Performance of Anatomically Designed Quadripolar Left Ventricular Leads: Results from the NAVIGATE X4 Clinical Trial

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Anatomically Designed Quadripolar LV Leads. Introduction: The safety and efficacy of a novel family of quadripolar left ventricular (LV) pacing leads designed to pace from nonapical regions of the LV with low pacing capture thresholds was studied in patients undergoing implantation of a cardiac resynchronization therapy defibrillator (CRT-D).

Methods and Results: Patients receiving a CRT-D were implanted with 1 of 3 ACUITY X4 leads (Spiral Long, Spiral Short, or Straight), designed to address coronary venous anatomical variability. Electrical performance and LV lead related complications were evaluated 3 and 6 months post implantation, respectively. 764 patients (68 ± 11 years, 66% male) were enrolled; 738 (97%) successfully implanted with an ACUITY X4 lead (Spiral L, n = 239, 31%; Spiral S, n = 281, 37%; Straight, n = 218, 29%). A targeted threshold ≤2.5 V was achieved in 644 (94%) patients. The median threshold from the best proximal electrode was lower than the tip electrode (0.9 V [IQR 0.7, 1.3] vs. 1.3 V [IQR 0.7, 2.5], p < 0.001) on Spiral leads. Irrespective of lead implanted, one of the proximal electrodes was the programmed cathode in most patients. The overall LV complication-free rate was 98%. LV lead dislodgment occurred in 8 (1%) patients. PNS occurred in 58 (8%) patients, but only 3 (0.4%) patients required surgical intervention.

Conclusion: The ACUITY X4 LV leads had low pacing thresholds particularly from proximal electrodes, a high incidence of pacing from the nondistal electrode, and low likelihood of dislodgment or PNS requiring surgical intervention. (ClinicalTrials.gov Identifier: NCT02071173) (J Cardiovasc Electrophysiol, Vol. 27, pp. 1199-1205, October 2016)

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Introduction

Cardiac resynchronization therapy (CRT) is an established therapy for patients with symptomatic heart failure, left ventricular (LV) dysfunction, and electrical dyssynchrony (as assessed by wide QRS duration, in particular left bundle branch morphology).1-5 Over time, the LV pacing leads have evolved from unipolar to bipolar to (most recently) quadripolar pacing leads. The 2 major advantages of quadripolar LV pacing leads are (1) they offer a greater opportunity to pace from a nonapical pacing electrode and (2) they mitigate the need for reoperation to manage complications because of the greater number of programming vectors available. However, the pacing capture threshold (PCT) of currently available LV leads increases when pacing from more proximal electrodes, and result in low utilization.5-9 Therefore, a new family of quadripolar LV leads was designed to ensure low PCTs from nonapical regions of the LV, while maintaining a high degree of stability and programming options to manage phrenic nerve stimulation (PNS). The aim of this study is to report the performance of these leads as ascertained through a Food and Drug Administration (FDA) mandated Investigational Device Exemption clinical trial.
to demonstrate the safety, performance and effectiveness of the ACUITY X4 LV pacing leads. The institutional review boards at each institution approved the study, and all subjects gave written informed consent.

The study sought to enroll a minimum of 748 patients with a standard indication for a CRT-defibrillator (CRT-D). A minimum of 534 spiral (either the Spiral L or S) and 214 straight leads were required per the study protocol. Patients with prior device implant, <12 months life expectancy, or a mechanical tricuspid valve were excluded. The choice of the LV lead from the ACUITY X4 family was left to the discretion of the implanting physician based on intraoperative coronary sinus venography. Guidance was provided to use the Spiral L lead if the target vessel terminated in the apical portion of the LV, use the Spiral S lead if the vessel terminated in the mid portion of the LV, or use the Straight lead if the vessel was short or narrow.

The prespecified primary safety endpoint evaluated 6-month LV lead-related complication rates, defined as lead-related adverse events resulting in permanent loss of pacing therapy, invasive intervention, injury or death, per protocol defined methods pursuant to ADVAMED and FDA Guidance documents, with a complication-free rate of ≥87% for the Spiral leads and ≥85% for the Straight lead. The prespecified primary efficacy endpoints consisted of 2 separate tests of electrical performance (assessed at 3-months postdevice implantation). These included (1) percent of patients with PCT ≤ 2.5 V in the final programmed configuration and (2) percent of patients in the Spiral L or Spiral S cohort with a PCT ≤ 2.5 V for the proximal electrodes within the bias; the endpoint had to be met in 75% of patients. Secondary endpoints evaluated indices of sensing and impedance.

A detailed protocol was utilized at the time of electrical measurements to assess the PCTs and for the presence of PNS at 7.5 V; all electrical testing used a 0.5 millisecond pulse width. First, the PCT and PNS threshold was measured for each electrode in either an extended bipolar (E1–RV coil; E2–RV coil; E3–RV coil; and E4–RV coil) or unipolar (E1-can; E2-can; E3-can; and E4-can) configuration. Approximately 80% of the time, investigators chose to assess in the extended bipolar configuration. Second, the 3 available true bipolar vectors incorporating the tip electrode were tested (E1–E2; E1–E3; and E1–E4). Third, the proximal electrode with the lowest PCT and without PNS was identified to determine the electrode with the best myocardial contact. This was termed the “best electrode,” and a true bipolar vector using this electrode was tested. For example, if E3 was deemed the best proximal electrode, the investigator evaluated the PCT and PNS thresholds using E3–E2 or E3–E4.

Statistical Analysis

Mean and standard deviation (mean ± standard deviation) or median and interquartile range (median [IQR]) were calculated for continuous variables. Counts and percentages were calculated for categorical variables. P-values were calculated with t-tests for continuous variables presented as a mean and standard deviation, Wilcoxon tests for continuous variables presented as median and IQR, and chi-square tests for categorical variables, unless otherwise noted. The endpoint assessing LV lead-related complication-free rate through 6 months was evaluated using the 180-day Kaplan–Meier estimator.
Anatomically Designed Quadripolar LV Leads

Results

Between April 2014 and July 2015, a total of 791 patients were enrolled in the study from 88 centers in the United States and followed for a median duration of 9.2 months (range: 0.1–15.1 months). Table 1 summarizes the demographics of the study cohort as well as their indications for CRT-D implantation. Ultimately, 764 patients underwent a CRT-D implantation procedure with an ACUITY X4 lead; the lead was successfully implanted in 738 (97%) of patients; 281 (37%) with Spiral S, 239 (31%) with Spiral L, 218 (29%) with Straight, 15 (2%) with a commercially available LV lead (details available in Table S1), and 11 (1%) were unable to be implanted. The implant success rate of the initially selected lead was 85.2%, an alternate lead was successfully implanted in additional 11.4% of patients. The median CRT-D implant procedure time was 86 (IQR 62,120) minutes, including a mean (IQR) of 7 (IQR 3,15) minutes to implant the LV lead (measured as the time from insertion of the LV lead into the delivery catheter to the first electrical measurement using the Pacing System Analyzer). The LV lead was implanted into an anterolateral, lateral or posterolateral branch of the coronary sinus in 687 (93%) of patients. Representative cases from the NAVIGATE X4 clinical trial are shown in Figure 2.

Lead Safety Performance

Within the first 6-months of device implantation, an LV lead related complication or observation was observed in 16 (2%) and 67 (9%) of 764 patients, respectively (Table 2). The complication-free rate from 0 to 6 months was 98.5% for the ACUITY X4 Spiral leads and 96.5% for the Straight lead. The most commonly observed complication was dislodgment of the LV lead, which occurred in 8 (1%) patients (75% occurred within the first day). There have been no unanticipated adverse device effects reported in this clinical study. As of July 17, 2015, 46 deaths have been reported, which represents 6% of enrolled patients. None of the deaths were adjudicated by the Clinical Events Committee to be related to the LV lead.

Electrode Performance

The ACUITY X4 leads met both primary effectiveness performance endpoints. In total, 644 (94%) patients had a PCT ≤ 2.5 V; 462 (96%) patients with Spiral leads (1.0 V [IQR 0.8, 1.4]), and 182 (90%) patients with a Straight lead (1.2 V [IQR 0.9, 1.8]). For the second pre-specified effectiveness endpoint, 441 (91%) patients implanted with a Spiral lead had a PCT ≤ 2.5 V from the best proximal electrode (0.9 V [IQR 0.7, 1.3]). The same analysis for the Straight leads found they were less likely to have a PCT ≤ 2.5 V (P = 0.003); overall, 169 (83%) of these patients had a PCT ≤ 2.5 V (1.3 V [IQR 0.9, 2.2]).

At the 3-month follow-up visit, the extended bipolar or unipolar PCT of the best proximal electrode had lower median value than the tip electrode for both the Spiral L (0.9 V [IQR 0.7, 1.3] vs. 1.3 V [IQR 0.7, 2.7], respectively, P < 0.001) and Spiral S (0.9 V [IQR 0.7, 1.2] vs. 1.3 V [0.8, 2.3], respectively, P < 0.001) leads (Fig. 3). Conversely, the PCT of the best proximal electrode on the straight lead was slightly increased compared to the tip electrode (1.2 V [IQR 0.9, 2.1] vs. 1.0 V [IQR 0.6, 2.0], P = 0.002). Irrespective of the ACUITY X4 LV lead implanted, LV pacing was programmed to occur from one of the proximal electrodes in most patients (74% vs. 26% from the distal (E1) electrode, P < 0.001, Fig. 4).

### TABLE 1

| Patient Demographics and Indications for CRT-D Implantation |
|-----------------------------------------------------------|
| **Number of patients**                                    |
| 791                                                       |
| **Age (years)**                                           | 68 ± 11          |
| **Male (n)**                                              | 525 (66%)        |
| **NYHA Heart Failure Class**                              | 221 (28%) / 534 (68%) / 19 (2%) |
| **LVEF (%)**                                              | 25 ± 7           |
| **QRS duration (milliseconds)**                            | 152 ± 23         |
| **QRS morphology: LBBB / RBBB**                           | 638 (81%) / 53 (7%) |
| **Co-morbidities**                                       |                  |
| **Hypertension**                                          | 651 (82%)        |
| **Diabetes mellitus**                                    | 303 (38%)        |
| **Chronic pulmonary disease**                             | 194 (25%)        |
| **Renal disease**                                         | 179 (23%)        |
| **Cerebrovascular disease**                               | 104 (13%)        |
| **Etiology for cardiomyopathy**                           |                  |
| **Ischemic / Nonischemic / Hypertrophic / Other**         | 364 (47%) / 364 (46%) / 17 (2%) / 12 (2%) |
| **CRT-D indications**                                    |                  |
| **LVEF ≤ 35%, sinus rhythm, LBBB with QRS duration ≥ 150 milliseconds, NYHA II, III, or ambulatory IV on GDMT** | 391 (49%)        |
| **LVEF ≤ 35%, sinus rhythm, LBBB with QRS duration 120–149 milliseconds, NYHA II, III, or ambulatory IV on GDMT** | 194 (25%)        |
| **LVEF ≤ 35%, sinus rhythm, non-LBBB with QRS duration ≥ 150 milliseconds, NYHA III or ambulatory IV on GDMT** | 38 (05%)         |
| **Atrial fibrillation and LVEF ≤ 35% on GDMT and (a) requires ventricular pacing or otherwise meets CRT criteria or (b) AV nodal ablation or pharmacological rate control will allow near 100% ventricular pacing with CRT** | 107 (14%)        |
| **On GDMT with LVEF ≤ 35% and are undergoing new device placement with anticipated significant (≥ 40%) ventricular pacing** | 109 (14%)        |

CRT-D = cardiac resynchronization therapy-defibrillator; GDMT = guideline directed medical therapy; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; RBBB = right bundle branch block

### RESULTS

Between April 2014 and July 2015, a total of 791 patients were enrolled in the study from 88 centers in the United States and followed for a median duration of 9.2 months (range: 0.1–15.1 months). Table 1 summarizes the demographics of the study cohort as well as their indications for CRT-D implantation. Ultimately, 764 patients underwent a CRT-D implantation procedure with an ACUITY X4 lead; the lead was successfully implanted in 738 (97%) of patients; 281 (37%) with Spiral S, 239 (31%) with Spiral L, 218 (29%) with Straight, 15 (2%) with a commercially available LV lead (details available in Table S1), and 11 (1%) were unable to be implanted. The implant success rate of the initially selected lead was 85.2%, an alternate lead was successfully implanted in additional 11.4% of patients. The median CRT-D implant procedure time was 86 (IQR 62,120) minutes, including a mean (IQR) of 7 (IQR 3,15) minutes to implant the LV lead (measured as the time from insertion of the LV lead into the delivery catheter to the first electrical measurement using the Pacing System Analyzer). The LV lead was implanted into an anterolateral, lateral or posterolateral branch of the coronary sinus in 687 (93%) of patients. Representative cases from the NAVIGATE X4 clinical trial are shown in Figure 2.

### LEAD SAFETY PERFORMANCE

Within the first 6-months of device implantation, an LV lead related complication or observation was observed in 16 (2%) and 67 (9%) of 764 patients, respectively (Table 2). The complication-free rate from 0 to 6 months was 98.5% for the ACUITY X4 Spiral leads and 96.5% for the Straight lead. The most commonly observed complication was dislodgment of the LV lead, which occurred in 8 (1%) patients (75% occurred within the first day). There have been no unanticipated adverse device effects reported in this clinical study. As of July 17, 2015, 46 deaths have been reported, which represents 6% of enrolled patients. None of the deaths were adjudicated by the Clinical Events Committee to be related to the LV lead.

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Figure 2. Fluoroscopic locations of ACUITY X4 leads: ACUITY X4 LV lead selected based on the patient’s coronary sinus venogram. Top: long, nontapering lateral vessel extending to the apex; this anatomy is ideally suited for the Spiral L lead. Middle: short, tapering lateral vessel; this anatomy is ideally suited for the Spiral S lead. Bottom: small, tortuous lateral vessel; this anatomy is ideally suited for the Straight lead.

### TABLE 2
ACUITY X4 Related Adverse Events With the First 6 Months

| Adverse Event Observed | Total Patients | Complication | Observation |
|------------------------|----------------|--------------|-------------|
| Extracardiac stimulation | 56 (7.3%) | 3 (0.4%) | 54 (7.1%) |
| Dislodgment            | 9 (1.2%)   | 8 (1.0%)  | 1 (0.1%)   |
| Elevated threshold     | 7 (0.9%)   | 0 (0.0%)  | 7 (0.9%)   |
| Unable to capture      | 4 (0.5%)   | 0 (0.0%)  | 4 (0.5%)   |
| Coronary venous perforation | 2 (0.3%) | 2 (0.3%) | 0 (0.0%) |
| Myocardial perforation | 2 (0.3%)   | 1 (0.1%)  | 1 (0.1%)   |
| Coronary venous dissection | 1 (0.1%) | 0 (0.0%)  | 1 (0.1%)   |
| Impedance out of range | 1 (0.1%)   | 1 (0.1%)  | 0 (0.0%)   |
| Incomplete connection to header | 1 (0.1%) | 1 (0.1%) | 0 (0.0%) |
| Total                  | **81 (10.6%)** | **16 (2.1%)** | **67 (8.8%)** |

1Patients may contribute to more than 1 adverse event.
2A “complication” was defined as a lead-related adverse events resulting in permanent loss of pacing therapy, invasive intervention, injury or death.

During predischarge testing, PNS could be detected in 281 (38%) of 733 patients. PNS most commonly occurred with E1 as the cathode, especially for Spiral L leads, and decreased with more proximal electrodes. True bipolar pacing within the proximal electrodes detected PNS in only 6% of patients (Fig. S1). Between hospital discharge and the 6-month follow-up visit, PNS was observed clinically in 58 (8%) patients, most commonly when the distal electrode was the programmed cathode (30 of 205 patients, 15%) instead of a proximal electrode (28 of 539 patients, 5%). The PNS could be eliminated with reprogramming in 55 (95%) patients; thus, surgical correction was necessary in only 0.4% of the entire study cohort.

At the 3-month follow-up visit, the mean R-wave amplitude in the programmed configuration was 17 ± 7 mV for the Spiral leads and 16 ± 7 mV for the Straight lead. The mean pacing impedance in the programmed configuration was 776 ± 266 Ω (Spiral) and 805 ± 304 Ω (Straight). The LV pacing impedance was significantly higher when pacing with a true bipolar configuration (1,301 ± 344 Ω) as compared with an extended bipolar or unipolar configuration (693 ± 215 Ω, P < 0.001).

### Discussion
There are several important findings from this study. First, a novel family of quadripolar LV leads, specifically designed to meet the needs of various coronary venous anatomies, can be successfully implanted in 97% of patients and is associated with low acute and chronic complication rates. Second, with
Figure 3. Pacing capture threshold comparison between electrodes: the pacing capture threshold (median and IQR) of extended bipolar or unipolar configurations at 3-month follow-up of the tip electrode (E1) compared to the best proximal electrode (E2, E3, or E4). The proximal electrode has lower thresholds on Spiral L and Spiral S leads, but not Straight leads.

Figure 4. Cathode utilization in final programming: distribution of the final programmed pacing cathode of the Spiral L, Spiral S, and Straight leads. Irrespective of lead design, most patients were paced from an electrode other than the tip electrode.
either Spiral LV lead, the PCT from 1 of the 3 proximal electrodes (E2, E3, or E4) spaced around the helical bias is lower than from the distal electrode. As a result, the device is programmed most commonly to pace from a proximal electrode, thereby increasing the ability to avoid pacing from apical regions of the LV. This is the first demonstration that LV pacing can be preferentially performed from a nonapical region of the LV without sacrificing lead stability or device longevity. Finally, PNS occurred in only 8% and was nearly always resolved by reprogramming either the pacing output or vector.

CRT has become accepted therapy in selected patients with heart failure. The LV pacing lead was initially implanted epicardially. Improvements in lead design and delivery tools led to a transvenous approach into a venous tributary of the coronary sinus, thus eliminating the morbidity and complexity inherent to epicardial LV lead implantation. However, these leads needed to be wedged into branch vessels for lead stability; as a result, electronic repositioning had limited success in eliminating PNS. Initial CRT clinical studies were all performed with unipolar or bipolar leads with these limitations. Quadripolar LV leads were developed to overcome this limitation and over time have become the standard of care during CRT device implantation procedures. It has been shown that commercially available quadripolar LV leads can be implanted successfully in most patients, have a low rate of dislodgement, and PNS can be eliminated with reprogramming in almost all patients. Importantly, in combination, these benefits have translated into improved patient survival as compared to patients receiving a bipolar LV lead.

It has been demonstrated that the site of LV pacing has an important impact on patient outcome with CRT. In a post hoc analysis of the MADIT-CRT trial, Singh et al. validated the fluoroscopic location of the leads implanted in the study and evaluated the impact on patient outcomes. The 14% of patients with leads in the apical third of the LV had a 2.4x risk of the composite endpoint of heart failure/death as well as a 5-fold increase in the risk of death alone. In addition, it has been demonstrated that pacing from the site of latest mechanical delay (which almost never occurs at the LV apex) further contributes to improved patient outcomes. Thus, current guidelines advocate avoiding apical pacing and targeting latest mechanical delay regions.

An additional benefit of nonapical pacing is that, irrespective of pacing configuration (unipolar, extended bipolar, true bipolar), PNS is less commonly observed when pacing is performed from the basal region of the heart. The proximal electrodes of the ACUITY X4 leads had lower rates of PNS both during acute evaluation (6% during true bipolar testing) and clinically during follow-up (5%).

Existing quadripolar LV leads were not designed to have robust PCTs when pacing from the more proximal electrodes, which are placed on straight sections of the lead body. For example, the extended bipolar PCT for the Quartet™ LV lead (St. Jude Medical, Sylmar, CA, USA) increased as the pacing electrode moved proximally (D1: 1.1 ± 1.2 V, M2: 2.0 ± 1.8 V, M3: 2.5 ± 2.1 V, P4: 4.1 ± 2.5 V). As a result, pacing incorporated the distal electrode for either true or extended bipolar pacing in 73% of patients. The extended bipolar PCT for Attain Performa LV leads (Medtronic, Minneapolis, MN, USA) also increased as the pacing electrode moved proximally (LV1: 1.0 ± 0.9 V, LV2: 1.3 ± 1.2 V, LV3: 1.5 ± 1.3 V, LV4: 2.1 ± 1.5 V), and the distal electrode was used as the cathode in 44% of patients. The results for the ACUITY X4 spiral leads are unique both within quadripolar as well as bipolar LV leads in that the PCT is lower on the proximal electrodes, and the strong majority of patients are programmed to utilize these electrodes.

Despite being programmed to a nontip electrode in the majority of patients, the pacing capture threshold was ≤ 2.5 V in 96% of patients implanted with a Spiral lead (90% implanted with a Straight lead). The median pacing threshold at 3 months was 1.0 V for Spiral and 1.2 V for Straight leads. This will provide implanting physicians options to pace closer to the basal region of the left ventricle regardless of patient anatomy and will have a positive effect on CRT-D longevity, as high LV pacing output has shown to be a strong determinant of increased battery drain and shorter times to elective replacement.

**Limitations**

The selection of the shape of LV lead and the final pacing cathode were left to the discretion of the implanting physician. Although this reflects the way the lead will be used in routine clinical practice, it limits direct comparisons across the lead types. In the interests of practicality, PCT and PNS were tested based on a prespecified algorithm, which did not examine all possible configurations. The location of the lead implant was not verified independently with off-line review of intraoperative fluorooscopy images and predischarges radiographs. Finally, although pacing predominantly excluded the distal electrode, the impact on long-term outcome remains yet undefined.

**Conclusions**

The ACUITY X4 LV leads are safe and effective with low PCT particularly from proximal electrodes, a high incidence of pacing from the nondistal electrode, and low likelihood of dislodgment or PNS requiring surgical intervention. This was especially true for the novel Spiral designed ACUITY X4 leads.

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**References**

1. Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De Marco T, Carson P, DiCarlo L, DeMets D, White BG, DeVries DW, Feldman AM: Comparison of Medical Therapy, Pacing and D in HF (COM- PANION) I. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med 2004;350:2140-2150.

2. Cleland J, Daubert J, Erdmann E, Freemantle N, Gras D, Kappenberger L, Tavazzi L: The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med 2005;352:1539-1549.

3. Moss AJ, Hall WJ, Cannom DS, Klein H, Brown MW, Daubert JP, Estes NA 3rd, Foster E, Greenberg H, Higgins SL, Pfeffer MA, Solomon SD, Wilber D, Zareba W; MADIT-CRT Trial Investigators: Cardiac-resynchronization therapy for the prevention of heart-failure events. N Engl J Med 2009;361:1329-1338.

4. Tang ASL, Wells GA, Talajic M, Arnold MO, Sheldon R, Connolly S, Hohnloser SH, Nichol G, Birnie DH, Sapp JL, Yee R, Healey JS, Rouleau JL: Resynchronization-Defibrillation for Ambulatory Heart Failure Trial Investigators. Cardiac-resynchronization therapy for mild-to-moderate heart failure. N Engl J Med 2010;363:2385-2395.
phrenic nerve stimulation (PNS) testing at predischarge. The data are presented reflective of the method used for testing. (A) Spiral L; (B) Spiral S; (C) Straight ACUITY X4 leads.

Table S1. Patients with a Failed Implant Using an ACUITY X4 Left Ventricular Lead.