Left Ventricle Three-Dimensional Quadripolar Lead Acute Clinical Study: The LILAC Study

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Aims: This multicenter acute clinical study was designed to verify novel three-dimensional (3D) quadripolar lead designs that can achieve ≤2.5 V average pacing capture threshold (PCT) not only at the apex, but also at the base of the left ventricle with phrenic nerve stimulation (PNS) avoidance for cardiac resynchronization.

Methods: During the implant procedure, up to two different left ventricular investigational leads were introduced and tested in the same target coronary vein based on the coronary sinus venogram in a wedged and unwedged position. Adverse events were collected in 30 days following the procedure.

Results: Eighty-seven leads were tested in 50 patients. When the best performing spiral electrode was chosen from each lead testing, the average of the best PCT on spiral in a wedged position was similar to the unwedged position (1.7 ± 1.5 V vs 1.9 ± 1.5 V, P = ns) and was similar to the wedged tip electrode average PCT (1.7 ± 1.5 V vs 1.6 ± 1.6 V, P = ns). In the majority of patients (89–96%), pacing was achievable in a mid-basal ventricular location without PNS.

Conclusions: This acute study demonstrated that a 3D quadripolar spiral lead design can achieve acceptable PCTs and avoid PNS without repositioning the lead at implant in the vast majority of patients. It also demonstrated that this lead design can achieve mid-basal ventricular stimulation with low PCT and good acute stability. (PACE 2015; 38:438–447)

quadripolar leads, cardiac resynchronization, lead design

Introduction

Cardiac resynchronization therapy (CRT) is recommended treatment for heart failure patients with a left ventricular (LV) ejection function (LVEF) <35% and wide QRS (>120 ms), especially in the presence of a typical left bundle branch block and New York Heart Association class II/IV on optimal medical therapy.1–3 There is also clinical evidence that CRT will benefit patients indicated for pacing in the presence of atrioventricular block when associated with a depressed LVEF < 40%.4,5 In addition, data are available suggesting that LV lead implantation should target viable regions of the left ventricle with a low scar burden6 as well as late local electrical activation.7 Furthermore, there is evidence that a “nonapical” region is associated with better clinical response.6,8

However, there are still important technical challenges. To achieve a successful implantation at the best LV lead location possible, implanters often face the challenges of high pacing threshold, phrenic nerve stimulation (PNS), or apical placement of the electrode to achieve lead stability and good pacing threshold. Additionally, at follow-up, high pacing threshold or PNS may appear. It is recognized that up to 13% of patients at follow-up will develop PNS, especially when the lead pacing site is located at the mid-lateral/posterior and apical sites. In some cases (1.6%), reoperations were needed to resolve symptoms.9 However, in
vast majority of the cases, this may be mitigated by reprogramming.\textsuperscript{9,10}

To improve the implant procedure success and lead location, quadripolar LV leads may offer more options to avoid PNS and target nonapical sites using different pacing vectors on the same lead, as long as the lead design permits capture with acceptable thresholds at multiple sites. It may offer the implanter the option of stability and good pacing capture without repositioning the lead at implant or during follow-up. Finally, it is also conceivable that a better hemodynamic response may be achieved with multipolar leads.\textsuperscript{11–17}

Coronary veins typically taper with smaller diameters in the distal or apical regions in comparison to larger diameters in more proximal or mid to basal regions. Because of the diameter disparity, it is often more difficult to achieve myocardial contact and, therefore, acceptable pacing thresholds in mid-to-basal regions where the best hemodynamic response could be achieved. Adding more electrodes on the lead will not necessarily provide an acceptable pacing threshold, unless the electrodes are in good myocardial contact in those regions. This multicenter acute clinical study was designed to verify that the novel three-dimensional (3D) quadripolar lead designs can achieve ≤2.5 V pacing threshold without changing the target vein not only at the apex, but also at the mid-base of the ventricle with PNS avoidance for cardiac resynchronization. Three different lead configurations were evaluated in order to finalize the optimal electrode placement on the spiral bias and the ideal lead distal straight tip lengths for further clinical human use.

Methods

The LILAC study (Left ventricular Lead Acute Clinical study) sponsored by Boston Scientific Corporation (BSC; St. Paul, MN, USA) was an acute, prospective, nonrandomized, multicenter feasibility clinical investigation that was conducted at nine centers in five countries worldwide. Patients were scheduled to have an LV lead implantation according to current CRT guidelines.\textsuperscript{1–3} Patients who met eligibility criteria for the study gave written informed consent prior to device implant.

During the implant procedure, up to two investigational leads were introduced and tested in the same target coronary vein. The target vein was chosen based on the occlusive coronary sinus venogram and implanting physician’s clinical judgment. The prototype lead was not repositioned in a separate vein in case of high threshold of PNS as a permanent LV lead would have been. The prototype lead was removed at the end of testing and a commercially available LV lead was implanted in the same vein if adequate or in another vein if required. Adverse events were collected in the 30 days following the procedure.

The study was conducted in accordance with the Declaration of Helsinki and all applicable local and national regulations in the countries of submission, and was approved by the Institutional Review Board of all participating hospitals.

Investigational Device

The new investigational quadripolar lead has a 5.2F lead body and 2.6F lead tip, with 3D spiral passive fixation set back from the tip, which leaves the tip with a straight tapered section to enhance maneuverability in tortuous anatomies. Two different straight tip lengths were designed to correspond to different vein lengths (Fig. 1). The straight tip lengths were chosen based on 50 human rotational venogram measurements (BSC, internal data). One electrode was located at the distal tip of the lead. The additional three electrodes spatially oriented on the 3D spiral were designed to overcome high pacing threshold challenges in the mid-base (proximal) ventricular region assuming spiral bias deploying in a vein where the lead could not be wedged may have better electrode-myocardium contact. The electrode placement range on the spiral was determined by the results from an acute 20-pig study conducted by BSC (internal data). The design would allow the lead to be reliably wedged in the most distal position possible in the branch vein for greater stability, while maintaining the ability to pace in a more proximal (mid-basal) location, which may significantly reduce any need to anatomically reposition the lead.

Three investigational quadripolar LV prototype leads S1, S2, and L1 (BSC Model RD1068-R01, R02, and R03) were evaluated. The difference between S1/S2 and L1 is the straight tip length (20 mm for S1/S2 and 35 mm for L1). The difference between S1 and S2 is the electrodes orientation on the 3D spiral (S1-E2 spiral electrode was 27 mm from the lead tip and S2-E2 was 23.5 mm from the lead tip) in order to cover the spiral region and find the optimal electrode placement.
locations on the spiral for further clinical use. The L1 spiral electrode orientation was the same as that of the S2 lead. The interelectrode spacing between the spiral electrodes was 7.5 mm (Fig. 1).

A pacing configuration switch box (BSC Model RD1068-R04) was interfaced between the pacing system analyzer (BSC model 3105) and the investigational quadripolar LV lead to test multiple pacing configurations without manually changing electrical connections at the lead terminals.

**Implant Methods**

During the CRT implantation procedure, up to two different lead models were tested on each patient according to venous anatomy. Two different lead positions were also tested (wedged and unwedged). After the venograms (right anterior oblique [RAO] and left anterior oblique views) were acquired and recorded, the targeted vein was selected by the implanter based on the venous anatomy and best clinical judgment. If a long vein (past the midline of the ventricle) was available, the L1 lead was tested first and then a short tip lead (either S1 or S2) was evaluated. If only a short vein was available, the S1 and/or S2 leads were tested. If two prototype leads were evaluated, both leads were evaluated in the same target vein in each patient. It was predefined that at least 15 leads of each model and 15 S1 + S2 in the same patient would be evaluated in order for the BSC Leads Design and Development Team to optimize the electrode locations on the spiral and select lead distal straight tip lengths for clinical use in humans. After testing, the investigational lead was removed and a market-released LV lead was implanted.

The pacing system analyzer was connected to the lead via a switchbox and cable interface. The return electrode, for use in unipolar pacing configurations, consisted of one of the following: a surface patch electrode placed in the left or right subclavian region (in 15 patients) or a sterile hemostat or other surgical tool placed in electrical contact with tissue at the cut-down site (in 35 patients). A higher unipolar pacing threshold was expected comparing to those using a right subclavian region (in 15 patients) or much smaller anode surface area using a return electrode due to different tissue path or much smaller anode surface area using either the surface patch or surgical instrument tissue contact. Each lead was tested with the following configurations: unipolar E1 (–); unipolar E2 (–); unipolar E3 (–); unipolar E4 (–); bipolar E1 (–) to E3 (+); bipolar E3 (–) to E1 (+) (see Fig. 1). Standard pacing parameters were measured (pacing threshold starting at 10 V at 0.5-ms pulse width, R-wave sensing amplitude, and pacing impedance at 5 V, 0.5 ms). Phrenic nerve or diaphragmatic stimulation threshold for each configuration was performed starting at 10 V at 0.5-ms pulse width.

Pacing capture threshold (PCT) was defined as the lowest voltage with continuous LV capture. PNS threshold was defined as the lowest voltage with palpable diaphragmatic stimulation.

After data from the initial lead tip wedged position were recorded, the lead was then retracted 1–2 cm to a mid-to-basal placement within the same vein, leaving the lead tip in a nonwedged position. The same electrical measurements were performed. All lead testing positions before and immediately after the testing were recorded with cine imaging in the RAO view for further offline analysis.

After the first lead model was withdrawn, the second lead model was positioned using the same methods as described earlier. The implanter would attempt to position the lead in the same location(s) as the first lead. The fluoroscopic images, pacing threshold, R-wave measurement, pacing impedance, and the presence of PNS at 10 V and its stimulation threshold at both wedged and unwedged positions were again collected. After finishing all the experimental testings, the prototype lead was withdrawn and a commercially available LV lead was implanted via the same delivery catheter.

**Data Analysis**

Offline analysis included standard pacing parameters in both wedged and unwedged vein locations, characterizing the success rate for the lead with the ability to achieve acceptable pacing parameters without PNS, and assessing the lead anatomical fit and acute fixation based on the cine analysis.

In each patient, the venogram and lead fluoroscopic images were analyzed using the RAO view to categorize lead positioning according to the basal, mid ventricular (mid), and apical classification (Fig. 2). The determination of fit was achieved by performing evaluation of both the venogram and LV lead fluoroscopic images using Sante DICOM viewer (Santesoft, Athens, Greece). Analyses were made in the still frame that best showed the coronary venous anatomy in diastole. Anatomical measurements were calibrated using the known delivery catheter diameter as a reference. In order to validate lead acute stability, all fluoro images before and after electrical measurement tests were reviewed offline. An acceptable position was defined when all four electrodes were within the target vessel and not in the great cardiac vein.
Figure 2. A representative coronary venogram divided into apical, mid, and basal sections (A); a representative wedged L1 lead with electrodes placed in mid-apical location (B); a representative unwedged L1 lead with electrodes placed in mid-basal location (C).

Statistics

Continuous variables are shown as mean ± standard deviation, while the categorical variables are shown as absolute and relative frequency. Unipolar PCT up to 10 V at each electrode in a wedged position was compared to the unwedged position using a two-sample t-test. The unipolar PCT was compared to the bipolar PCT using a paired t-test. The P value for comparing unipolar PCT of four electrodes at wedged position is derived from analysis of variance. A two-sided P value less than 0.05 was considered statistically significant. Statistical analyses were generated using SAS 9.3 (SAS Institute Inc., Cary, NC, USA).

Results

A total of 54 patients were enrolled to LILAC study. Of the 54 patients: coronary sinus access failed in two patients; in two additional patients, the prototype lead was introduced but could not be placed inside a target vessel for testing due to tortuous anatomy. The remaining 50 patients were tested with the prototype leads. The baseline patient characteristics are presented in Table I.

Among the 50 patients, 87 leads (L1:22, S1:35, and S2:30) were tested in a wedged position. There were fewer unwedged positions tested (L1:14, S1:21, and S2:24) since in some cases the venous anatomy would not allow an unwedged position or the patient’s clinical status precluded more extensive testing.

Lead Position (Wedged Only)

A total of 22 L1 leads were tested. Among those, 20 had good quality fluoroscopic images for final analysis. Eleven (55%) long tip leads were placed at the mid-apex position (tip electrode at the apex and spiral electrodes at the LV mid) and nine (45%) were at the mid-base position (tip electrode at the mid and spiral electrodes at the LV base). When a long tip lead was chosen based on the venogram, 100% of the long tip leads fit in the targeted coronary vein.

A total of 65 S1 and S2 leads were tested in the study. Among those, seven leads from four patients had their spiral electrodes implanted in the great cardiac vein, four leads had no images recorded, and one had very poor fluoro images. Thus, 53 lead fluoro images were used for the electrode anatomic position evaluation. Twenty-two (41%) short tip leads were placed at mid-apex positions, 26 (49%) at mid-base locations, four (8%) at mid-mid locations (both tip and spiral electrodes at the mid of LV), and one (2%) at the apex-apex location (both tip and spiral electrodes at the apex of LV).

In 93% of patients, the tip electrode and spiral electrodes of all lead types were placed in two different anatomical segments. In patients with acceptable lead implant position (excluding four patients with spiral electrode(s) of a lead in the great cardiac vein), 25 patients had the lead implanted in a lateral vein, 20 in a posterior vein, and one in an anterior vein.

| Characteristic                  | Results (%) |
|--------------------------------|-------------|
| Age (years)                    | 66 ± 9      |
| Male gender                    | 46 (85)     |
| Left ventricular ejection fraction (%) | 26 ± 7     |
| QRS duration (ms)              | 149 ± 34    |
| NYHA class I                   | 2 (4)       |
| NYHA class II                  | 17 (31)     |
| NYHA class III                 | 34 (63)     |
| NYHA class unknown             | 1 (2)       |
| Ischemic cardiomyopathy        | 25 (46)     |

NYHA = New York Heart Association; SD = standard deviation.
Table II.

Average Unipolar Pacing Capture Thresholds at Each Electrode, Wedged and Unwedged Position

| Mean PCT V@0.5 ms | Tip Electrode | Spiral Electrode | Best PCT Electrode on Spiral |
|-------------------|--------------|-----------------|-----------------------------|
|                   | E1 Unipolar  | E2 Unipolar     | E3 Unipolar                 | E4 Unipolar     | E2 or E3 or E4 Unipolar |
| Wedged            |              |                 |                             |                 |                          |
| 1.6 ± 1.6         | 2.2 ± 1.9    | 2.5 ± 1.8       | 3.6 ± 2.5                   | 1.7 ± 1.4       |
| Unwedged          | 2.4 ± 2.1*   | 2.4 ± 1.9       | 3.5 ± 2.3**                 | 4.2 ± 2.1       | 1.9 ± 1.5                |

*P < 0.05 E1 wedged versus unwedged. **P = 0.01 E3 wedged versus unwedged. PCT = pacing capture threshold.

Figure 3. Individual unipolar pacing capture threshold from all lead models in a wedged position. Each lead data are plotted with one unique color. The best on spiral electrode occurs 22 times at E2, 12 times at E3, and 14 times at E4.

Electrical Performance

Table II summarizes the mean unipolar PCT in wedged and unwedged positions for all lead models combined. In a wedged position, the mean pacing thresholds of E1, E2, and E3 electrodes were ≤2.5 V, and E4 electrode was at 3.6 V (P < 0.001). The unwedged mean PCT of all four electrodes was higher than those of the corresponding wedged position. However, when the best performing spiral electrode was chosen from each lead testing, the mean of the best PCT on spiral in a wedged position was similar to the unwedged position (1.7 ± 1.5 V vs 1.9 ± 1.5 V, P = ns) and was similar to the wedged tip electrode average pacing threshold (1.7 ± 1.5 V vs 1.6 ± 1.6 V, P = ns). Figure 3 illustrates individual unipolar PCT data in a wedged position. The median value of each electrode PCT was always lower than the mean PCT for all four electrodes, indicating more data were clustered below mean PCT value. Although E1, E2, and E3 individual PCT clustered in the lower region of the plot and E4 PCT spread more along whole measurable range, some of the E4 electrodes had the lowest PCT and served as the best spiral electrode. The occurrence of the only best spiral electrode on the lead with PCT ≤ 2.5 V and no PNS were 22 times...
Figure 4. Percentage of times at least one electrode had an acceptable capture threshold (PCT ≤ 2.5 V or PCT ≤ 3.5 V without PNS). PCT = pacing capture threshold; PNS = phrenic nerve stimulation.

at E2 electrode, 12 times at E3 electrode, 14 times at E4 electrode. As shown in Table II, the mean PCT of the best electrode on the spiral was 1.7 V (median 1.0 V), which was very close to the distal tip electrode E1 (mean 1.6 V, median 1.0 V). This confirms that this lead would be able to provide two distinct zones of pacing with one at the lead tip (mid to apical) and one at the spiral location (mid to base).

In a wedged position, 87%, 67%, or 35% of the patients had one electrode, two electrodes, or all three electrodes on spiral with PCT ≤ 2.5 V, respectively. In an unwedged basal position, more than 80% of patients had at least one unipolar vector option on the spiral with PCT ≤ 2.5 V.

The mean electrode PCT for each lead model as well as the mean of the best spiral electrode in a wedged position were calculated and compared. As expected, the lowest mean PCT in four electrodes was achieved at the tip for all model leads in wedged positions. The more basal location was associated with a higher PCT. However, the best performing electrodes on the 3D spiral, even if more basal than the tip electrode, were associated with an acceptable PCT comparable to all distal tip electrodes in a wedged position. The mean of the best PCT on spiral for S1 lead model was 1.9 ± 1.7 V, for S2 lead model 1.6 ± 1.4 V, and for L1 lead model 1.7 ± 1.3 V. The mean sensing R waves of all lead types at each measurement configuration were ≥5 mV. The mean pacing impedances were within the acceptable range (300–2,000 Ω).

Figure 4 summarizes the percentage of time at least one electrode had an acceptable PCT (≤2.5 V or ≤3.5 V free of PNS or PNS threshold 3 V higher than the PCT) using unipolar configurations only. Overall, 89–96% had at least one electrode on the lead with acceptable PCT without PNS (one zone pacing), 87–93% had at least one electrode on the 3D spiral with acceptable PCT without PNS (proximal zone pacing), and 61–80% had both the tip electrode and at least one electrode on the 3D spiral with acceptable PCT without PNS (two-zone pacing). If bipolar PCTs were collected and included in the analysis, the success rate could have been even higher (not performed due to time constraint during the implantation procedure).

PNS Occurrence

Twenty-four of 46 analyzed patients encountered PNS at 10 V with 0.5-ms pulse width while the leads were wedged. The incidence and average stimulating threshold at each electrode location is summarized in Table III. The majority of PNS was encountered distally (at E1) or apically.
Table III.  
PNS Occurrence, Mean PNS Threshold at Each Electrode Location, and Mean PCT at Those Electrodes that Encountered PNS

| PNS at 10 V @ 0.5 ms | E1 Unipolar | E2 Unipolar | E3 Unipolar | E4 Unipolar | E1–E3 Bipolar | E3–E1 Bipolar |
|----------------------|-------------|-------------|-------------|-------------|--------------|--------------|
| Occurrence (No. of patients) | 19          | 12          | 9           | 7           | 16           | 14           |
| Mean PNS threshold (V)     | 3.2 ± 2.0   | 4.3 ± 2.2   | 4.7 ± 1.6   | 6.2 ± 3.0   | 4.8 ± 3.3    | 5.3 ± 2.0    |
| Mean PCT (V)              | 1.4 ± 1.4   | 1.8 ± 2.3   | 2.0 ± 1.8   | 2.6 ± 3.2   | 1.9 ± 1.9    | 2.5 ± 1.7    |

PCT = pacing capture threshold; PNS = phrenic nerve stimulation.

mean PNS threshold was also the lowest at E1 and gradually increased from E1 to E4 (apical to basal location of the heart). The mean PCT at each electrode configuration that encountered PNS is summarized in Table III as well. The bipolar E1–E3 and E3–E1 stimulation increased the mean PNS threshold by 1.6 V ($P < 0.01$) and 0.5 V ($P = \text{ns}$) compared to the corresponding E1 and E3 unipolar mean PNS threshold; the bipolar mean PCT increased only by 0.5 V ($P < 0.01$) for both. By switching E1 from unipolar pacing to E1–E3 bipolar pacing, 42% (10/24) of E1 electrode became free (>10 V) of or without (>3 V higher than PCT) PNS and only 8% (2/24) had slightly lowered PNS threshold; by switching E3 from unipolar to E3–E1 bipolar pacing, 31% (5/16) E3 electrode became free of or without PNS and at the same time, 38% (6/16) had lowered PNS threshold (Fig. 5).

No investigational device-related adverse effects occurred during this acute study.

**Limitations**

This study was an acute feasibility study limited to a small, however, cross geographical population. The study was not powered or designed to evaluate clinical outcomes. Since this was an acute lead prototype validation study for BSC new lead design and development purposes and the lead had to be removed after testing, for patient safety concern the testing duration was limited to 30 minutes or less. Up to two leads and four lead positions were tested; only six vector data were collected. The bipolar vectors among the E2, E3, and E4 were not collected, which may have more favorable effect on PNS avoidance due to shorter electrode distance compared to E1–E3 and E3–E1 and equal electrode surface area, which could avoid anode pacing phenomenon observed in E3–E1 bipolar pacing. In addition, unipolar thresholds were measured using a surgical tool as the anode. Lower thresholds could have been recorded using the pulse generator instead.

In order to validate the electrode position on spiral, an acceptable position was defined when all four electrodes were within the target vessel and not in the great cardiac vein. If the lead position was unacceptable, the corresponding electrode measurement data were excluded from the electrical parameter analysis. A total of four patients’ data were excluded from the analysis for reasons described earlier. It is recognized that excluding the data from these patients may create some bias on the study results.

Since this is an acute human study and the prototype leads were removed after the measurements, a chronic human study will be needed to evaluate the lead long-term stability and threshold values.

**Discussion**

This acute study demonstrated that a novel quadripolar 3D spiral lead design can achieve acceptable pacing thresholds with PNS avoidance and without lead repositioning in CRT patients. It also demonstrated that this 3D lead design can achieve mid-basal ventricular stimulation most of the time with acceptable stimulation threshold and acute stability. Of note, the prototype lead was not repositioned in a separate vein to obtain even better measurements such as the implanter would do in a clinical implant. It is possible that in clinical practice, such a lead design could perform even better when implanted in the best suitable vein location. The lead design has a distal tip electrode and three clustered spiral electrodes located more proximally. Two zone pacing (mid-apical and mid-base) with this lead was achieved by similar average capture pacing threshold at tip electrode (1.6 V) and at the best proximal spiral electrode (1.7 V; Table II). It was expected that the pacing threshold would be lower toward the apical location and higher toward the base due to vein size and myocardial contact. However, our data showed that regardless of where the spiral was located, whether in a small or a large vein, in
a wedged or an unwedged position, there is at least one electrode on the 3D spiral that would face the myocardium with an acceptable pacing threshold (≤2.5 V). In many cases, two or even all three spiral electrodes had ≤2.5 V pacing threshold. The PNS occurrence was found more frequently at apical, mid-lateral, and mid-posterior LV sites in a 1,307 patients study. LV stimulation at mid-basal sites might be the ideal location to manage the PNS. However, a proximal LV lead placement to avoid PNS may increase the risk of lead dislodgement and encounter higher LV pacing threshold. Furthermore, high LV pacing thresholds affect battery longevity and increase the risk of postimplant PNS due to higher pacing output.

Clinical studies of a market-released quadripolar lead aiming at successful PNS mitigation via 10 programmable vectors reported the need of repositioning the lead away from the target vein at implant in 37% and 40% of cases which is higher than conventional LV lead implantations. Repositioning in the Quartet trials might be due to PNS, high mid-basal pacing threshold, and the lead anatomical unfit. In this study, using different quadripolar lead designs with two different tip lengths and spiral electrodes, acceptable PCT without PNS was achieved in more than 90% of patients in the first implanted target vein.

Only unipolar PCT data up to 10 V @ 0.5 ms were used for mean data calculation and success
rate analysis in this study. Prior data demonstrated that unipolar pacing threshold provides a relative threshold ranking among the electrodes, which is associated to the proximity of each electrode to viable myocardium. It should be noted that the unipolar anode used in the study was mostly a surgical tool in the surgical field, not the RV coil or pulse generator which has much bigger surface area and may achieve lower threshold.

PNS occurrence may be as high as 37% of patients at implant. In this study, we observed even higher incidence (52%) due to more electrodes on the lead than conventional LV leads, more lead positions evaluated, and two leads tested in the same vein in each patient. By switching from unipolar to bipolar (electronic repositioning) at E1 electrode location, more electrodes became available for pacing without PNS. However, by switching from E3 unipolar pacing to E3–E1 bipolar pacing, more PNS occurred. It could be caused by E1 anode pacing due to lower PNS threshold at E1 and smaller E1 electrode surface area than the spiral electrode surface area. E1 as an anode in such cases should be avoided. A bipolar pacing configuration with a much shorter bipole (E2–E3 or E4–E3) may have even more favorable effect on PNS avoidance.

In this study, seven leads from four patients (8%) had their short tip spiral electrodes implanted in the great cardiac vein that was unfit for the leads. In clinical practice, this location is rarely suitable for CRT and rarely used.

With more electrodes and potentially more vectors to choose from for pacing and pacing zone switching capability, this new quadripolar lead design could successfully mitigate the PNS without repositioning the lead and achieve midventricular or basal site pacing. Thus the use of such leads in clinical practice, where implanters would attempt many veins to avoid PNS or use many more pacing configurations to achieve acceptable PCT at best anatomical location, may prove to be even better than this acute study measurements.

Conclusions

This acute pilot study using three different 3D quadripolar lead designs demonstrated human anatomic fit and good electrical performance associated with PNS avoidance. The range of spiral electrode placement and straight tip lengths were adequate in this tested group of patients. Multiple zone pacing where a nonapical segment can be adequately paced was also achieved. This acute study has contributed to the BSC design and development of new quadripolar leads and will offer to the implanters better options at time of implantation and hopefully better clinical outcomes in CRT.

References

1. Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA III, Freedman RA, Gettes LS, Gillinov AM, et al. 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2013; 61:66–675.

2. Exner DV, Birnie DH, Moe G, Thibault B, Philippin F, Healey JS, Tang AS, et al. Canadian Cardiovascular Society Guidelines on the use of cardiac resynchronization therapy: Evidence and patient selection. Can J Cardiol 2013; 29:182–195.

3. Brignole M, Auricchio A, Baron-Esqviais G, Bordachar P, Boriani G, Breithardt OA, Cleland J, et al. 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: The Task Force on Cardiac Pacing and Resynchronization Therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). Europace 2013; 15:1070–1118.

4. Martinelli FM, de Siqueira SF, Costa R, Greco OT, Moreira LF, D’Avila A, Heist EK. Conventional versus biventricular pacing in heart failure and bradyarrhythmia: The COMBAT study. J Card Fail 2010; 16:293–300.

5. Curtis AB, Worley SJ, Adamson PB, Chung ES, Niazi I, Sherfesee L, Shinn T, et al. Biventricular pacing for atrioventricular block and systolic dysfunction. N Engl J Med 2013; 368:1585–1593.

6. Khan FZ, Virdée MS, Palmer GR, Pugh PJ, O’Halloran D, Elsik M, Read PA, et al. Targeted left ventricular lead placement to guide cardiac resynchronization therapy: The TARGET study: A randomized, controlled trial. J Am Coll Cardiol 2012; 59:1509–1518.

7. Gold MR, Yu Y, Singh JP, Stein KM, Bigersdorf-Green U, Meyer TE, Seth M, et al. The effect of left ventricular electrical delay on AV optimization for cardiac resynchronization therapy. Heart Rhythm 2013; 10:988–993.

8. Thebault C, Donal E, Meunier C, Gervais R, Gerritse B, Gold MR, Abraham WT, et al. Sites of left and right ventricular lead implantation and response to cardiac resynchronization therapy observations from the REVERSE trial. Eur Heart J 2012; 33:2662–2671.

9. Biffi M, Exner DV, Croessegh GH, Ramza B, Coutu B, Tomassoni G, Kragin W, et al. Occurrence of phrenic nerve stimulation in cardiac resynchronization therapy patients: The role of left ventricular lead type and placement site. Europace 2013; 15:77–82.

10. Goetze S, Defaye P, Bauer A, Merkel M, Bizeau O, Treusch S, Contzen K, et al. Phrenic nerve stimulation in CRT patients and benefits of electronic lead repositioning: The ERACE trial. J Interv Card Electrophysiol 2013; 38:1–9.

11. Forleo GB, Della Rocca DG, Papavasilieou LP, Molfetta AD, Santini L, Romeo F. Left ventricular pacing with a new quadripolar transvenous lead for CRT: Early results of a prospective comparison with conventional implant outcomes. Heart Rhythm 2011; 8:31–37.

12. Mehta PA, Shetty AK, Squire M, Bostock J, Rinaldi CA. Elimination of phrenic nerve stimulation occurring during CRT: Follow-up in patients implanted with a novel quadripolar pacing lead. J Interv Card Electrophysiol 2012; 33:43–49.

13. Sperzel J, Danischel W, Gutleben KJ, Kragin W, Mortensen P, Connelly D, Trappe HJ, et al. First prospective, multi-centre clinical experience with a novel left ventricular quadripolar lead. Europace 2012; 14:365–372.

14. Forleo GB, Mantica M, Di BL, Panattoni G, Della Rocca DG, Papavasilieou LP, Santamaria M, et al. Clinical and procedural outcome of patients implanted with a quadripolar left ventricular lead: Early results of a prospective multicenter study. Heart Rhythm 2012; 9:1822–1828.

15. Ohlow MA, Lauer B, Brunelli M, Daralammouri Y, Goller C. The use of a quadripolar left ventricular lead increases successful implantation rates in patients with phrenic nerve stimulation.
and/or high pacing thresholds undergoing cardiac resynchronisation therapy with conventional bipolar leads. Indian Pacing Electrophysiol J 2013; 13:58–65.

16. Valzania C, Eriksson MJ, Biffi M, Boriani G, Gadler F. Acute changes in electromechanical parameters during different pacing configurations using a quadrupolar left ventricular lead. J Interv Card Electrophysiol 2013; 38:61–69.

17. Asbach S, Hartmann M, Wengenmayer T, Graf E, Bode C, Biermann J. Vector selection of a quadrupolar left ventricular pacing lead affects acute hemodynamic response to cardiac resynchronization therapy: A randomized cross-over trial. PLoS One 2013; 8: e67235.

18. Blendea D, Shah RV, Auricchio A, Nandigam V, Orencole M, Heist EK, Reddy VY, et al. Variability of coronary venous anatomy in patients undergoing cardiac resynchronization therapy: A high-speed rotational venography study. Heart Rhythm 2007; 4:1155–1162.

19. Singh JP, Klein HU, Huang DT, Reek S, Kuniss M, Quesada A, Barsheshet A, et al. Left ventricular lead position and clinical outcome in the multicenter automatic defibrillator implantation trial-cardiac resynchronization therapy (MADIT-CRT) trial. Circulation 2011; 123:1159–1166.

20. Biffi M, Bertini M, Ziacchi M, Gardini B, Mazzotti A, Massaro G, Diemenger I, et al. Management of phrenic stimulation in CRT patients over the long term: Still an unmet need? Pacing Clin Electrophysiol 2011; 34:1201–1208.

21. Biffi M, Zanon F, Bertaglia E, Padeletti L, Varbaro A, De ST, Boriani G, et al. Short-spaced dipole for managing phrenic nerve stimulation in patients with CRT: The “phrenic nerve mapping and stimulation EP” catheter study. Heart Rhythm 2013; 10:39–45.

22. Biffi M, Foerster L, Eastman W, Eggen M, Grenz NA, Sommer J, De ST, et al. Effect of bipolar electrode spacing on phrenic nerve stimulation and left ventricular pacing thresholds: An acute canine study. Circ Arrhythm Electrophysiol 2012; 5:815–820.