Late-Breaking Clinical Trials
This Could Change My Practice

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**D-LBCT04-01**

**COMPARISON OF OUTCOMES AMONG PATIENTS IMPLANTED WITH A TINED, LEADLESS VERSUS TRANSVENOUS SINGLE-CHAMBER VENTRICULAR PACEMAKER IN THE NOVEL MICRA COVERAGE WITH EVIDENCE DEVELOPMENT STUDY**

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**Introduction:** The safety and efficacy of the Micra leadless pacemaker have been demonstrated in multiple clinical trials. Performance of the device in a large, real-world population with a contemporaneous comparison to transvenous pacemakers has not been examined. We sought to compare patient characteristics and chronic (6-month) complications among patients implanted with Micra leadless VVI pacemakers (M-VVI) and transvenous VVI pacemakers (TV-VVI) in the U.S. Medicare population.

**Methods:** The Micra Coverage with Evidence Development (CED) Study is a prospective, longitudinal study designed to evaluate the effectiveness of the M-VVI pacemaker in the Medicare population. The Micra CED Study protocol was approved by the Centers for Medicare and Medicaid Services to meet national coverage requirements and enrols all Medicare Fee-for-Service patients implanted with M-VVI and TV-VVI. To allow for 6 months of follow up, patients implanted with M-VVI between the first date of Medicare coverage, March 9, 2017, and June 30, 2018 were identified using Medicare claims data linked to manufacturer device registration data. All TV-VVI patients from facilities with M-VVI implants during the study period were obtained directly from the Medicare claims. Patients with less than 12 months of continuous enrollment in Medicare prior to M-VVI or TV-VVI implant and patients with evidence of a prior CIED were excluded. Relevant pre-specified complications including dislodgement, infection, and pocket complications were identified using procedure and diagnostic codes. Unadjusted Fine-Gray competing risk models and models adjusted with propensity score overlap weights were used to compare chronic complications between treatment groups.

**Applications:** There were 3,726 M-VVI and 7,246 TV-VVI patients implanted during the study period. Compared to TV-VVI patients, the M-VVI patients were more likely to have ESRD (12.5% vs. 2.3%, $P < 0.0001$), renal dysfunction (48.7% vs. 41.5%, $P < 0.0001$), and a higher Charlson Comorbidity Index score (5.1 vs. 4.5, $P < 0.001$). Patients implanted with a M-VVI had a significant reduction in chronic complications compared to patients implanted with a TV-VVI (adj. HR, 0.34, 95% CI, 0.28-0.43, $P < 0.0001$; unadj. HR, 0.38, 95% CI, 0.31-0.47, $P < 0.0001$). Acute (30-day) effusion/perforation/tamponade was not significantly different between the M-VVI and TV-VVI patients.

**Next Steps/Future:** Despite the M-VVI patients having more comorbidities than TV-VVI patients, the leadless pacemaker population experienced a 66% reduction in chronic complications in this first real-world, contemporaneous, comparative effectiveness study.

**D-LBCT04-02**

**PREDICTED BENEFIT OF THE IMPLANTABLE CARDIOVERTER DEFIBRILLATOR: THE MADIT-ICD BENEFIT SCORE**

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**Introduction:** The benefit of the ICD for primary prevention is not uniform. We present the first prediction model for ICD-Benefit that integrates the predicted risk for arrhythmic events vs. non-arrhythmic mortality in all ICD patients enrolled in the MADIT trials.

**Methods:** For the purpose of this study we established the MEGA-MADIT Database, combining all landmark MADIT trials (MADIT-II, MADIT-Risk, MADIT-CRT, and MADIT-RIT). Best-subsets Fine-and-Gray analysis was used to develop prognostic models for ventricular tachyarrhythmic events (VTE) (event of interest) or death without prior VTE (competing event). The two competing risk models were subsequently integrated to form the MADIT-ICD Benefit Score.

**Applications:** Eight clinical factors (male, age<75 years, prior non-sustained VT, LVEF <20%, no aspirin, no beta-blocker, and digitalis or diuretic use) were identified as predictors of VTE; and 5 clinical factors (age≥75 years,
prior CABG, diabetes, HF hospitalization, amiodarone use) as predictors of death without prior VTE (Fig. 1A). The two competing models were combined to form the MADIT-ICD Benefit Score (Fig. 1B). Increasing ICD Benefit Score was directly correlated with the 4-year predicted risk of VTE, and inversely correlated with the 4-year predicted risk of death without a prior arrhythmia (29 vs. 7%, respectively; p<.0001), with the highest potential for life-years saved by the ICD. In contrast, patients in the Lowest MADIT-ICD Benefit Group had a similar risk of VTE vs. death without a prior arrhythmia (19% vs. 18%, respectively; p=0.72), with the lowest potential for life-years saved by the ICD. Internal validation confirmed model stability with similar C indices (0.66 and 0.67).

**Next Steps/Future:** Based on the landmark MADIT trials, we propose the MADIT-ICD Benefit Score which predicts the likelihood of ICD benefit through personalized assessment of the risk of VTE weighed against the risk of non-arrhythmic mortality. The Score may be used for shared decision-making in potential ICD candidates.

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**ASSESSMENT OF ABSOLUTE RISK OF LIFE-THREATENING CARDIAC EVENTS IN LONG QT SYNDROME PATIENTS**

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**Introduction:** Risk stratification in long QT syndrome (LQTS) patients is important for optimizing patient care and informing clinical decision making. We developed a model for prediction of 5-year absolute risk of the first life-threatening arrhythmic event in LQTS patients.

**Methods:** The Rochester-based LQTS Registry included the phenotypic cohort of 1,509 LQTS patients with QTc ≥470ms, and the genotypic cohort of 1,288 patients with a single LQT1, LQT2, or LQT3 mutation. We developed two separate risk prediction models which included pre-specified time-dependent covariates of beta-blocker use, syncope (never, syncope while off beta blockers, and syncope while on beta blockers), sex by age < and ≥ 13 years, baseline QTc, and genotype (for the genotypic cohort only).

Follow-up started from enrollment in the registry and was censored at each patient’s 50th birthday, date of death due to reasons other than sudden cardiac death, or last contact, whichever occurred first. The predictive models were externally validated in an independent cohort of 1,481 genotyped LQTS patients from Pavia, Italy.

**Applications:** In Rochester dataset, there were 77 endpoints in the phenotypic cohort during a median follow-up of 9.0 years, and 47 endpoints in the genotypic cohort during a median follow-up of 9.8 years. The time-dependent extension of Harrell’s generalized C-statistics for the phenotypic model and genotypic model were 0.784 (95% CI: 0.740 - 0.827) and 0.785 (95% CI: 0.721 - 0.849), respectively, in the Rochester cohort. In the Pavia cohort, 57 patients developed the endpoint. The C-statistics obtained from external validation in the Pavia cohort were 0.700 (95% CI: 0.610-0.790) and 0.711 (95% CI: 0.631-0.792) for the two models, respectively. Based on the above models, an online LQTS risk calculator estimating a 5-year risk of life-threatening arrhythmic events was developed.

**Next Steps/Future:** This study developed two risk prediction algorithms for phenotype and genotype positive LQTS patients separately. The estimated 5-year absolute risk can be used to quantify a LQTS patient’s risk of developing life-threatening arrhythmic events and thus assisting in clinical decision making regarding prophylactic ICD therapy.

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**ABLATION OF REFRACTORY VENTRICULAR TACHYCARDIA WITH A HEATED-SALINE NEEDLE CATHETER FOR ENHANCED RADIOFREQUENCY (SERF) ABLATION WITH CREATION OF TRANSMURAL LESIONS: A FIRST-IN-MAN FEASIBILITY STUDY**
Ablation of VT is limited by the ability to create deep lesions. Endocardial intramural needle ablation using heated Saline Enhanced Radiofrequency (SERF) energy uses convective heating to increase heat transfer and create lesions of controllable size that are transmural when needed (Figure). This first-in-human trial is evaluating the safety and initial efficacy for intramural, SERF needle ablation in patients with refractory VT.

**Methods:** Thirty-two subjects who had ICDs, EF 20-60%, therapies (shock/ATP) for VT in the 3-6 months pre-ablation were treated at 6 centers (Canada, USA). VTs were induced and mapped. The SERF needle catheter (Thermedical Durablate) was used to create 1-5 cm² intra-lesions to target the VT(s). Acute procedural success was defined as non-inducibility of the clinical VT. Patients underwent follow-up at 30 days, 3, and 6 months. ICD’s were interrogated at all follow-ups to determine VT recurrence.

**Applications:** Patients (91% male, 66±10 yrs, EF 35±11%, 56% ischemic cardiomyopathy) had a median of 45 ICD interventions (shock/ATP) for VT in the 3-6 months pre-ablation. The study catheter was used to deliver an average of 10±5 lesions per case, with an average of 430s±295s of RF time. Average time spent with the study catheter was 1.9±1.0 hours, with total procedural duration of 4.5±1.5 hours. Acute procedural success was 100% for eliminating clinical VT. With current average follow-up of 5 months (n=28) there has been an 89% reduction in ICD therapies and all patients have had reduction in ICD interventions (see figure). Median ICD therapies are zero. Complications were 2 acute deaths (bowel infarct and cardiogenic shock), 2 mild strokes with recovery, and worsening of a pre-existing pericardial effusion requiring drainage (n=1).

**Next Steps/Future:** Intramural needle ablation using heated saline shows acceptable initial safety and encouraging efficacy with a clinically significant reduction in VT burden and density. Full 6 month results for the trial will be presented in additional patients.

**Remote monitoring (RM) of pacemakers (PMs) can improve patient outcomes, and high RM adherence is associated with greater benefit. However, adoption and adherence to RM remain suboptimal. New generation PM and biventricular pacemaker (CRT-P) devices use Bluetooth® low-energy to communicate directly with patient-owned smart devices through a novel app-based platform. This provides automatic data transmission without the need of a bedside console and allows the patient to use a smartphone or tablet as their transmitter. The impact of this technology on RM adherence in PM patients is unknown and this evaluation was designed to understand it.

**Methods:** The BlueSync® Field Evaluation was a prospective, multi-center study measuring the success rate of scheduled transmissions in PM patients using the MyCareLink Heart™ mobile app (MCLH) through 12 months. Patients were enrolled in the evaluation from April 2018 through December 2018 and 1-year follow up was completed in December 2019. Scheduled transmission success was compared to 3 historic control groups from the Medtronic de-identified CareLink™ database: 1) PM patients requiring a wand to communicate with a bedside console (active transmission), 2) PM patients with wireless automatic communication with the bedside console (active and passive transmission); 3) defibrillator patients with similar automatic communication (Table).

**Applications:** For 12 months, 245 BlueSync evaluation patients (64.8 ± 15.6 years, 58.4% men) had a total of 953 scheduled transmissions of which 902 were successfully completed (94.6%). This was superior to all three control groups (Table), even after matching groups by age, number
of device chambers and gender (P < 0.001.) In addition, scheduled transmission success for 811 patients (69.1 ± 12.2, 62.3%, men) using MCLH outside of the study for at least 12 months was 92.8% (2,365 scheduled and 2,194 completed), suggesting that the real-world experience outside the field evaluation is similar.

Next Steps/Future: Twelve-month experience with the first of its kind app-based RM system for PM or CRT-Ps demonstrates a high rate of successful scheduled transmissions and was superior to predicate systems.

| TABLE 3: RM SUCCESS PERFORMANCE DESCRIPTIONS |
| Evaluation Group | Control 1 | Control 2 | Control 3 |
| Device Type | MyCareSync™ PA/CRT-P | PA/CRT-P | PA/CRT-P | KO/CRT-O |
| Monitor Mode | App-based | Manual | Automatic | Automatic |
| Monitor Location (App) | MCL Heart | CareLink™ (245Q) | MyCareLink™ (245Q) | MyCareLink™ (245Q) |
| Control | Field Evaluation | Historical Real-world retrospective | Historical Real-world retrospective | Historical Real-world retrospective |
| Number of Patients | 245 | 138,540 | 69,306 | 47,421 |
| Scheduled Transmissions | 953 | 350,200 | 203,622 | 167,517 |
| Completed Transmissions | 952 | 204,977 | 157,344 | 141,043 |
| Transmission Success (95% CI) | 94.6% (93.1% - 95.9%) | 60.0% (59.7% - 60.2%) | 77.3% (77.1% - 77.6%) | 86.6% (86.3% - 86.9%) |
| Difference to MCLHeart app (95% CI) | -34.7% (32.4% - 37%) | -17.3% (15% - 18.6%) | 8.1% (5.7% - 10.4%) |
| P-value Superiority | < 0.001 | < 0.001 | < 0.001 |

*Control group inclusion criteria: US patients at least 16 years of age activated first transmission monitor task plan of CareLink™ from 17 January 2019 to 27 December 2019, followed for at least one year after activation with a minimum of one scheduled transmission in this year and did not perform transmission with another monitor during this time period.