Boston Scientific

CLINICAL SUMMARY

GDT1000 SENSING ACUTE STUDY

CAUTION: Federal law restricts this device to sale by or on the order of a physician trained or experienced in device implant and follow-up procedures.

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CLINICAL STUDY - SUMMARY OF GDT1000 SENSING ACUTE STUDY

CLINICAL STUDY POPULATIONS

GDT1000 study included patients indicated for a CRT-D device. Excluded from the study were patients meeting any of the following criteria:

- Having no intrinsic P and/or R waves at implant
- Having a pre-existing unipolar pacemaker that was not to be explanted/ abandoned
- Enrolled in a concurrent study that would confound the study results
- Having ventricular tachyarrhythmias associated with a reversible cause (e.g., digitalis toxicity, hypoxia, sepsis, transient electrolyte imbalance, acute myocardial infarction, electrocution, or drowning)
- Women who were pregnant or planned to become pregnant
- Having a prosthetic mechanical tricuspid heart valve

SUMMARY

This clinical investigation was a 50 patient, multi-center, acute study conducted at seven (7) centers in the United States. The main purpose of this clinical investigation was to characterize the performance of the new Automatic Gain Control (AGC) sensing platform, with the Dynamic Noise Adjustment (DNA) feature, that is used in both COGNIS and TELIGEN devices. The AGC sensing platform was studied using a Guidant Acute Sensing Device (GASD) system, a non-implantable device containing the COGNIS/TELIGEN system board, hardware, and firmware required for sensing intracardiac signals. The study enrolled a total of 50 patients and was conducted in two phases. In the first phase, 28 of 30 patients completed protocol testing. The algorithm was modified after the first phase, and it was re-evaluated in the second phase, in which 17 of 20 patients completed protocol testing. Of the five patients who did not complete testing in the two phases, three were attempts, and two were intents.

STUDY DESIGN

Four scenarios were tested, including different combinations of sensed atrial signals (AS), paced atrial signals (AP), sensed ventricular signals (VS), and paced ventricular signals (VP), i.e., AS/VS, AS/VP, AP/VS, and AP/VP. Sensing algorithm performance was analyzed from patients' real-time electrograms (EGM) and electronic signals. Primary analysis was performed by visually reviewing the EGM and markers of the printed strips for proper sensing, as well as for instances of undersensing and oversensing.

Additional analysis included tabulating the sensed and paced events stored in the patient data files from the patient CD-ROM. During this tabulation, unexpected events were noted. An example of an unexpected event is a sensed event during an AP/VP testing scenario. The sensed event could be a real event, such as a PVC, or an oversensed event. These unexpected events were evaluated by viewing the electronic signals stored in the patient data files and correlating these signals to the printed strips.

Methods

The sensitivity, specificity, positive predictive value, rate of oversensing, and rate of undersensing of the sensing algorithm were analyzed for each chamber. A true positive (TP) is the number of intrinsic/paced signals appropriately sensed, a false positive (FP) is the number of intrinsic/paced signals from the opposite chamber oversensed, a false negative (FN) is the number of intrinsic/paced signals undersensed, and a true negative (TN) is the number of intrinsic/paced signals from the opposite chamber appropriately not sensed. The sensing sensitivity was calculated as TP/(TP+FN), specificity as TN/(TN+FP), positive predictive value (PPV) as TP/(TP+FP), rate of oversensing as FP/(TP+FP), and rate of undersensing as FN/(TP+FN).

The sensing performance results from the first phase of the study are provided and compared to the results from the second phase in order to demonstrate the improvement in the operation of the updated sensing algorithm following the between-phase changes. Results from the second phase of the study are the most clinically relevant, as they reflect the performance of the final sensing algorithm implemented in the COGNIS/TELIGEN devices.

The GDT1000 protocol did not pre-specify acceptable sensitivities, specificities, PPV, rates of oversensing, or rates of undersensing for the RA, RV, and LV channels.

STUDY RESULTS

Demographic Data

The table below shows the characteristics of the patients implanted or attempted (Table 1).

Table 1. All patients implanted or attempted, Phase 1 and Phase 2

Characteristic	Measurement	Phase 1 Result (N=29)	Phase 2 Result (N = 19)
Age at implant	Mean ±SD	65.8 ±12.2	68.1 ± 9.6
	Range	[44.6, 85.5]	[51.3, 81.8]
Gender [N (%)]	Female	14 (48.0)	14 (74.0)
	Male	15 (52.0)	5 (26.0)
NYHA Class [N(%)]	III	27 (93)	19 (100)
	IV	2 (7)	0 (0)
LVEF (%)	Mean ± SD	22.4 ± 7.7	23.5 ± 6.4
	Range	[10.0, 35.0]	[15.0, 35.0]
QRS Duration	Mean ±SD	161 ± 29	149 ± 30
	Range	[124, 248]	[106, 220]
Cardiac Disease [N (%)]	Nonischemic Cardiomyopathy	14 (48)	7 (37)
	Ischemic Cardiomyopathy, CAD	10 (34)	9 (47)
	Hypertension	3 (10)	0 (0)
	Coronary Artery Disease (CAD)	1 (3)	0 (0)
	Ischemic Cardiomyopathy, no CAD	1 (3)	3 (16)
	Valvular Heart Disease	0 (0)	1 (5)
	Other	0 (0)	1 (5)

Lead Position

In this study, the position of each lead was per physician's discretion. A majority of the atrial leads in the first/second phase of the study were placed in the right atrial appendage (19/12) with the remaining placed in the lateral wall (5/2), septal wall (2/3), and unspecified location (1/0). A majority of the right ventricular leads were implanted in the right ventricular apex, with the remaining placed in the septal wall (0/1) and unspecified location (1/0). A majority of the left ventricular leads were implanted in the lateral, postero-lateral, or posterior wall (21/15), with the remaining placed in an antero-lateral, anterior, or postero-septal location (4/3).

Lead Configurations

In this study, both RA and RV leads used a bipolar configuration, which was not programmable. The LV lead configuration programming was per physician's discretion. In the first phase, 20 patients had LV sensing programmed to the LVtip>>LVring configuration, four to LVtip>>RVcoil, and one to LVtip>>Can. In the second phase, 13 patients had LV sensing programmed to the LVtip>>LVring configuration, and four to LVtip>>RVcoil.

Lead Performance

The lead performance, including pacing threshold, pacing impedance and sensing amplitude, were measured at implant by a commercially available Pacing System Analyzer (PSA). The results are provided in the table below (Table 2).

Table 2. Lead performance

Measurement	Lead Location	Number of Leads: Phase 1	Mean ± SD: Phase 1	Number of Leads: Phase 2	Mean ± SD: Phase 2
Pacing Impedance (Ω)	Left Ventricle	25	1034 ± 394	18	779 ± 227
	Right Atrium	28	520 ± 161	17	519 ± 112
	Right Ventricle	29	816 ± 263	18	649 ± 206
Pacing Threshold (V)	Left Ventricle	25	1.9 ± 1.4	18	1.3 ± 1.0
	Right Atrium	28	1.1 ± 0.7	16	1.2 ± 0.6

Table 2. Lead performance

Measurement	Lead Location	Number of Leads: Phase 1	Mean ± SD: Phase 1	Number of Leads: Phase 2	Mean ± SD: Phase 2
	Right Ventricle	29	1.0 ± 0.4	18	0.8 ± 0.3
Sensing Amplitude (mV)	Left Ventricle	25	14.1 ± 7.6	18	13.2 ± 7.3
	Right Atrium	28	2.9 ± 1.5	16	3.7 ± 3.3
	Right Ventricle	29	12.3 ± 6.2	18	13.4 ± 7.0

Sensing Performance

In the first phase of the study, a total of 55,207 signals were recorded, including 54,151 appropriate sensed intrinsic and paced beats and 1,056 inappropriate sensed events (223 undersense and 833 oversense events). The sensing algorithm used in the first phase achieved the sensitivities, specificities, positive predictive values (PPV), rates of undersensing (1-sensitivity), and rates of oversensing (1-PPV) are summarized in the table below (Table 3).

Table 3. Summary of Sensing Performance - First Phase

	Sensitivity (Rate of Undersensing)	Specificity	Positive Predictive Value (Rate of Oversensing)	Appropriate Sensed Beats	Inappropriate Sensed Beats: Undersense	Inappropriate Sensed Beats: Oversense
Right Atrial Channel	100% (0%)	96.81%	97.03% (2.97%)	19,478	0	615
Right Ventricular Channel	100% (0%)	98.94%	98.86% (1.14%)	18,439	0	216
Left Ventricular Channel	98.63% (1.37%)	99.99%	99.99% (0.01%)	16,054	223	2
Totals				54,151	223	833

In the second phase of the study, a total of 35,998 signals were recorded including 35,831 appropriate sensed intrinsic and paced beats and 171 inappropriate sensed events (2 undersense and 169 oversense events). The upgraded sensing algorithm used in the second phase achieved the sensitivities, specificities, positive predictive values (PPV), rates of undersensing (1-sensitivity), and rates of oversensing (1-PPV) summarized in the table below; the table also summarizes the results of the analysis from the second phase (Table 4).

Table 4. Summary of Sensing Performance - Second Phase

	Sensitivity (Rate of Under-sensing)	Specificity	Positive Predictive Value (Rate of Over-sensing)	Appropriate Sensed Beats	Inappropriate Sensed Beats: Undersense	Inappropriate Sensed Beats: Oversense
Right Atrial Channel	100% (0%)	98.64%	98.54% (1.46%)	11,372	0	168
Right Ventricular Channel	100% (0%)	100%	100% (0%)	12,230	0	0
Left Ventricular Channel	99.98% (0.016%)	99.99%	99.99% (0.008%)	12,227	2	1
Totals				35,831	2	169

Comparing the performance between the two phases, there were 1,056 inappropriate sensing events out of 55,027 signals (1.919%) in the first phase of the study, and a total of 171 inappropriate sensing events out of 35,998 signals (0.475%) in the second phase of the study, reflecting a 75.2% reduction in inappropriate sensing events from phase one to two.

Oversense Events

During the analysis of the first phase data, some unexpected oversense events were identified. There were a total of 831 oversense events in the RA (615) and RV (216) channels in phase one. The majority of the RA and RV oversense events were attributed to an artificial event introduced while pacing. This type of oversense was observed in 6 patients in the RA channel and 7 patients in the RV channel. The results for the second phase of the study demonstrated that oversensing artificial events observed in the first phase of the study were successfully eliminated by using

the upgraded GASD system. There were no artificial events introduced in the second phase of the study.

In the second phase, a total of 168 oversense events in the RA channel were observed in one patient. This patient had an intrinsic P-R interval greater than 300 ms. In order to complete the AP/VS test scenario, the device was programmed with a LRL = 80 bpm and AV Delay = 300 ms, which is the maximum allowable AV Delay in a CRT-D device. At the end of the AV Delay, no intrinsic activity occurred and the device paced both ventricles. These paced beats were oversensed by the atrial channel. If the atrial blanking period were programmed to a larger value, atrial oversensing would have been eliminated. Therefore, excluding this patient's AP/VS test scenario from the analysis, there were no undersensing or oversensing events in the RA channel.

In one patient, the single oversense event in the LV channel was caused by noise.

Undersense Events

LV undersense events (223) in the first phase of the study primarily occurred in one patient whose LV intrinsic amplitude was less than 1.0 mV, which is much smaller than the clinically acceptable threshold. This small LV intrinsic amplitude resulted in undersensing some LV events.

Two LV undersense events occurred in the second phase of the study. A potential cause for the LV undersense events was premature ventricular contractions while atrial pacing.

Conclusions

This acute study demonstrated excellent sensitivity (100% in the RA, 100% in the RV, and 99.98% in the LV channels), specificity (98.64% in the RA, 100% in the RV, and 99.99% in the LV channels), and positive predictive values (98.54% in the RA, 100% in the RV, and 99.99% in the LV channels). In conclusion, the new sensing platform evaluated in the GDT1000 study will be implemented in COGNIS/TELIGEN devices.

By excluding one patient's oversensed events that could be eliminated by programming a longer atrial blanking period, the modified specificity and positive predictive values in the RA channel are 100% and 100% (oversensing eliminated). While the GDT1000 protocol did not pre-specify acceptable sensitivities, specificities, or PPV values, a Sensing Tape Testing DAT report for COGNIS/

TELIGEN on file at Boston Scientific CRM[1] reported a 99.96% sensitivity (0.04% Undersensing) and a 99.97% positive predictive value (0.03% Oversensing) for the RV channel in normal sinus rhythm. Using the RV values as a benchmark (RA and LV values were not calculated), the results of this study compare favorably.

1. Sensing Tape Testing Design Analysis Test report 100019-687 Revision A describes testing performed in which the COGNIS/TELIGEN sensing platform is modeled and compared to a previous Guidant device, CONTAK RENEWAL TR. The analysis was performed using 219 patient rhythms from the Gold Development Database, including normal sinus rhythm and atrial and ventricular arrhythmias.

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