

Tachycardia detection performance of implantable loop recorders: results from a large 'real-life' patient cohort and patients with induced ventricular arrhythmias

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Aims	Implantable loop recorders (ILRs) are valuable for diagnosing arrhythmias. We evaluated tachycardia detection per- formance of the Medtronic Reveal [®] ILR with FullView TM Software.
Methods and results	The rate of occurrence of tachycardia detection [supraventricular tachycardia, ventricular tachycardia (VT), and ventricular fibrillation (VF)] and the percentage of appropriately detected tachycardias were determined from all 2190 ILR patients that transmitted to CareLink over a 4-month period (total follow-up = 135.6 patient-years). All 1909 tachycardia episodes were reviewed. Episodes with actual heart rate above the programmed tachycardia detection rate were classified as appropriate. Sensitivity to detect true ventricular arrhythmias was assessed in another group of 215 patients undergoing implantable cardioverter defibrillator (ICD) implant testing. Skin electrodes represented ILR electrodes. Induced VF (404 episodes) and VT (93 episodes) were processed by an emulation of FullView Software. Generalized estimation equation analysis adjusted for multiple episodes per patient. In the CareLink cohort, 68.7% (63.9% adjusted) of detected episodes had tachycardia above the detection rate. Of 1642 episodes detected in the VT zone (12.1 episodes/patient-year), 78.8% (79.0% adjusted) had tachycardia above the detection rate. Of 267 episodes detected in the fast VT zone (1.9 episodes/patient-year), 6.7% (9.4% adjusted) had tachycardia above the detection rate. Of 267 episodes detected in the fast VT zone (1.9 episodes were observed in 10 patients. In the ICD patient cohort, 95.9% (96.5% adjusted) of induced VT/VF segments were correctly detected at nominal rate cutoffs. When VT detection was set to 130 b.p.m. (to include the slowest VT), 99.0% (99.3% adjusted) were correctly detected.
Conclusion	The majority (63.9%) of detected tachycardias contained true tachycardia. Sensitivity to detect induced VT/VF was 99.3%.
Keywords	Implantable loop recorder • ECG monitoring • Ventricular tachycardia • Ventricular fibrillation • Arrhythmia detection • Algorithms

Introduction

Implantable loop recorders (ILRs) have demonstrated clinical benefit in patients with unexplained syncope and symptoms that may be related to arrhythmias.¹⁻³ Current ILRs offer heart rhythm monitoring with both a manual activation of

electrocardiogram (ECG) storage in response to symptoms and an automated detection and storage of suspected arrhythmias, including asystole, bradycardia, tachycardia, and atrial fibrillation. Automated detection of arrhythmias is essential to detect asymptomatic arrhythmias. Several reports have indicated added clinical benefit from the automated detection features.^{4–7} However,

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What's new?

- The Reveal Implantable Loop Recorder with FullView Software demonstrated very high sensitivity to detect induced ventricular tachycardia /ventricular fibrillation (99.3%).
- The majority (63.9%) of detected tachycardia episodes in ambulatory patients contained true tachycardias.

inappropriate detections that result from noise, oversensing, or undersensing have limited the overall clinical value of automated tachycardia detection.^{7–10} Furthermore, the sensitivity of ILR's to detect ventricular arrhythmias has not been reported. The purpose of this study is to determine the tachycardia detection performance of new ILR software (Medtronic Reveal[®] DX/XT with FullViewTM Software).

Methods

Ventricular tachycardia and fast ventricular tachycardia detection algorithm

The ILR detects tachycardias by sensing ventricular activations, determining the intervals between sensed ventricular activations (R-R intervals), and then detecting periods of consistently short R-R intervals according to the programmed tachycardia detection parameters. Ventricular activations are sensed by first filtering the raw ECG signal (0.5-95 Hz, sampled at 256 Hz) with a 10-32 Hz bandpass filter. The filtered signal is then rectified and compared with an autoadjusting threshold with linear decay.¹¹ A sensed ventricular activation occurs when the rectified signal exceeds the threshold value. A blanking period of 150 ms is enforced following each sensed ventricular activation. The R-R intervals are then determined with 10 ms resolution. The device includes two rate zones for tachycardia detection: ventricular tachycardia (VT) (for slower tachycardias) and fast VT (FVT) (for faster tachycardias). Although the rate zones are labelled VT and FVT, these zones are intended for detection of all tachycardias, including supraventricular tachycardia (SVT). The VT zone extends from a programmed VT interval up to the programmed FVT interval (maximum range is 520-250 ms). The FVT zone extends from the programmed FVT interval up to the blanking period (maximum range is 400–150 ms). R-R intervals that fall within the VT zone increment a VT interval counter. A single R-R interval that is longer than the VT and FVT zones resets the VT interval counter. The value of the VT interval counter is held for R-R intervals in the FVT zone. If the VT interval counter reaches the programmed threshold number of beats, then the episode is stored in the VT bin.

Preliminary FVT detection occurs if a programmed number of R-R intervals out of a buffer of recent R-R intervals (e.g. 30 of the most recent 40 R-R intervals) fall within the FVT zone. Following preliminary FVT detection, a noise rejection algorithm is applied to exclude episodes detected because of noise. If at the moment of preliminary FVT detection, at least one of the most recent 12 R-R intervals is <220 ms and the raw ECG signal for the 781 ms immediately preceding the preliminary FVT detection point contains >20 negative inflection points (i.e. changes from positive to negative signal slope), then the episode is considered noise. Otherwise, FVT detection is confirmed. Following noise detection, the VT and FVT counters are cleared and can begin to increment again towards detection.

After a VT or FVT episode is detected, episode termination occurs when either eight consecutive R-R intervals are longer than the programmed VT interval or the median of 12 R-R intervals is consistently longer than the programmed VT interval over a period of 20 s. Each stored VT or FVT episode consists of 30 s of ECG preceding detection and up to 27 s of ECG leading up to episode termination. A total of 27 min of ECG storage is available for automatically detected episodes. Episodes are overwritten if memory is filled, but at least three episodes of each episode type remain in memory.

Databases

Two databases were analysed to determine the tachycardia detection performance of the new algorithm.

Clinical Performance Database

The Clinical Performance Database included spontaneous episodes collected by ILRs. Data from implanted devices were telemetered from the patient to the CareLink data server (Medtronic Inc.), and were then transferred into a de-identified database. Patients with implanted devices that had FullView software, transmitted data from 31 July 2011 to 25 November 2011, had FVT and VT detection enabled, and had ECG storage for FVT and VT episodes enabled, were included. If a patient had more than one transmission of data during this time, only the first transmission was selected. Each transmission included all stored episodes (up to 27 episodes with ECGs can be stored in the VT or FVT bins), as well as the date, time, and programmed parameters for each detected episode. There were a total of 2190 data transmissions from 2190 separate patients. Devices were programmed according to physician discretion. The database included stored electrograms, markers of sensed cardiac events, programmed parameters, and the duration of follow-up.

Induced Ventricular Tachycardia/Ventricular Fibrillation Database

The Induced VT/Ventricular Fibrillation (VF) Database contained recordings of induced VT and VF obtained from 215 patients undergoing implantable cardioverter defibrillator (ICD) implant testing. The recordings were obtained after ethics committee approval at each of the 10 study sites, and each subject provided informed consent. Three skin electrodes were placed on the left thorax in the shape of a right triangle (see Figure 1), with spacing approximating that of the ILR (43 mm). The base of the triangle was positioned with 20 mm on each side of a vertical line that was placed half way between the midsternal and midaxillary lines. The base of the triangle was positioned at the level of the nipple line in males and at the level of the inframammary crease in females. The height of the triangle was 40 mm. Three ECG vectors (representing possible orientations of ILRs) were recorded continuously by a GE Prucka system with 0.5-100 Hz filter settings and 977 Hz sample rate. Programmed electrical stimulation was applied via an implanted ventricular defibrillation lead, until either a ventricular arrhythmia was induced or the physician deemed that VT was not inducible. Ventricular fibrillation was induced by 50 Hz burst pacing. Segments of VF and VT leading up to initial detection were included. Segments between therapies (if a shock failed to convert the rhythm) were also included if they were at least 6 s in duration.

Analysis

Clinical Performance Database

Analysis of the Clinical Performance Database predominantly addressed the rate of occurrence of detected tachycardias (i.e. how

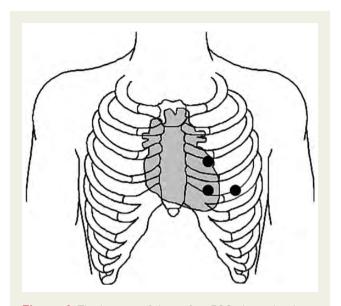


Figure I The location of the surface ECG electrodes during collection of the induced VT/VF Database.

often they occurred) and the positive predictive value of detecting true tachycardias (i.e. what percentage of detected tachycardias had appropriately high true heart rates for detection). Because detected SVTs can have important clinical implications, all forms of tachycardia [VT, VF, SVT, atrial fibrillation (AF) with rapid ventricular response, or ST] were considered appropriate detections if the actual heart rate was in the programmed tachycardia detection zones. Each stored VT and FVT episode was adjudicated independently by two authors (R.W.S. and R.W.) to determine rhythm truth and to determine whether the actual heart rate of the recorded episode was appropriate for detection. If the device memory was filled such that the oldest detected episodes during follow-up did not contain ECG, an effective follow-up duration was calculated according to the date of the oldest available episode with ECG. For example, if the follow-up duration was 30 days but only episodes collected in the last 7 days had ECG storage, then the effective follow-up duration was 7 days.

Induced Ventricular Tachycardia/Ventricular Fibrillation Database

Analysis of the Induced VT/VF Database addressed device sensitivity to detect ventricular tachyarrhythmias. The segments of induced VT and VF were post-processed by an emulation of Reveal DT/XT with Full-View Software. The emulation matched the ECG filtering, sensing, detection, and noise rejection of the actual device. As result of the limited duration of episodes, the detection thresholds for duration of VT and FVT were set to 12 beats and 12 of 16 beats, respectively (16 beats and 30 of 40 beats, respectively, are the nominal settings in Reveal and the settings used in most patients in the clinical performance database). The rate cutoff for FVT was set to 230 b.p.m. (i.e. the nominal value) and at 130 b.p.m. All other sensing and detection parameters were left at nominal values (see *Table 1*).

Statistical methods

Tachycardia detection performance was adjusted for multiple episodes per patient according to the methods described by Wilkoff. $^{\rm 12}$

Table I Programmed parameters for tachycardia detection in 2190 patients

Parameter	Value	% of Patients
VT duration (beats)	5	1.6
	12	4.9
	16 (n)	90.4
	24	1.8
	32	1.0
	48	0.3
VT detection interval (ms)	<340	3.6
	340 (n)	62.2
	>340	34.2
FVT duration (beats)	9 of 12	0.8
	12 of 16	4.9
	18 of 24	6.4
	24 of 32	2.8
	30 of 40 (n)	85.1
FVT detection interval (ms)	<260	2.0
	260 (n)	78.5
	>260	19.5
Stability	Off (n)	92.1
Onset	Off (n)	93.5

n, nominal setting.

Clinical Performance Database

The percentage of detected tachycardias that contained appropriate heart rates for detection was adjusted for the correlation effect of multiple episodes per patient according to the GENMOD procedure of SAS v9.2 (SAS institute Inc.). A logistic regression model with a single explanatory variable (nominal vs. non-nominal device programmed settings) was used to compare detection performance between patients that were programmed to nominal tachycardia detection and those that were not.

Induced Ventricular Tachycardia/Ventricular Fibrillation Database

Sensitivity to VT/VF was calculated as the percentage of rhythm segments that were detected as VT or FVT before the end of the available data. A random effects model with compound symmetry correlation structure was used to adjust the VT/VF sensitivity to account for the correlation effect of multiple episodes per patient and multiple ECG recordings for each episode (according to the GLIMMIX procedure of SAS v9.2).

Results

Clinical performance

Table 1 summarizes the programming of tachycardia detection parameters for the 2190 patients with ILR's that transmitted data. In 330 of these 2190 patients (15.1%), 1909 VT and FVT episodes were recorded. The remaining 1860 patients had no detected tachycardias. The effective total follow-up duration was 135.6 patient-years for VT detection and 138.0 patient-years for

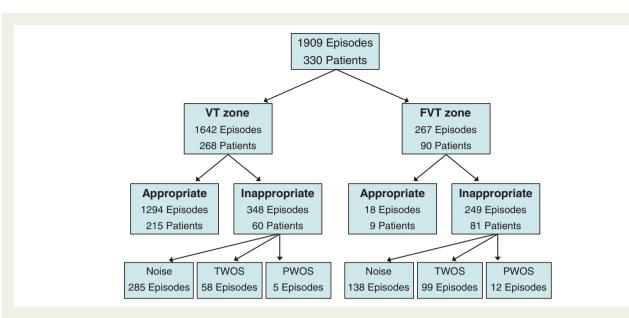


Figure 2 Summary of the detected VT and FVT episodes in the clinical performance database. TWOS, T-wave oversensing; PWOS, P-wave oversensing.

FVT detection (effective follow-up durations differed because of memory storage).

Figure 2 summarizes the detected episodes. Of the 1909 episodes, 1642 were detected in the VT zone in 268 patients and 267 episodes were detected in the FVT zone in 90 patients. On average, 12.1 VT episodes and 1.9 FVT episodes were detected per patient-year of monitoring. Of the 1909 total episodes detected, 68.7% [adjusted: 63.9%, 95% confidence interval (CI): (58.7-68.8%)] contained a true tachycardia with a ventricular rate that was appropriate for detection (VT and SVT combined-note that the ILR does not distinguish between SVT and VT). Of the 1642 episodes detected in the VT zone only, 78.8% [adjusted: 79.0%, 95% CI: (73.8-83.4%)] contained a true tachycardia. The remaining 348 (21%) episodes were inappropriate detections of noise (285 episodes, 17% of total), T-wave oversensing (58 episodes, 4% of total) or P-wave oversensing (five episodes, 0.3% of total). Of the 267 episodes detected in the FVT zone only, 6.7% [adjusted: 9.4%, 95% CI: (5.0-17.2%)] contained a true tachycardia (total of 18 episodes). The remaining 249 episodes were inappropriate detections of either noise (138 episodes, 52% of total, see Figure 3, top panel), T-wave oversensing (99 episodes, 37% of total, see Figure 3, middle panel), or P-wave oversensing (12 episodes, 4% of total).

There was a large disparity between the percentages of appropriately detected episodes in the VT (79.0%) and FVT (9.4%) zones. As shown in *Figure 2*, the VT zone had 1294 appropriate detections and the FVT zone had only 18. In contrast, the inappropriate detections were similar for the VT (348 episodes) and FVT (249 episodes) zones. Thus, the disparity between the FVT and VT zones resulted from a much lower incidence of true tachycardias in the FVT zone, not from more frequent inappropriate detections in the FVT zone.

Of the 1909 detected tachycardias, only 12 (10 patients) were adjudicated as true VT/VF (*Figure 3*, bottom panel). Two of the

true VT/VF episodes were detected in the FVT zone and 10 were detected in the VT zone. *Figure 4* summarizes tachycardia detection on a per-patient basis. Of the 2190 patients, 330 (15.1%) had a detected tachycardia, 217 (9.9%) had a true tachycardia with ventricular rate that was appropriate for detection, and 10 (0.5%) had true VT/VF.

Of the 2190 patients, a subset of 1147 had all VT and FVT detection parameters set to nominal values (see *Table 1*). In this subset, a total of 311 VT and 85 FVT episodes were detected in 90 patients. On average, 3.7 VT episodes and 1.0 FVT episodes were detected per patient-year of monitoring. There was no significant difference in the proportion of appropriate FVT or VT detections between patients that were programmed to nominal detection parameters (raw: 65.7%, adjusted: 59.6%) and patients that were not programmed to nominal detection parameters (raw: 69.5%, adjusted 65.5%; P = 0.31).

Induced ventricular tachycardia/ ventricular fibrillation performance

From the 215 patients with induced VT/VF, a total of 404 segments of VF and 93 segments of VT were acquired, each with at least 6 s duration. Each rhythm was recorded simultaneously in three vectors, resulting in 1491 recorded ECG segments. Loss of contact of the skin electrodes led to exclusion of 16 segments. Thus, 1475 total ECG segments were available for analysis.

Figure 5 summarizes the results on induced VT/VF. At the nominal ILR detection rate cutoffs of 230 b.p.m. for FVT and 176 b.p.m. for VT, 1415 of 1475 [95.9%, adjusted: 96.5%, 95% CI: (94.2–97.9)] segments of VT/VF were successfully detected before the end of the available data. Of the 60 segments of VT/VF that were not detected, 40 were VT with rate <176 b.p.m., so they could not be detected at the nominal detection rate. Nineteen segments either had R-wave undersensing or variable R-wave

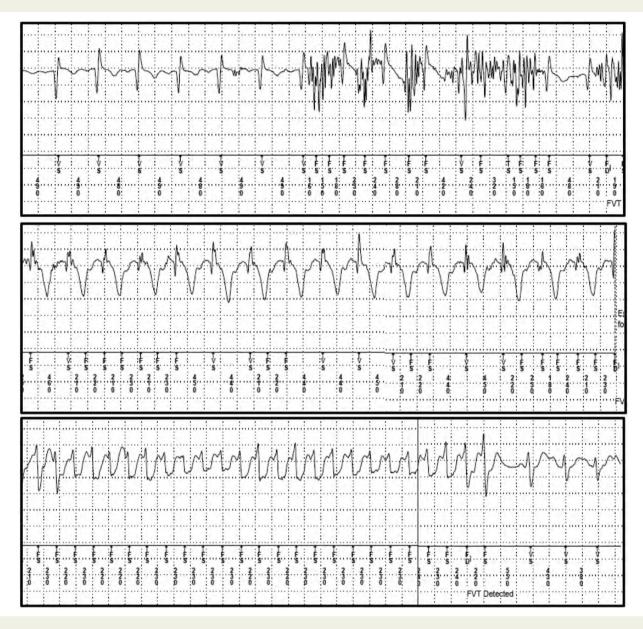


Figure 3 *Top*: Inappropriate detection of FVT because of noise. The noise abruptly stopped near the point of FVT detection (far right in the panel), so the noise rejection criteria failed to detect the noise. *Middle*: Inappropriate detection of FVT because of T-wave oversensing. Detection occurs at the far right of the panel. *Bottom*: Appropriate detection of a VT. The tachycardia spontaneously terminated one beat after detection occurred.

sensing within a QRS complex such that the FVT criteria were not met and/or the VT counter was reset (*Figure 6*). The remaining segment reached initial FVT detection criteria on two occasions but detection was rejected because the noise rejection criteria reset the FVT counter (*Figure 7*). Therefore, 20 of 1475 (1.4%) recorded vectors had VT/VF underdetection. However, all but one episode was detected in at least one of the three separate vectors recorded for each episode. No particular vector angle accounted for underdetection.

When the rhythm segments were re-processed with VT detection set to 130 b.p.m. (to include the slowest of the induced VTs),

all but 14 segments, instead of 60, were detected [sensitivity = 99.0%, adjusted sensitivity = 99.3%, 95% CI: (98.0–99.8%)]. Of the 14 segments of VT/VF that were not detected, most (12 of 14) were VF with undersensing (including the example of *Figure 6*). The remaining two segments reached initial detection criteria but were rejected because of the noise rejection criteria. One of these two segments is the same as that in *Figure 7*. The other segment was successfully detected when VT detection was set to 176 b.p.m., but not when VT detection was set to 130 b.p.m. This occurred because the initial detection criteria were met one R-R interval earlier when VT rate was 130 b.p.m.

The noise rejection criteria encountered 22 negative inflection points at the slower detection rate, which was enough to reject detection and reset the counters. When the VT rate was 176 b.p.m., only 20 negative inflection points were encountered at this faster rate cutoff, which was not enough to reject the rhythm as noise.

Discussion

Given that adequate detection of tachycardias has major therapeutic implications, including catheter ablation or anticoagulation for SVT and atrial fibrillation, and defibrillator implantation for ventricular arrhythmias, we sought to evaluate the accuracy of a new automated tachycardia detection algorithm for the Reveal[®] ILR. We have shown that 63.9% of detected tachycardias obtained by implanted ILRs contain a true tachycardia and that ILR sensitivity

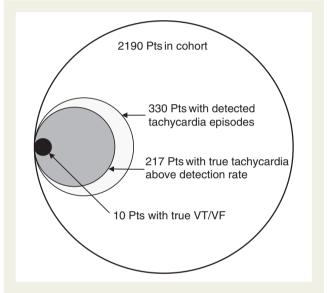


Figure 4 Tachycardia detection results summarized on a perpatient basis. Pts, patients.

to detect VT/VF is very high (96.5% at nominal rate cutoffs and 99.3% when the device is programmed to detect slower VT). Furthermore, our data provide insights in to the 'real-life' prevalence of ventricular and supraventricular arrhythmias in a large, unselected population undergoing ILR implantation.

To detect rare, episodic, but therapeutically relevant events, a high sensitivity is important. Hence, our finding in patients with induced VT/VF are reassuring. The 63.9% positive predictive value of detected tachycardias suggests that recorded episodes need to be reviewed to establish rhythm truth, and especially to distinguish arrhythmias from artefacts. This is consistent with another validation of automated ILR detection for atrial fibrillation compared with 'ground truth' Holter ECG recordings.¹³ The finding that tachycardia episode detection is rare (only 3.7 VT episodes and 1.0 FVT episodes/patient-year of monitoring at nominal device settings) and that tacyhcardias are detected in a small proportion of patients (consistent with prior estimates¹⁴), suggests that reviewing detected tachycardia episodes is of low burden. Inappropriate detection of tachycardia resulted from oversensing of noise, or T-waves, with rare occurrences of P-wave oversensing. Although programming a higher sensitivity setting (i.e. higher than the nominal 35 μ V setting) decreases the risk of oversensing, it also increases the risk of undersensing and inappropriate diagnosis of asystole.¹¹

Retaining the nominal device settings for tachycardia detection led to a substantial reduction in the incidence of detected episodes compared with non-nominal device settings (3.7 vs. 12.1 VT episodes detected per patient-year and 1.0 vs. 1.9 FVT episodes detected per patient-year). However, the percentage of detected episodes that contained true tachycardia did not differ significantly between nominal and non-nominal programming (P = 0.31). Table 1 suggests that deviations from nominal programming were predominantly towards detection of slower tachycardias and shorter duration of tachycardias, which favour increased incidence of detected episodes.

Although the incidence of spontaneous VT/VF in this cohort was very rare (12 true VT/VF episodes in 138 patient-years of monitoring, the equivalent of 1 true VT/VF episode for every

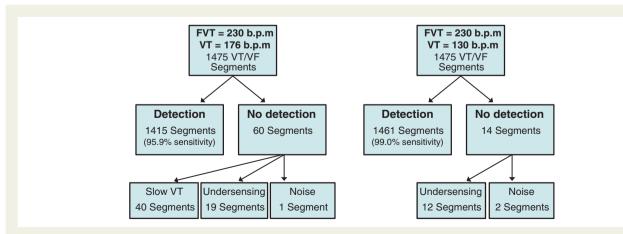
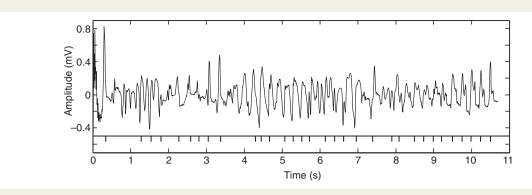
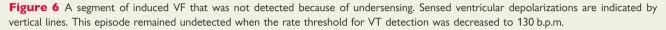


Figure 5 *Left:* Summary of detection of induced VT/VF segments when detection parameters were set to nominal values. *Right:* Summary of detection of induced VT/VF segments when the rate threshold for VT detection was decreased to 130 b.p.m.





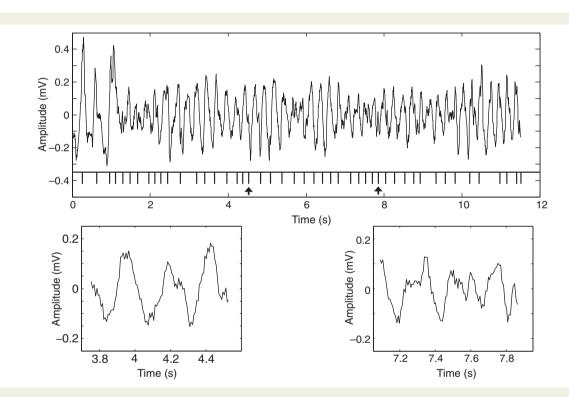


Figure 7 A segment of induced VF that was not detected because of the noise rejection criteria. Sensed ventricular depolarizations are indicated by vertical lines. The two arrows indicate locations of preliminary FVT detection. The lower panels show the signals during the 781 ms preceding each preliminary detection. These segments resulted in rejection of detection and clearing of detection counters because they contained too many transitions from positive to negative slope.

11.5 patient-years), the ILR had VT/VF sensitivity that approximated that of ICDs.¹² The actual VT/VF sensitivity of the device is likely to be higher than our results, because the Induced VT/ VF Database had limited episode durations and episodes that were not detected by the end of the available data may actually be delayed detection rather than failure to detect. As with ICDs, extending the detection zone in an effort to detect slower rhythms increases the probability that a detected tachycardia will not be VT.¹⁵ The low burden of detection in the FVT zone (1.0/ patient-year at nominal device settings) suggests that device memory will be sufficient to retain a true VT/VF when it occurs.

Limitations

The analysis of sensitivity to VT/VF was based upon induced rhythms recorded from skin electrodes. The limitations of this test environment could have influenced the results. Although we tested multiple vectors in the typical location of ILR implants, actual ILR implant locations in individual patients could differ

A strong correlation exists between ECG from surface recordings and ECG from implanted ILRs,¹⁶ especially in resting states. The use of skin electrodes and external equipment may create a different noise environment than that of a chronically implanted device, but since the implanted device is less susceptible to noise,¹⁶ skin recordings would, if anything, underestimate implanted device performance.

This study did not address the possibility of underdetection of SVT with rapid ventricular rate, but the demonstrated high sensitivity to VT/VF strongly suggests a similarly high sensitivity to SVT.

In this analysis of the positive predictive value of ILR detection, we considered detection of any rhythm with an appropriately high ventricular rate to be an appropriate detection. In contrast, the positive predictive value of ICD detection considers only detection of true VT and VF rhythms to be appropriate. The difference in definition of appropriate detection lies in the clinical application of the device. Although ICDs are intended for detection and treatment of VT and VF, ILRs are indicated for the monitoring of symptomatic arrhythmias, which can include SVT or rapidly conducted AF as well as VT. Thus, detection of SVT, rapidly conducted AF, VT, and VF by the ILR can all convey important clinical information.

Conclusion

For those patients receiving the Medtronic Reveal DX/XT with FullView software, automatic detection can be expected to capture almost all (>95%) VT/VF episodes. The new Reveal noise rejection algorithm apparently has negligible impact on sensitivity to detect VT/VF. Owing to the occasional oversensing of noise, detections of tachycardia by ILRs need to be adjudicated. However, detections of tachycardia are relatively rare, so the burden of adjudication is low.

Conflict of interest: K.J.V. is a consultant for Medtronic and Atricure and is a speaker for Medtronic. R.W.S. and R.W. are

employees and shareholders of Medtronic. P.K. is a consultant for Medtronic and has received research grants from Medtronic, St. Jude Medical, and Omron.

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