in the SA group. The incidence of stroke and AF recurrences were significantly reduced in the SA group, and remained significant even after adjustment for all covariables incl. CAD (stroke: HR 0.31, [0.12-0.92], p=0.019, AF recurrences: HR 0.44, [0.31-0.62], p<0.001).

Next Steps/Future: Concomitant SA of AF is associated with a greater likelihood of maintaining sinus rhythm and a decreased risk of stroke. Additional long-term follow-up is needed to see the broader benefits of AF ablation.

S-LBCT03-05

REAL-TIME ELECTROGRAM ANALYSIS FOR DRIVERS OF ATRIAL FIBRILLATION (RADAR): A MULTI-CENTER, FDA-IDE, CLINICAL TRIAL OF PERSISTENT AF

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Introduction: Beyond PVI, the optimal ablation strategy for persistent AF (PerAF) is undefined. Extra-PV driver domains associated with fibrotic regions are thought to be responsible for maintaining AF, but recent methods employing phase mapping have been limited by spatial resolution, with consequent concerns about artefactual rotor “creation”. In a first-in-human multicenter, single arm, FDA IDE trial (NCT03263702; IDE#G170049) we studied a novel system designed to identify these driver domains at high resolution using conventional EGM signal processing.

Methods: The RADAR system (AFTx, Inc) was used in tandem with a conventional mapping system (NavX, Abbott Inc), with spatio-electrical data from the latter streamed real-time to the RADAR system. After PVI with a standard force-sensing irrigated RF catheter, high density LA (n=64 pts) and RA (n=8 pts) maps of AF were created using a 20 pole spiral catheter (Abbott Inc) - each 20 sec acquisition included EGM/catheter location data from both the spiral and CS catheter. Using the stationary CS catheter, the computational algorithm identified recurring CS activation patterns to define “phases” of AF, and then reconstructed panoramic 3D conduction vector maps for each phase to identify focal and rotational activity in AF. Voltage data suggestive of fibrotic borders were fused - highlighting driver domains to target for ablation. No other empiric ablation was permitted. AADs were stopped by 8 wk, within the 3 mo blanking period. The primary endpoint is 12 mo freedom from AF.

Applications: At 4 centers, we enrolled 64 drug-refrac-
tory PerAF pts (age 64±9 yrs; male 73%; BMI 31±6; LA 54±10mm; duration of continuous AF: 13±36 mo, longest 240 mo; *de novo* - 38 pts; redo - 26 pts, with 2±1 prior procedures). RADAR mapping and ablation times were 22±5 and 28±20 min. An average of 3±1 LA drivers and 2±1 RA drivers were identified. No adverse events were associated with the RADAR procedure. Over a follow up of 9±3 mo, 72% of patients remain AF/AT/AFL free and 83% remain AF free, off all AADs.

**Next Steps/Future**: In a first-in-human FDA IDE study, this novel mapping system guided ablation of AF driver domains with promising 1-year outcomes in a persistent AF cohort.

### S-LBCT03-06

**PULSED FIELD ABLATION FOR PULMONARY VEIN ISOLATION: LESION DURABILITY AND CHRONIC SAFETY**

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**Introduction**: Pre-clinical studies revealed that pulsed field ablation (PFA) preferentially ablates myocardial tissue. We previously reported that PFA isolates PVs acutely, but little is known about lesion durability or chronic safety with this novel energy source. We report these outcomes from 2 first-in-human PFA trials (**IMPULSE** - NCT03700385; **PEFCAT** - NCT03714178).

**Methods**: A penta-spline over-the-wire catheter (Farapulse Inc) was placed at each PV ostium in a flower petal or basket pose (**Figure**). A custom generator delivered proprietary bipolar waveforms (WF): either monophasic with general anesthesia (plus paralytics to address skeletal muscle stimulation) or biphasic with sedation (given minimal muscle stimulation) without esophageal temp monitoring or devia.

Electroanatomical voltage mapping was performed immediately post-ablation and again during ~3 mo remap studies.

**Applications**: At 2 sites, 81 PAF pts (age 58.1 ± 10.8 yr; 74.1% male; LA 41 ± 5 mm) were treated. All PVs (315/315, 100%) were acutely isolated by monophasic (n=15) or biphasic (n=66) PFA with ≤ 3 min elapsed delivery/pt, skin-to-skin procedure time = 92±27 min (including 18±10 min for voltage mapping), PFA catheter dwell time = 34±17 min, and fluoroscopy time = 13±7 min. Adenosine triggered reconnection in 0 of 315 PVs (0%). Of 63 eligible pts, 46 (73%) underwent remapping at 89±29 days. With successive WF refinement, results improved to 100% durable PVI (55/55 PVs; 14 pts) using the most recent PFA WF eligible for remapping (**Biphasic 3**; **Figure**). After 1 procedural Primary AE (pericardial tamponade), there were no additional Primary AEs over 171±131 days follow-up (30 pts at 6 mo, 15 at 1 yr) including: no stroke/TIA (brain MRI negative in 13 scanned pts, including DWI), no phrenic injury, no PV stenosis by 3mo CT/MRI (29 pts) or invasive remapping, no esophageal injury (EGD and MRI-T2/LGE negative for damage in 29 & 8 pts). The 6 and 12 mo Kaplan-Meier estimates of freedom from AF/AFL/AT are 90.6±4.7% and 87.1±5.6%, respectively.

**Next Steps/Future**: Pulsed field ablation with this novel catheter allowed facile rapid PVI, under sedation when using biphasic waveforms, with excellent durability and excellent chronic safety (with optimized waveforms).