Late-Breaking Clinical Trials
Innovation Boulevard
D-LBCT02
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D-LBCT02-01
LEFT BUNDLE BRANCH PACING AS A NOVEL STRATEGY FOR CARDIAC RESYNCHRONIZATION THERAPY: RESULTS FROM INTERNATIONAL LBBP COLLABORATIVE STUDY GROUP

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Introduction: Cardiac resynchronization therapy (CRT) using biventricular pacing (BVP) or His bundle pacing (HBP) is effective in patients with heart failure (HF), bundle branch block or RV pacing. Intraseptal left bundle branch pacing (LBBP) has been reported as an alternative option for CRT. The aim of the study was to assess the feasibility and outcomes of LBBP in CRT candidates in an international, multicenter, collaborative study.

Methods: LBBP was attempted in patients with LVEF<50% and indications for CRT/pacing at 8 international centers. Indications, procedural and pacing parameters, NYHA class, HF hospitalization, echocardiographic data and lead complications were assessed. LBBP was performed as a rescue or primary approach to achieve CRT utilizing SelectSecure 3830 pacing lead. LBB capture was assessed by the presence of: LBB potentials, paced RBBB morphology, nonselective (NS) to selective (S) or myocardial capture, peak LV activation time (pLVAT)<90ms in V6, response to programmed stimulation.

Applications: LBBP was attempted in 325 pts and CRT was successfully achieved in 277 (85%); failure due to incomplete CRT 27, failed deep septal deployment 21. Age 71±13 yrs, female 37%, HTN 68%, DM 38%, CAD 47%. Ischemic CMP 36%, nonischemic CMP 59%; LVEF <35% in 65 pts. QRS morphology at baseline: LBBB 42%, RBBB 18%, IVCD 12%, RVP 13%, narrow 16%. Procedure and fluoroscopy duration were 105±54 and 19±16 min. LBBP threshold and R-wave amplitudes were 0.76±0.5V@0.5ms and 11.5±6.8mV at implant and remained stable during mean f/u of 6±5 months. LBBP resulted in significant narrowing of QRS from 156±32ms to 137±22ms (p=0.0001) with pLVAT of 83±16ms. EF improved from 32±9 to 44±11% (p<0.0001). LBB capture evidence, echo and clinical outcomes and complications will be presented.

Next Steps/Future: LBBP is feasible, safe and provides an alternative option for cardiac resynchronization therapy. LBBP provides remarkably low and stable pacing thresholds. Insights from this study may provide better electrophysiologic understanding of LBBP and its role in CRT. Randomized, controlled trials comparing conduction system pacing to BVP will be necessary.

D-LBCT02-02
LONGER TERM RESULTS FROM A PHASE I/II STUDY OF EP-GUIDED NONINVASIVE CARDIAC RADIOABLATION FOR TREATMENT OF VENTRICULAR TACHYCARDIA (ENCORE-VT)

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Introduction: A prospective trial of noninvasive cardiac radioablation for patients with treatment-refractory ventricular arrhythmias demonstrated acceptable safety profile with 11% serious adverse event (SAE) rate, 94% reduction in ventricular tachycardia (VT) episodes, and 89% overall survival (OS) at 6 months. Because adverse radiation effects are often delayed, longer-term safety of this technique is important.

Methods: Arrhythmogenic scar regions were targeted by combining noninvasive anatomic and electrical cardiac imaging with a standard stereotactic body radiation therapy
workflow followed by delivery of a single fraction of 25 Gy to the target. SAEs were defined as CTCAE v4.0 grade 3-5 events possibly, probably, or definitely related to treatment. Efficacy was tracked using ICDs or 24-hour PVC burden comparing 6 months before treatment to 6-month intervals after treatment.

**Applications:** 19 patients underwent treatment. Median LVEF = 25%. 74% were NYHA 3 or 4. 53% had VT storm despite antiarrhythmic medication (median=2) and catheter ablation (median=1). Median follow-up was 34 months (range 7.9-60.1). 1-, 2- and 3-year OS was 74%, 53% and 46% (Figure). Nine deaths occurred: 1 unrelated (pancreatitis), 4 unlikely (accident, amiodarone toxicity, VT recurrence), and 4 possible (2 heart failure, 2 VT recurrence). Late SAEs (>6 month) were rare: 2 pericardial effusions (treated with oral colchicine) and 1 gastropericardial fistula (successful surgical repair).

Persistent reductions in VT episodes (defined as anti-tachycardia pacing and ICD shock) were observed in each 6-month time period after treatment (Figure). ICD shocks were reduced from a median of 4 (range 0-30) before treatment to median 0 for each 6-month time period. Complete freedom from VT was uncommon.

**Next Steps/Future:** In a high-risk cohort of patients with treatment-refractory ventricular arrhythmia, noninvasive cardiac radioablation was associated with markedly reduced VT burden that persisted through the first 3 years. Three SAEs related to treatment were observed > 2 years after treatment. Vigilant long-term follow-up will define the full safety profile of this novel therapy.

**D-LBCT02-03**

**PULSED AF: FIRST HUMAN EXPERIENCE AND ACUTE PROCEDURAL OUTCOMES USING A NOVEL PULSED FIELD ABLATION SYSTEM**

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**Introduction:** Pulmonary vein isolation (PVI) is a cornerstone of catheter ablation for atrial fibrillation (AF), and rapidly evolving technologies are poised to improve the safety and efficacy of this procedure. Irreversible electroporation using pulsed field ablation may be highly selective for myocardial tissue, improving the efficiency of PVI while potentially minimizing collateral damage to non-myocardial tissues. PULSED AF is a first-in-human study evaluating the safety and efficacy of pulsed field ablation for PVI.

**Methods:** PULSED AF (NCT04198701) is a non-randomized, prospective, multi-center, global, pre-market clinical study performed in Australia, Canada, United States and Europe. It is evaluating the PulseSelect™ system (Medtronic Inc) which delivers bipolar, biphasic pulsed electric fields through a circular multi-electrode array catheter to perform PVI. Patients undergoing first-time ablation for either paroxysmal or persistent AF (less than one year) are eligible. Study endpoints are AF recurrence >30 seconds and procedural safety. Patients will ultimately be followed for 12-months post-ablation. AF monitoring is being performed by weekly trans-telephonic transmission and intermittent Holters at 6 and 12 months.

**Applications:** Baseline demographics and acute, 30-day procedural outcomes (including acute efficacy and safety, esophageal temperatures, and phrenic nerve results) will be reported for the full cohort of the first-in-human usage of the PulseSelect™ system (N=20). Acute electrical isolation was achieved in 100% of patients to date and there have been no tamponades, strokes or phrenic nerve injuries. Upon conclusion, the study will report the rate of arrhythmia-free survival at 12 months, and pre-specified secondary and ancillary endpoints, including: procedural outcomes, quality of life, and arrhythmic symptoms. Further details will be reported on the full set of patients at the time of abstract presentation.

**Next Steps/Future:** The PULSED AF study results will provide safety and efficacy outcomes in a first-in-human cohort receiving pulsed field ablation for both paroxysmal and persistent AF patients. This will be followed by a large, global, prospective, multi-center trial.

**D-LBCT02-04**

**POINT-BY-POINT PULSED FIELD ABLATION (+/- RADIOFREQUENCY ABLATION) TO TREAT ATRIAL FIBRILLATION: A FIRST-IN-HUMAN TRIAL**

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Introduction: The tissue selectivity of pulsed field ablation (PFA) provides safety advantages over RF ablation. One-shot PFA catheters for PVI exist, but they don’t permit flexible lesion sets - eg, linear lesions. In a first-in-human trial (NCT041141007, NCT04194307), a novel lattice-tip ablation catheter able to deliver either focal RF or PF energy, was used to treat PAF or PerAF with either: i) PFA posteriorly and RFA anteriorly (RF/PF), or ii) PFA only (PF/PF).

Methods: The 8Fr lattice catheter has a compressible 9 mm nitinol tip, and is used with a custom mapping system and RF & PF generators (Sphere-9, Prism-1, HexaGen respectively; Affera Inc). Toggling between energy sources, point-by-point PV encirclement was performed using a biphasic PFA (2-5 sec; 24-32 Amp) posteriorly, and either temp-controlled irrigated RFA (Tmax 73°C; 5 sec) or PFA anteriorly. PVI was confirmed with bidirectional lines. In a first-in-human trial (35 RF / 8 PF) lines, with therapy duration times of 4.7±3.5 min. There were no device complications; there were 4 vascular injuries. Post-procedure EGD revealed mild esophageal mucosal thermal injury in 2 of 36 RF/PF and 0 of 24 PF/PF pts. Brain MRI revealed DWI+/FLAIR- and DWI+/FLAIR- asymptomatic lesions in 4 and 3 of 52 pts, respectively; the initial ACT was lower in MRI-positive (255±26 sec) vs MRI-negative (349±84 sec) pts (p<0.00001). Only 1 pt (of 29; 3.4%) with ACT >300 had an MRI-positive lesion (DWI+/FLAIR-).

Next Steps/Future: The focal lattice catheter could safely and rapidly ablate AF using a combined RF/PF approach (capitalizing on the safety of PFA and the years of experience with RFA) or a PF-only approach.

Applications: At 3 centers (11 operators), a 76-pt cohort (age 59 ± 9.9 yrs; M / F = 50 / 26; PAF / PerAF = 55 / 21) underwent either RF/PF (40 pts; 47.4±16.2 lesions/pt) or PF/PF (36 pts; 53.1±14.4 lesions/pt) ablation. The PVI therapy duration time (transpiring from first to last lesion) was 22.6±3.3 min/pt. Linear lesions included 13 mitral (4 RF / 1 RF+PF / 8 PF), 33 LA roof (12 RF / 21 PF) and 43 CTI (35 RF / 8 PF) lines, with therapy duration times of 5.1±3.6, 1.8±2.4 and 2.4±2.2 min/pt, respectively. All lesion sets were acutely successful. Total fluoroscopy time was 4.7±3.5 min. There were no device complications; there were 4 vascular injuries. Post-procedure EGD revealed minor mucosal thermal injury in 2 of 36 RF/PF and 0 of 24 PF/PF pts. Brain MRI revealed DWI+/FLAIR- and DWI+/FLAIR+ asymptomatic lesions in 4 and 3 of 52 pts, respectively; the initial ACT was lower in MRI-positive (255±26 sec) vs MRI-negative (349±84 sec) pts (p<0.00001). Only 1 pt (of 29; 3.4%) with ACT >300 had an MRI-positive lesion (DWI+/FLAIR-).

Next Steps/Future: The focal lattice catheter could safely and rapidly ablate AF using a combined RF/PF approach (capitalizing on the safety of PFA and the years of experience with RFA) or a PF-only approach.

D-LBCT02-05

UNDERSTANDING OUTCOMES WITH THE S-ICD IN PRIMARY PREVENTION PATIENTS WITH LOW EJECTION FRACTION (UNTOUCHED) TRIAL PRIMARY RESULTS

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Introduction: The Subcutaneous ICD (S-ICD) has been shown to be safe and effective for sudden cardiac death prevention. Previous S-ICD studies’ patients (pts) had few comorbidities, high left ventricular ejection fraction (EF) and received more inappropriate shocks (IS) than in transvenous (TV) ICD trials. The UNTOUCHED trial was designed to evaluate IS with prescriptive programming and enhanced discrimination algorithms in an ICD pt population similar to landmark TV ICD trial pts: primary prevention pts with reduced EF.

Methods: Primary prevention pts with EF ≤35% were prospectively enrolled if they had no pacing indication, NYHA class IV or end-stage renal failure. Devices implanted with or without SMART Pass™ filter enabled were programmed with therapy delivery for rates ≥200 beats per minute (bpm) and discrimination for rates ≤250 bpm. Pts were followed for 18 months (mos). The primary endpoint is the IS free rate compared to a 91.6% performance goal, derived from the MADIT-RIT study. Kaplan-Meier analyses were performed to evaluate IS, all cause shock, and complication-free rates. Multivariable proportional hazard analysis was performed to determine predictors of endpoints.

Applications: In 1111 of 1116 pts, S-ICD devices were implanted and included in endpoint analyses. The cohort had a mean age of 55.8±12.4 years, 74.4% men, 23.4% black race, 53.5% with ischemic heart disease, 87.7% with heart failure and an EF of 26.4±5.8%. Freedom from other cardiac OS, 1.4% for non-cardiac OS, and 0.1% for other. All cause shock free rate was 90.6% (LCL 89.0%), meeting performance goal of 85.8%. Conversion success rate for appropriate, discrete episodes was 98.4%. Complication free rate was 92.7%.

Next Steps/Future: This study shows high S-ICD efficacy
and safety with contemporary devices and programming despite the “sickest” cohort studied to date. The inappropriate shock rate (3.1% at one year) is the lowest reported for the S-ICD and lower than many TV device studies using contemporary programming to reduce IS (5% in MADIT-RIT).