Efficacy of a New Discrimination Algorithm: Results from a Multicenter Dual-Chamber ICD Clinical Trial

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Summary

Appropriate discrimination of ventricular tachyarrhythmias and supraventricular tachyarrhythmias has improved with the introduction of dual-chamber implantable defibrillators (ICDs). However, even in fifth-generation devices, inappropriate therapy can still be delivered due to a misdiagnosis of supraventricular tachyarrhythmias. This investigation evaluated the new SMART Detection timing-based discrimination algorithm included in the Phylax AV ICD. Between February 1999 and September 2000, 192 patients received a Phylax AV ICD in this prospective multicenter trial. A total of 1415 sustained spontaneous or induced tachyarrhythmia episodes with associated stored IEGMs were retrieved from the ICD and reviewed by study investigators; 267 episodes were supraventricular tachycardias, and 1148 ventricular tachycardias or ventricular fibrillation episodes. The sensitivity for detection of sustained VT or VF was 100 %, and specificity of the algorithm for discriminating supraventricular tachyarrhythmias from VT/VF was 93.3 % (249 of 267 episodes). The overall results from this clinical study demonstrate a significant improvement in discrimination success of the Phylax AV compared to other dual-chamber ICDs.

Key Words

Dual-chamber ICD, arrhythmia classification, algorithms, detection specificity, prospective studies

Introduction

As implantable cardioverter-defibrillators (ICDs) continue to evolve, the focus of innovation in these devices over the past five years has been to reduce size and enhance diagnostic features. However, delivery of inappropriate ventricular therapy for benign supraventricular tachycardias (SVTs) remains the most frequent clinical side effect in ICD patients [1-3]. Atrial fibrillation in particular is cited most often as the cause for inappropriate shocks [4-6], which occurs in up to 41 % of all single-chamber ICD patients [2,7-9]. A high incidence of inappropriate therapy due to misclassification of SVT as ventricular tachycardia (VT) remains a significant problem.

Dual-chamber ICDs, first introduced in 1997, held the promise of improved specificity in the detection of SVTs. However, subsequent clinical results have shown that these dual-chamber discrimination algorithms provide only incremental improvements over their single-chamber predecessors. The results of a recent, dual-chamber ICD study involving the Gem DR and Jewel AF (Medtronic, USA) models showed that SVTs are responsible for 19 % of episodes diagnosed as VT [10]. In another study involving the Ventak Mini ICD (Guidant, USA), 52 (24 %) of 218 atrial fibrillation or flutter episodes were treated inappropriately [11]. The aim of the Phylax AV study was

Lead model		Number of leads
Elox		18
FH		2
Polyrox	(Biotronik, Germany)	15
Retrox		45
Synox		19
Fineline	(Guidant, USA)	5
Sweet Tip		4
Thinline	(Intermedics, USA)	2
CapSure	(Medtronic, USA)	2
CapSureFix		6
Tendril DX	(Pacesetter, USA)	65
Oscor	(Sulzer Oscort, Switzerland)	14

Table 1. Distribution of atrial leads.

to demonstrate improvements in safety and clinical efficacy of a new SMART Detection (Biotronik, Germany) discrimination algorithm incorporated in this dual-chamber ICD.

SMART Detection

The atrioventricular classification algorithm incorporated in the Phylax AV ICD performs an arrhythmia analysis in a stepwise fashion by continuously monitoring the rate and relative relationships of atrial (A) and ventricular (V) signals. Classification is based on five tests applied simultaneously to both the atrial and ventricular rhythm on an ongoing basis. These tests include an assessment of averaged A and V rates and an evaluation of A and V stability. Stability of the rhythm is computed by comparing the current measured interval in either the atrium or the ventricle to a moving average of the previous four intervals. A ratio check of atrial events to ventricular events is also performed. In addition, a P-R trend test evaluates the coupling interval of A and V events over time, specifically confirming or ruling out monotonic changes of the atrial and ventricular signals. Finally, an Onset criterion is used in a limited fashion to distinguish sinus tachycardias with a gradual rate increase from ventricular tachyarrhythmias characterized by a sudden increase in heart rate. The Onset criterion is only applied if a 1:1 relationship between atrial and ventricular events is present during a tachyarrhythmia episode.

Duration (days)	Number of implants
≤ 30	9
31 – 60	6
61 – 90	7
91 – 180	49
> 180	121

Table 2. Implant Duration. n = 192.

Materials and Methods

A U.S. Food and Drug Administration (FDA) clinical study was conducted to evaluate the Phylax AV dual-chamber ICD from February 1999 to October 2000 in which a total of 23 investigational centers participated. The purpose of this prospective study was to evaluate the safety and efficacy of this ICD as well as the ability of the device to distinguish between VTs and SVTs. Candidates for participation were required to meet standard ACC/AHA Guidelines for ICD implantation [12]. These guidelines included either survival of at least one episode of cardiac arrest (manifested by a loss of consciousness) due to a VT, or recurrent, poorly tolerated sustained VT. Contraindications for participation in the study were the same as for a standard ICD. The Phylax AV study protocol specified ventricular fibrillation (VF) induction testing at implant, and standard device interrogation and lead evaluations at hospital pre-discharge and subsequent follow-up visits to be scheduled every 3 months until study completion.

All Phylax AV dual-chamber defibrillators were implanted with either a Kainox SL lead or a SL-ICD lead (Biotronik) in the ventricle but with any atrial sensing and pacing lead. The most common atrial lead used in the study was the Tendril DX (St. Jude Medical, USA) followed by the Retrox (Biotronik) (Table 1).

Diagnostics available in the Phylax AV include event recording of tachyarrhythmia detection and subsequent therapy status, high-resolution storage of IEGMs, and episode recording of events in which therapy was withheld (SMART Detection success). This occurred whenever SMART Detection classified the event as an SVT. All stored tachyarrhythmia events in the ICD were retrieved from the device and made available for review by clinical investigators.

		Patients
Patient age (years)	Mean ± SE	66 ± 1
	Range	22 – 87
Gender	Male	166 (86.5 %)
	Female	26 (13.5 %)
Left ventricular ejection fraction	Mean ± SE	31 ± 1 %
	Range	5 – 65 %
Primary cardiac disease	CAD	151 (78 %)
	Nonischemic or dilated cardiomyopathy	1 (0.5 %)
	Valvular disease	30 (15.6 %)
	Primary electrical disease	7 (3.6 %)
	Other cardiac diseases	3 (1.6 %)
Primary tachyarrhythmia	VF/VT	80 (41.7 %)
	MVT	127 (66.1 %)
Concomitant therapy	No concomitant therapy	99 (51.6 %)
	Antiarrhythmic drug therapy	93 (48.4 %)

Table 3. Patient Demographics. n = 192; SE = standard error of the mean; CAD = coronary artery disease; VF = ventricular fibrillation; VT = ventricular tachycardia; MVT = monomorphic ventricular tachycardia.

Results

Patient Demographics

All data are presented as mean values ± standard error of the mean (SE). A total of 192 patients were enrolled in the Phylax AV study with a cumulative implant duration of 1717.9 patient months and a mean implant duration of 8.9 ± 0.4 months (Table 2). Other patient demographics were as follows: The mean patient age was 66 ± 1 years, and ranged from 22 to 87. Patient gender in this study was 86.5 % male. The mean left ventricular ejection fraction of this patient group was 31 % ± 1 % with a range of 5 – 65 %. Coronary artery disease was the primary disease in 78 % of patients enrolled, followed by valvular disease (15.6 %), primary electrical disease (3.6 %), and other cardiac diseases (1.6 %). Monomorphic VT was the primary tachyarrhythmia in 66.1 % of patients, while 41.7 % had prior ventricular fibrillation or polymorphic VT events (Table 3).

ICD

The Phylax AV ICD was specifically selected because of its dual-chamber bradycardia pacing capability in 88 (45.8 %) patients, while SVT discrimination was listed as the reason for implant in 140 (72.9 %) patients. Other considerations were listed in an additional five (2.6 %) patients. Note that an investigator could indicate more than one reason for selecting the dual-chamber ICD.

Safety Margin Evaluation

Study investigators were required to evaluate the safety margin of VT/VF conversions at the time of device implantation. Two options were provided in the protocol. The investigator could perform two successful conversions at 20 J or less, or conduct step-down defibrillation threshold (DFT) testing. Testing results from each of these categories are summarized as follows:

		P-wave	Pacing threshold	Pacing impedance
Implant	No. of tests	196	197	200
	Mean ± SE	3.6 ± 0.1 mV	0.8 ± 0.1 V	483 ± 10 Ω
	Range	0.2 – 7.8 mV	0.2 – 7.2 V	300 – 1280 Ω
Pre-discharge follow-up	No. of tests	194	193	200
	Mean ± SE	3.6 ± 0.1 mV	0.7 ± 0.1 V	466 ± 9 Ω
	Range	0.2 – 7.8 mV	0.1 – 5.2 V	310 – 1240 Ω
3-month follow-up	No. of tests	140	141	145
	Mean ± SE	4.0 ± 0.2 mV	1.3 ± 0.1 V	16.3 ± 0.7 Ω
	Range	0.2 – 7.8 mV	1.2 – 5.8 V	280 – 980 Ω
Other follow-ups	No. of tests	494	479	522
	Mean ± SE	3.8 ± 0.1 mV	1.2 ± 0.1 V	473 ± 5 Ω
	Range	0.2 – 7.8 mV	0.1 – 7.2 V	260 – 1050 Ω

Table 4. P-wave amplitude, atrial pacing threshold, and atrial pacing impedance.

		R-wave	Pacing threshold	Pacing impedance
Implant	No. of tests	199	201	202
	Mean ± SE	15.0 ± 0.6 mV	0.6 ± 0.1 V	606 ± 7 Ω
	Range	4.2 – 32.0 mV	0.1 – 1.7 V	400 – 1080 Ω
Pre-discharge follow-up	No. of tests	201	198	200
	Mean ± SE	14.3 ± 0.6 mV	0.7 ± 0.1 V	556 ± 6 Ω
	Range	2.5 – 32.0 mV	0.1 – 6.4 V	400 – 800 Ω
3-month follow-up	No. of tests	138	147	147
	Mean ± SE	16.3 ± 0.7 mV	1.2 ± 0.1 V	613 ± 9 Ω
	Range	2.8 – 32.0 mV	0.1 – 5.2 V	390 – 970 Ω
Other follow-ups	No. of tests	494	512	527
	Mean ± SE	15.0 ± 0.3 mV	1.2 ± 0.1 V	579 ± 5 Ω
	Range	2.0 – 32.0 mV	0.1 – 7.2 V	350 – 1000 Ω

Table 5. R-wave amplitude, ventricular pacing threshold, and ventricular pacing impedance.

- Two successes at 20 J or less: There were 158 tests performed in this category. The average converting energy was 13.9 ± 0.3 J with a range of 4 – 20 J.
- Step-down DFT testing: There were 27 tests performed of this type. The mean converting energy was 10.2 ± 0.9 J with a range of 2 – 20 J.

Lead Evaluation

The Phylax AV was used to evaluate lead measurements, including P- and R-wave amplitudes, pacing threshold, as well as pacing impedance at the time of implant, predischarge, and each scheduled follow-up. These data are presented in Tables 4 and 5.

Specificity

During the course of the study, the Phylax AV classified 267 SVT episodes out of 1415 total tachyarrhythmias. Of the 267 episodes, 113 (42.3 %) were identified as sinus tachycardia, 17 (7.2 %) as atrial flutter, 110 (46.6 %) as atrial fibrillation, and 27 (11.4 %) as other SVTs such as paroxysmal atrial tachycardia or junctional tachycardias (Table 6). These SVTs were distributed over 25 (13 %) of the 192 total patients enrolled. In addition to the episodes mentioned, tachyarrhythmia therapy was appropriately inhibited for an additional 144 atrial tachyarrhythmias because no therapy was programmed in the tachyarrhythmia zone (monitoring only).

Of the 113 sinus tachycardia episodes classified, 26 (23 %) resulted in inappropriate ventricular therapy. In addition, none (0 %) of the 17 atrial flutter episodes, seven (6 %) atrial fibrillation episodes, and ten (37 %) of all other atrial tachyarrhythmias resulted in inappropriate ventricular therapy. Of the 43 SVT episodes resulting in inappropriate ventricular therapy, only 18 resulted from an unsuccessful classification of the SMART Detection algorithm (Table 7). In most cases, misclassification of SMART Detection resulted from tachyarrhythmias having a sudden onset with 1:1 AV conduction such as PAT or junctional tachycardia.

	No. of patients	No. of episodes	No. of episodes resulting in appropriately withheld therapy	No. of episodes resulting in inappropriately withheld therapy
Sinus tachycardia	14	113	87 (77 %)	26 (23 %)
Atrial flutter	3	17	17 (100 %)	0 (0 %)
Atrial fibrillation	6	110	103 (94 %)	7 (6 %)
Other atrial arrhythmias	9	27	17 (63 %)	10 (37 %)
Total	25	267	224 (84 %)	43 (16 %)

Table 6. Atrial tachyarrhythmia episodes.

	Detected in VT zone	Detected in VF zone (single-chamber algorithm)	Detection due to safety timer
Sinus tachycardia	9	0	17
Atrial flutter	0	0	0
Atrial fibrillation	0	3	4
Other atrial tachycardias	9	1	0
Total	18 (6.7 %)	4 (1.5 %)	21 (7.9 %)

Table 7. Detection categories of inappropriate therapy. n = 267.

There were three episodes in which sinus tachycardia resulted in inappropriate VT detection. Each of these was resolved by reprogramming the onset parameter.
All other cases of inappropriate therapy for atrial tachyarrhythmias were not related to SMART Detection, but rather to

- the expiration of the safety timer,
- the classification of these arrhythmias in the VF zone, or
- the deactivation of SMART Detection.

In addition, 18 (6.7 %) of the 267 SVTs classified in the Phylax AV clinical study resulted in inappropriate therapy. Therefore, specificity of SMART Detection in the Phylax AV demonstrated in this clinical study was 93.3 % (Table 8).

Sensitivity

The Phylax AV detected a total of 1148 VT episodes during this clinical investigation. The sensitivity of the Phylax AV for appropriate detection of VTs is 99.4 % (Table 9). Three of the 1148 VTs were not appropriately detected because the rate of the VT was slower than the programmed detection rate. However, these episodes of inappropriate detection were not related to this algorithm. Therefore, the sensitivity of the SMART Detection algorithm for appropriately detecting VT is 100 %.

Discussion

The SMART Detection algorithm incorporated in the Phylax AV defibrillator has demonstrated excellent specificity to a wide variety of SVTs, as evidenced in the Phylax AV clinical investigation. VTs were appropriately classified and treated even when tachyarrhythmias were ongoing in the both the atrium and the ventricle (dual tachycardias). In addition, the SMART algorithm was able to discriminate all episodes of atrial flutter regardless of the A to V conduction ratio. Although detection of VT was clearly demonstrated in the Phylax AV trial, careful programming for VT should be exercised to ensure appropriate VT/VF detection.
Specificity of the SMART algorithm appeared to falter most frequently during tachyarrhythmias that had a 1:1 A-V conduction ratio. In this rhythm classification, the algorithm utilizes an Onset test for differential diagnosis from VT with retrograde conduction (Figure 1). The default setting of Onset in the Phylax AV is 20 %. Previous published studies have indicated that the specificity of Sudden Onset for atrial tachycardias in single-chamber ICDs is between 88.5 % and 92.3 % when the Onset parameter is programmed between 19 % and 25 % [13]. It is interesting to note that this discrimination efficacy is quite similar to the overall specificity of SMART (93.3 %). This suggests that atrial tachyarrhythmias conducted in a 1:1 A-V ratio may pose the greatest challenge to the SMART algorithm.

Total No. of atrial tachyarrhythmias	No. of atrial tachyarrhythmias resulting in inappropriate therapy	Specificy
267	18	93.3 %

Table 8. Specificity of the SMART Detection algorithm.

Total No. of ventricular tachyarrhythmias	No. of ventricular tachyarrhythmias appropriately detected	Sensitivity
1148	1141	99.4 %

Table 9. Sensitivity of the SMART Detection algorithm.

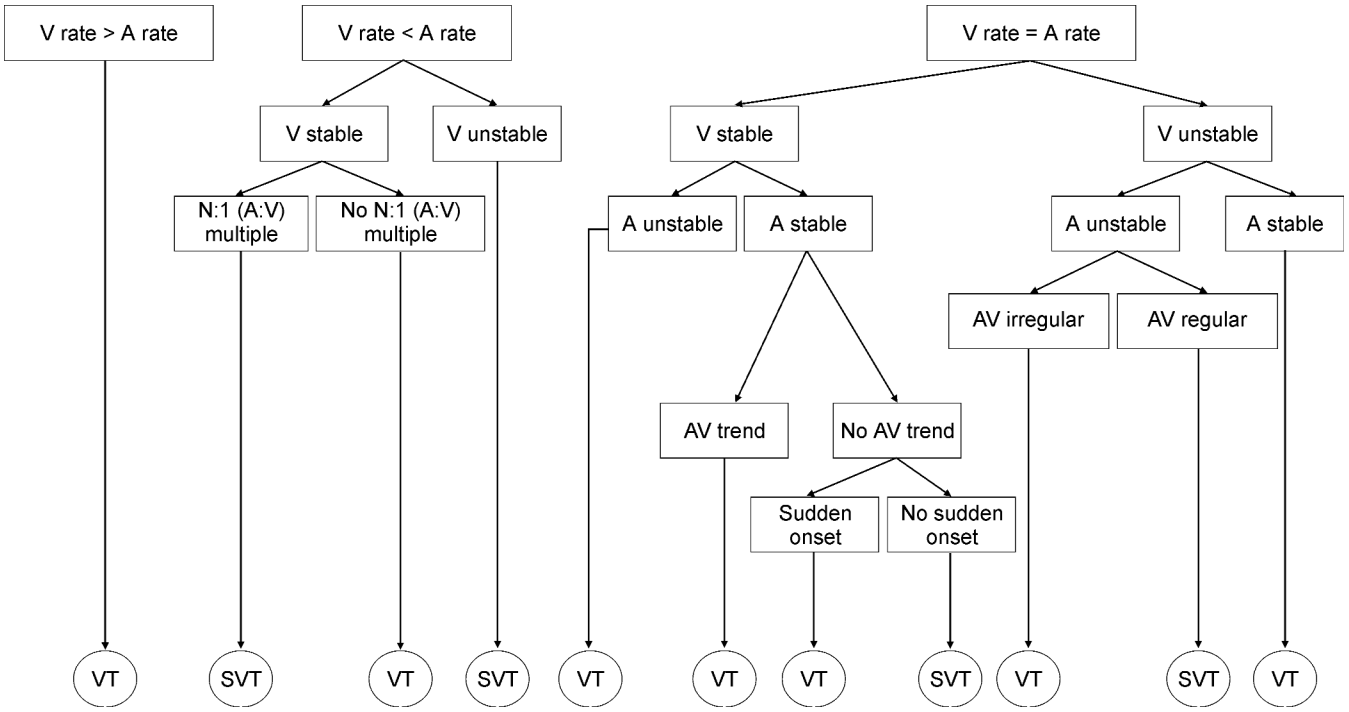

Figure 1. SMART Detection flow chart. A = atrial; V = ventricular; AV = atrioventricular; SVT = supraventricular tachyarrhythmia; VT = ventricular tachycardia.

The clinical results presented here demonstrate that the SMART Detection algorithm incorporated in the Phylax AV represents a significant improvement in specificity compared with previous single-chamber ICDs and other currently available dual-chamber ICDs. For example, a recently published comparison of the Ventak AV ICD (Guidant, USA) reported that inappropriate therapy was applied to 41 % of all atrial fibrillation/flutter episodes [10]. The Photon DR ICD (St. Jude Medical, USA) evinces an 84 % specificity [14], and the GEM III DR (Medtronic, USA) has an 85.8 % specificity [15].

Conclusion

The results of this controlled clinical trial indicate that the SMART Detection algorithm incorporated in the Phylax AV ICD provides a significant benefit to patients by providing superior differentiation between ventricular and supraventricular arrhythmias. Furthermore, this high level of performance in tachyarrhythmia discrimination success (93.3 %) has been demonstrated by 143 patient years of experience through the Phylax AV clinical trial.

Phylax AV Investigators Group

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