Failure to Treat Life-Threatening Ventricular Tachyarrhythmias in Contemporary Implantable Cardioverter–Defibrillators

Implications for Strategic Programming

See Editorial by Krainski and Birgersdotter-Green

BACKGROUND: In clinical trials, manufacturer-specific, strategic programming of implantable cardioverter–defibrillators (ICDs), including faster detection rates, reduces unnecessary therapy but permits therapy for ventricular tachycardia/ventricular fibrillation (VF). Present consensus recommends a generic rate threshold between 185 and 200 beats per minute, which exceeds the rate tested in clinical trials for some manufacturers. In a case series, we sought to determine the relationship between programmed parameters and failure of modern ICDs to treat VF.

METHODS AND RESULTS: We reviewed cases in which normally functioning ICDs failed to deliver timely therapy for VF from April 2015 to January 2017 at 4 institutions. Of 10 ambulatory patients, 5 died from untreated VF, 4 had cardiac arrests requiring external shocks, and 1 was rescued by a delayed ICD shock. VF did not satisfy programmed detection criteria in 9 patients (90%). Seven of these patients had slowest detection rates that were consistent with generic recommendations but not tested in a peer-reviewed trial for their manufacturer’s ICDs. Manufacturer-specific factors interacted with fast detection rates to withhold therapy, including strict VF episode termination rules, enhancements to minimize T-wave oversensing, and features that restrict therapy to regular rhythms in ventricular tachycardia zones. Untreated VF despite recommended programming accounted for 56% of sudden deaths and 11% of all deaths during the study period.

CONCLUSIONS: Complex and unanticipated interactions between manufacturer-specific features and generic programming can prevent therapy for VF. More data are needed to assess the risks and benefits of translating evidence-based detection parameters from one manufacturer to another.
Reliable sensing and detection of ventricular fibrillation (VF) and rapid, life-threatening ventricular tachycardia (VT) was a challenge for early implantable cardioverter–defibrillators (ICDs). Manufacturers responded with improved technology; in this century, reports of failure to treat life-threatening VT or VF have been rare and limited to one1–4 or a few patients.5,6

WHAT IS KNOWN
- In clinical trials, manufacturer-specific, strategic programming of implantable cardioverter–defibrillators (ICDs) reduces unnecessary therapy but permits therapy for ventricular tachycardia/fibrillation.
- Present guidelines provide generic programming recommendations. For some ICDs, these recommendations are extrapolated from evidence obtained using other manufacturer’s ICDs with different sensing and detection features.

WHAT THE STUDY ADDS
- No patient with manufacturer-specific, programming validated in a clinical trial failed to receive an initial, timely shock for ventricular fibrillation.
- Most patients who did not receive timely ventricular fibrillation shocks had ICDs programmed consistent with guidelines extrapolated from evidence obtained using another manufacturer’s ICDs with different sensing and detection features.
- More data are needed to assess both the benefits and risks of applying generic programming recommendations to specific ICDs in which these recommendations have not been validated clinically.

In the last decade, investigators focused on preventing unnecessary ICD therapies by strategic programming, including faster detection rates, longer detection times, discriminators for supraventricular tachycardia (SVT), and enhancements to prevent oversensing.7 Clinical studies8–13 report that strategic programming reduces unnecessary therapies without withholding therapy for life-threatening VT/VF. Each study used ICDs from a single manufacturer. Programmed parameters were strictly controlled within each study, but they varied among studies. The 2015 HRS/EHRA/APHRS/SOLAECE Consensus Statement on Optimal ICD Programming and Testing7 (Consensus Statement) provides generic programming recommendations. For some ICDs, these recommendations are necessarily extrapolated from evidence obtained using another manufacturer’s ICDs with different sensing and detection features. In a series of cases, we sought to determine the reasons that contemporary ICD systems failed to deliver therapy for life-threatening VT/VF in the era of strategic programming.

METHODS
Patient Selection
The 10 patients were ambulatory, expected to live >1 year, and did not have an acute illness. They met these criteria: (1) a shock for life-threatening VT/VF was either not delivered or delayed significantly, resulting in death or a major adverse event. For simplicity, we refer to failure to deliver timely therapy. (2) The ICD system functioned normally. (3) VT/VF detection and therapies were programmed ON. (4) The amplitude of sinus-rhythm R waves exceeded 5 mV at implant and follow-up. Index events occurred from April 2015 to January 2017. No patient who met the inclusion criteria was excluded. Patients 1 to 8 were programmed and followed at 1 of the 4 participating
restrictive programming than tested in clinical trials.8–13

Consensus Statement and its Appendix B permits more preferred value to 200 beats per minute. For some ICDs, the range of acceptable thresholds extends from the pre-

tive treatment. For primary prevention patients, preferred rate thresholds vary from 185 to 188 beats per minute; guidelines. For primary prevention patients, preferred rate thresholds vary from 185 to 188 beats per minute; within guidelines. For primary prevention patients, preferred rate thresholds vary from 185 to 188 beats per minute; the range of acceptable thresholds extends from the preferred value to 200 beats per minute. For some ICDs, the Consensus Statement and its Appendix B permits more restrictive programming than tested in clinical trials,8–13 restricting therapy to faster rates.

RESULTS

Table 1 summarizes patient demographics. Table I in the Data Supplement shows device and implant data. Table 2 shows programmed parameters. One column indicates whether rate threshold programming complied with the generic recommendations of the Consensus Statement (consensus recommendations) and by extension was within guidelines as determined by Appendix B. A second column indicates whether the rate threshold equaled Appendix B’s preferred thresh-

old for the specific manufacturer. Table 3 summarizes manufacturer-specific features that contributed to failure to deliver timely shocks.

Of the 8 patients who underwent implant testing, all had reliable sensing and detection of VF (maxi-
mum delay 1 s). Overall, 5 patients died of untreated VF, 4 patients required external defibrillation, and 1 patient was rescued by the ICD after aborted shocks. There was no evidence of a primary cause of cardiac arrest (eg, acute myocardial infarction, pulmonary embolus) in the 5 survivors or 3 patients who died after prolonged resuscitation. The flow chart in Figure 1 summarizes reasons for failure to deliver VF therapy.

Programming Consistent With Generic Consensus Recommendations (Cases 1 to 8)

In cases 1 to 8, rate thresholds complied with generic consensus recommendations; and SVT-VT discriminators complied with manufacturer preferences in Appendix B.7

Premature VF Episode Termination (Cases 1 and 2)

In 2 cases, ICDs detected VF, but the device-defined VF episode terminated prematurely because of intermittent undersensing.

Case 1

A 66-year-old man with a primary prevention St. Jude Medical ICD had VF that was detected rapidly and defibrillated with a single shock. His physician found no change in clinical status and made no changes in programming or medication. Two months later, the patient had a witnessed, out-of-hospital cardiac arrest. Paramedics defibrillated him from VF 13 minutes after collapse. Spontaneous circulation returned, but he died of anoxic encephalopathy.

Analysis. Figure 2 shows that the stored electro-
gram (EGM) began with monomorphic VT slower than the programmed VT detection interval (315 ms, 190 beats per minute); this VT degenerated to VF. The ICD detected VF, but terminated the device-defined VF episode prematurely (Return to Sinus), aborting the shock because it undersensed VF EGMs. After this, the ICD neither detected VF nor stored EGMs before paramedics performed external defibrillation. The shock would have been delivered if the VT interval had been programmed to the clinically validated value of 333 ms (180 beats per minute)12 rather than the manufacturer-preferred value (Consensus Statement Appendix B7; Figure 2 and Figure I in the Data Supplement).

Case 2


Analysis. Figure 3 shows that premature episode termination occurred for the initiating VT because anti-
tachycardia pacing slowed the VT to 318 to 332 ms (180–189 beats per minute) below the rate threshold of
300 ms (200) beats per minute. This episode would not have terminated prematurely if the VT interval had been programmed to the clinically validated value of 333 ms (180 beats per minute). VT then degenerated to VF. Three VF episodes terminated prematurely because of undersensing. It is likely that sensing enhancements designed to prevent T-wave oversensing contributed to undersensing VF (Figure II in the Data Supplement).

### Table 1. Clinical Data

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, y</th>
<th>Sex</th>
<th>Heart Disease</th>
<th>LVEF</th>
<th>NYHA Class</th>
<th>Indication</th>
<th>β Blocker</th>
<th>Antiarrhythmic</th>
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<tbody>
<tr>
<td>1</td>
<td>66</td>
<td>M</td>
<td>CAD</td>
<td>0.30</td>
<td>2</td>
<td>1°→2° (VF)</td>
<td>Y</td>
<td>Amiodarone</td>
</tr>
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<td>2</td>
<td>76</td>
<td>M</td>
<td>CAD</td>
<td>0.40</td>
<td>1</td>
<td>2° (VF)</td>
<td>Y</td>
<td>N</td>
</tr>
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<td>3</td>
<td>62</td>
<td>M</td>
<td>CAD</td>
<td>0.25</td>
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<td>1°</td>
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<td>N</td>
</tr>
<tr>
<td>4</td>
<td>79</td>
<td>M</td>
<td>CAD</td>
<td>0.20</td>
<td>3</td>
<td>1°→2° (VT)</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>5</td>
<td>41</td>
<td>M</td>
<td>CAD</td>
<td>0.18</td>
<td>3</td>
<td>1°</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>6</td>
<td>87</td>
<td>M</td>
<td>CAD</td>
<td>0.35</td>
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<td>N</td>
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<td>7</td>
<td>75</td>
<td>M</td>
<td>CAD</td>
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<td>2° (VF)</td>
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<td>67</td>
<td>M</td>
<td>NICM</td>
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<td>2</td>
<td>2° (VF)</td>
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<td>N</td>
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<td>9</td>
<td>14</td>
<td>M</td>
<td>Vasospastic MI</td>
<td>0.35</td>
<td>2</td>
<td>1°→2° (VT)</td>
<td>N</td>
<td>Amiodarone</td>
</tr>
<tr>
<td>10</td>
<td>44</td>
<td>M</td>
<td>NICM</td>
<td>0.20</td>
<td>3</td>
<td>1°→2° (VT)</td>
<td>Y</td>
<td>Amiodarone Mexiletine</td>
</tr>
</tbody>
</table>

1° indicates primary prevention for implantable cardioverter–defibrillator (ICD), 2° indicates secondary prevention for ICD, 1°→2° indicates primary prevention indication at implant with a subsequent VT or VF requiring ICD therapy. CAD indicates coronary artery disease; LVEF, left ventricular ejection fraction; M, male; MI, myocardial infarction; N, no; NICM, nonischemic cardiomyopathy; NYHA, New York Heart Association; VF, ventricular fibrillation; VT, ventricular tachycardia; and Y, yes.

### Table 2. Programmed Parameters

<table>
<thead>
<tr>
<th>Case</th>
<th>Sensitivity (mV)</th>
<th>Sensing Enhancements</th>
<th>Monitor (beats per minute/ms); Duration</th>
<th>VT/VT1 (beats per minute/ms); Duration</th>
<th>FVT/VT2 (beats per minute/ms); Duration</th>
<th>VF (beats per minute/ms); Duration</th>
<th>Programmed Rate Threshold Consistent with?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.5*</td>
<td>LFA, Decay Delay 60 ms, Threshold Start 50%, SecureSense</td>
<td>OFF</td>
<td>OFF</td>
<td>190/315*; 24 intervals</td>
<td>No (VT2 and VF)</td>
<td>Yes</td>
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<tr>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2</td>
<td>0.3</td>
<td>Decay Delay 60 ms, Threshold Start 62.5%</td>
<td>OFF</td>
<td>OFF</td>
<td>200/300*; 30 intervals</td>
<td>No (VT2 and VF)</td>
<td>Yes</td>
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<td></td>
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<tr>
<td>3</td>
<td>0.3</td>
<td>None</td>
<td>150/400; 32 intervals</td>
<td>OFF</td>
<td>OFF</td>
<td>No (VF)</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>0.5*</td>
<td>LFA, Decay Delay 60 ms, Threshold Start 50%, SecureSense</td>
<td>OFF</td>
<td>OFF</td>
<td>200/300*; 18 intervals</td>
<td>No (VT2 and VF)</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>5</td>
<td>0.3</td>
<td>T-wave rejection, RV lead noise, LIA</td>
<td>Monitor 150/400; 44 intervals</td>
<td>OFF</td>
<td>188/320*; 40 intervals</td>
<td>No (VF)</td>
<td>Yes</td>
</tr>
<tr>
<td>6</td>
<td>0.3</td>
<td>T-wave rejection, RV lead noise, LIA</td>
<td>OFF</td>
<td>150/400; 32 intervals</td>
<td>200/300*; 30/40 intervals</td>
<td>No (VF)</td>
<td>Yes</td>
</tr>
<tr>
<td>7</td>
<td>0.8</td>
<td>None</td>
<td>150/400*; 26 intervals</td>
<td>OFF</td>
<td>182/330*; 22 intervals</td>
<td>No data</td>
<td>Yes</td>
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<tr>
<td>8</td>
<td>0.6</td>
<td>None</td>
<td>160/375; 30 s</td>
<td>OFF</td>
<td>200/300*; 5 s</td>
<td>Yes11</td>
<td>Yes</td>
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<tr>
<td>9</td>
<td>0.5*</td>
<td>LFA, Decay Delay 60 ms, Threshold Start 50%; SecureSense</td>
<td>OFF</td>
<td>169/355; 18 intervals</td>
<td>200/300*; 30 intervals</td>
<td>No2</td>
<td>No</td>
</tr>
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<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>0.3</td>
<td>T-wave rejection, RV lead noise, LIA</td>
<td>OFF</td>
<td>167/360; 32 intervals</td>
<td>200/300*; 30/40 intervals</td>
<td>No (FVT, VF)</td>
<td>No</td>
</tr>
</tbody>
</table>

FVT indicates fast VT zone; LFA, low-frequency attenuation filter; LIA, Lead Integrity Alert; RV, right ventricular; VF, ventricular fibrillation; and VT, ventricular tachycardia.

*Values indicate sensing thresholds and detection rate thresholds not tested in clinical trials.

1° indicates primary prevention for implantable cardioverter–defibrillator (ICD), 2° indicates secondary prevention for ICD, 1°→2° indicates primary prevention indication at implant with a subsequent VT or VF requiring ICD therapy. CAD indicates coronary artery disease; LVEF, left ventricular ejection fraction; M, male; MI, myocardial infarction; N, no; NICM, nonischemic cardiomyopathy; NYHA, New York Heart Association; VF, ventricular fibrillation; VT, ventricular tachycardia; and Y, yes.
VF Never Detected (Cases 3 to 7)

In 4 cases, the ICD did not detect the index episode of VF.

Case 3
A 62-year-old man with a primary prevention Medtronic cardiac resynchronization therapy ICD died suddenly and unexpectedly in his bedroom. A Lead Integrity Alert was triggered by double-counted EGMs and transmitted to a remote monitoring network.

Analysis. Figure 4 and Figure III in the Data Supplement show transmitted EGMs. In each Figure, Panel 1 shows the onset of monomorphic VT as a device-defined non-sustained episode, triggered by intervals that are transiently shorter than the VF detection interval of 300 ms. EGMs from multiple nonsustained episodes over the next 46 minutes show that VT slowed to cycle length 290 to 330 ms and degenerated to polymorphic VT/VF. Monomorphic VT would have been detected with a clinically validated VF interval of 330 ms (182 beats per minute); transmitted data are insufficient to determine whether detection would have occurred with the validated value of 320 ms (188 beats per minute).

Case 4
A 79-year-old man with a primary prevention St. Jude Medical cardiac resynchronization therapy ICD had monomorphic VT with cycle length 260 to 280 ms in December 2016 that was detected and treated in the VT zone (240–300 ms). In January 2017, he had a witnessed cardiac arrest while sitting in a chair. Cardiopulmonary resuscitation was performed until paramedics arrived 9 minutes later and defibrillated him from polymorphic VT/VF to sinus rhythm (Figure IVA in the Data Supplement). He died despite pro-

Table 3. Causes of Failure of Timely VF Therapy

<table>
<thead>
<tr>
<th>Case</th>
<th>Recommended Programming</th>
<th>ICD Response to Clinical Arrhythmia</th>
<th>Root Cause of Failure to Treat Clinical VT/VF</th>
<th>Additional Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vertical</td>
<td>VT (Cycle Length)</td>
<td>VT: Rate</td>
<td>Features to prevent T-wave oversensing*</td>
</tr>
<tr>
<td>1</td>
<td>Yes</td>
<td>No therapy (395–345 ms)</td>
<td>VF: Premature episode termination; rate and duration</td>
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<tr>
<td>2</td>
<td>Yes</td>
<td>270–320 ms</td>
<td>Therapy delay &gt;1 min</td>
<td>Premature episode termination</td>
</tr>
<tr>
<td>3</td>
<td>Yes</td>
<td>No therapy (300–320 ms)</td>
<td>VF: Rate</td>
<td>Features to prevent T-wave oversensing*</td>
</tr>
<tr>
<td>4</td>
<td>Yes</td>
<td>No therapy</td>
<td>Rate and duration</td>
<td>Features to prevent T-wave oversensing</td>
</tr>
<tr>
<td>5</td>
<td>Yes</td>
<td>No therapy (310–350 ms)</td>
<td>VT: Rate, Consecutive interval counting</td>
<td>Rate and duration</td>
</tr>
<tr>
<td>6</td>
<td>Yes</td>
<td>No therapy</td>
<td>VF: Rate and duration</td>
<td>Consecutive interval counting (VT zone)</td>
</tr>
<tr>
<td>7</td>
<td>Yes</td>
<td>No therapy (344–375 ms)</td>
<td>Therapy delay 14 min</td>
<td>Rate and stability</td>
</tr>
<tr>
<td>8</td>
<td>Yes</td>
<td>No therapy (375–345 ms)</td>
<td>No therapy after 6th shock</td>
<td>Rate and duration</td>
</tr>
<tr>
<td>9</td>
<td>No</td>
<td>No therapy (345–360 ms)</td>
<td>VT: Rate</td>
<td>Rate and duration</td>
</tr>
<tr>
<td>10</td>
<td>No</td>
<td>No therapy (300–330 ms)</td>
<td>Therapy delay 9 min</td>
<td>Rate and duration</td>
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</table>

ICD indicates implantable cardioverter-defibrillator; VF, ventricular fibrillation; and VT, ventricular tachycardia.

*Decay Delay, Threshold Start, low-frequency attenuation (LFA) filter.

Figure 1. Flow chart summarizes implantable cardioverter-defibrillator (ICD) programming and reasons for failure to deliver timely ventricular fibrillation (VF) therapy.
Figure 2. Case 1. Stored electrogram (EGM) displays 3 of 4 continuous panels showing filtered atrial EGM (A Sense Amp), filtered right ventricular (RV) sensing EGM (V Sense Amp), shock EGM (RV coil Can, discrimination), dual-chamber markers, ventricular intervals in ms, and timeline in s (Figure I in the Data Supplement).

Panel 1 shows ongoing monomorphic ventricular tachycardia (VT) at cycle length of 387 to 395 ms, slower than (Continued)
longed resuscitation. During resuscitation, he had 3 episodes of monomorphic VT that the ICD detected and treated.

**Analysis.** Figure IVB in the Data Supplement shows the first of 3 similar episodes. Each persisted for an unknown duration with cycle length slower than the VT interval (300 ms) before accelerating into the VT zone. The subsequent stored VTs suggest that untreated VF may have begun with VT slower than the detection interval and that this VT degenerated to VF, which was undersensed.

**Case 5**
A 41-year-old man suffered an arrhythmic cardiac arrest on in-hospital telemetry, the night after elective implantation of a primary prevention Medtronic ICD. He had no metabolic abnormalities, and he received no antiarrhythmic drugs. After resuscitation, he required inotropic support and underwent heart transplantation 6 weeks later.

**Analysis.** Figure 5A shows that initial episode of low-frequency VF did not fulfill the programmed detection criteria for either VF (18/24 intervals shorter than 300 ms) or VT (40 consecutive intervals, 300–319 ms). Double counting triggered the Lead Integrity Alert, which extended the number of intervals to detect VT to 30 of 40. After external defibrillation, monomorphic VT occurred and degenerated to polymorphic VT with cycle length 310 to 350 ms (Figure VB in the Data Supplement). This required a second external defibrillation (Figure 5C Panel 2). High-frequency VF recurred 2 s later (Figure 5C Panel 3; Figure V in the Data Supplement).

**Case 6**
An 87-year-old man with complete heart block and a primary prevention Medtronic cardiac resynchronization therapy ICD had a cardiac arrest while sleeping. His caregiver called 911. Paramedics found him in VF and defibrillated him to pulseless electric activity, but he did not regain spontaneous circulation. The ICD transmitted a Lead Integrity Alert.

**Analysis.** The transmitted EGMs in Figure VI in the Data Supplement show VF with undersensing that never fulfilled the detection criteria for VF (30/40 intervals shorter than 300 ms). Further, detection of VT did not occur despite a slow VT interval (400 ms) because Medtronic uses consecutive interval counting in the VT zone. Undersensing or entrance block caused occasional device-measured intervals slower than the VT interval, which repeatedly reset the VT count to 0 (Figure VI in the Data Supplement).

**Case 7**
A 75-year-old man with long-standing atrial fibrillation had an ICD implanted in 1994 for out-of-hospital VF and upgraded in 2011 to a Biotronik cardiac resynchronization therapy ICD. In 2015, his electrophysiologist increased the VT detection interval to 400 ms after the patient had suspected arrhythmic syncope. One month later, he had a witnessed cardiac arrest followed by immediate cardiopulmonary resuscitation. Paramedics found him in VF and defibrillated him to pulseless electric activity. He died after a prolonged resuscitation including repetitive sequences of VF.

**Analysis.** Relevant ICD parameters include detection intervals consistent with recommended secondary prevention programming (VT1: 400 ms, VT2: 330 ms, VF: 260 ms) and nominal values of single-chamber SVT-VT discriminators: Onset at 20% and Stability at 24 ms. Undersensing of low-amplitude VF EGMs after high-amplitude VF EGMs was critical in erroneous premature termination of the device-defined VF episode and aborting the shock. Arrows in Panel 3 denote that 6 sequential VF EGMs are not sensed after a high amplitude because EGM amplitude decreases faster than dynamically adjusting sensitivity can adapt. Features to prevent T-wave undersensing may also have contributed to undersensed EGMs. Signals with comparably low amplitude were sensed reliably toward the end of Panel 2 (Figure I in the Data Supplement). The final undersensing event occurs at 21.2 s (Panel 4) after 3 sequentially undersensed EGMs with amplitude 0.91 to 1.1 mV (third upward arrow). Undersensing these EGMs results in a device-defined ventricular interval of 852 ms (VS marker). The subsequent EGM is sensed accurately with an interval of 332 ms (black box), resulting in the fifth consecutive binned, VS interval (†) and premature episode termination. However, if VT detection had been programmed to clinically tested value of 333 ms, the 332 ms interval would have been unclassified (−), and premature episode termination would not have occurred. Because the ICD completed charging during the 852 ms interval (end of line of asterisks), it would have delivered the shock synchronous with the EGM ending the 254 ms interval after the † EGM (first binned VT or VF interval after charging). STIM indicates ventricular antitachycardia pacing; VS, ventricular sensed event; and VVI, ventricular demand pacing.
Figure 3. Case 2. Stored electrograms (EGMs) display filtered right ventricular (RV) dedicated bipolar sensing EGM (V Sense Amp), ventricular markers, ventricular intervals in ms, and timeline in s.

These multiple device-defined episodes were recorded during a single clinical ventricular tachycardia/ventricular fibrillation (VT/VF) episode. A, Monomorphic VT. Discontinuous Panels 1 and 3 show that VT begins an unknown time before the recording. The VT cycle length straddles the Sinus VT boundary of 300 ms so that multiple intervals in Panel 2 remain unclassified. VT is detected at 15.4 s in Panel 3 (VT(ATP—-…)) and antitachycardia pacing (ATP) is delivered immediately (STIM markers). After ATP, VT slows to 318 to 332 ms in the Sinus zone, resulting in episode termination (Return to Sinus; B) VF. The next stored EGM recorded about a minute later showed detection of VF. It is likely that the monomorphic VT degenerated (Continued)
zone that did not fulfill the Onset criterion and was thus classified as SVT (Figure 6A). The stored EGM in Figure 6B was recorded 13 minutes later and shows VF. Because of intermittent undersensing, the calculated ventricular cycle length (276 ms) was in the VT2 zone, so the Stability algorithm was applied and determined that the rhythm was irregular. Thus, the ICD classified VF as SVT and withheld therapy (Figure 6).

**Postshock Undersensing (Case 8)**

**Case 8**

A 67-year-old man underwent Boston Scientific ICD implantation with an integrated bipolar lead after out-of-hospital VF. One month later, he suffered a witnessed cardiac arrest. Paramedics arrived 12 minutes later and defibrillated VF after a long resuscitation. With prolonged hospitalization, the patient recovered completely and underwent VT ablation.

**Analysis.** Figure VII in the Data Supplement shows monomorphic VT that degenerated to VF, which was detected and defibrillated to sinus rhythm. This initiated a repetitive sequence of recurrent VF followed by successful defibrillation. However, the amplitude of the sensed EGMs decreased progressively in successive postshock recurrences of VF until they were undersensed consistently and VF remained undetected (Figure VII in the Data Supplement).

**Deviation From Consensus Programming (Cases 9 to 10)**

In case 9, the VT interval was set to 300 ms after apparently successful ablation of slower VT; the patient presented with VT slower than 300 ms and subsequent undersensed VF (Figure VIII in the Data Supplement). In case 10, the VT detection interval was not increased after antiarrhythmic drug treatment was changed (Figure IX in the Data Supplement; Data Supplement).

**Completeness of the Data Set**

No patient who met the study criteria was knowingly excluded. We reviewed all cardiac arrests and other deaths in ICD patients during the study period at the 2 institutions that tracked these data. These institutions contributed 8 of 10 cases, including 3 of the 4 cardiac arrest cases and all 5 fatal cases. There were no other resuscitated cardiac arrests during the study period.

Of 47 total decedents during the study period, 9 died suddenly. In addition to the 5 study patients who died, 2 patients died of pulseless electric activity, 1 patient with a fractured defibrillation lead died of VF that was detected but not defibrillated, and 1 patient died suddenly without postmortem ICD interrogation (Table II in the Data Supplement). Thus, failure to detect VF despite recommended programming was responsible for 5 of 8 adjudicated sudden deaths (62%), 56% of total sudden deaths, and 11% of all deaths in ICD patients.

**DISCUSSION**

We present a series of contemporary ICD patients who did not receive timely VF shocks. Our principal finding is that, in most patients, ICD programming deviated from values validated in manufacturer-specific, clinical trials,8–13 which form the evidence base for the Consensus Statement,7 but they complied with more restrictive, generic recommendations of the Consensus Statement. Failure to detect VF despite generically recommended programming was the most common cause of sudden death at the 2 centers that tracked these data. These data suggest that differences in sensing and detection methods among manufacturers may limit the applicability of generic programming recommendations.

**Prior Studies: Programming Sensing and Detection of VT/VF**

In the last decade, randomized clinical trials8–12 and prospective observational studies8,13 in primary prevention patients found that faster rate thresholds of 180 to 200 beats per minute and longer durations of at least 6 to 12 s reduce unnecessary shocks8–13 and may reduce mortality.18 Programmed parameters were tightly controlled within each study using ICDs from a single manufacturer, but varied among studies using different manufacturers’ ICDs. Importantly, studies report no deaths from untreated VT/VF. Programmed, slowest rate thresholds were 182 to 188 beats per minute for Medtronic ICDs8–10,13 (VF zone), 180 beats per minute for St. Jude ICDs12 (VT zone), and 200 beats per minute for Boston Scientific ICDs11 (VF zone). Data on strategic programming of secondary prevention patients are limited to subgroup analyses of 1 randomized19 and 1 observational study,13 each using Medtronic ICDs; these data support programming 188 beats per minute if the clinical VT is faster than this rate.
Figure 4. Case 3. Electrograms (EGMs) and interval plot transmitted with Lead Integrity Alert.
Atrial, right ventricular (RV) wide-band filtered sensing channel (RV Tip-RV Ring), and dual-chamber marker channel are shown.
Panel 1, Onset of monomorphic ventricular tachycardia (VT) at 10:02. Event storage is triggered by the 8 intervals (Continued)
The Consensus Statement relied on this evidence to develop generic programming recommendations including a range of reasonable heart rate cutoffs that are inclusive of those proven in good-quality trials. Its online Appendix B provides manufacturer-preferred examples intended to best approximate the recommended behaviors for each available ICD model.

Present Study
In contrast to clinical trials in which no patient died from untreated VT/VF with manufacturer-specific programming, we report patients with adverse outcomes. Overall, failure of VF to satisfy programmed detection criteria was critical in 9 of our 10 patients (90%, all but patient 8). Patients 1 to 8 had programming consistent with generic Consensus Statement recommendations. However, in patients 1 to 6, programming was inconsistent both with manufacturer-specific, clinical trials and manufacturer-preferred values (online Appendix B). In patient 7, programming complied with manufacturer-preferred values, but these values had not been validated in a peer-reviewed, clinical study. Programming a detection rate validated clinically for the manufacturer’s ICD would have resulted in prompt shocks for at least 4 other patients (1–3, 10); of these, patient 1 would not have received prompt shocks with manufacturer-preferred programming.

Our cases illustrate how variability of VF within patients necessitates a safety margin for detection: all 8 ICDs tested at implant detected VF reliably with the settings that failed to detect the index VF; 2 detected spontaneous VF or rapid VT before the index VF (cases 1, 4), and 1 detected VF after external defibrillation (case 5). Overall, failure of VF therapy accounted for 11% of deaths in ICD patients. In prompt shocks for at least 4 other patients (1–3, 10); of these, patient 1 would not have received prompt shocks with manufacturer-preferred programming.

In postmortem series, Tseng et al reported that similar failures accounted for 6% of deaths in ICD patients.

Interaction of Manufacturer-Specific Features With Generic Programming

Counting Methods, Detection Duration, and SVT Discriminators
Manufacturers use different methods to count ventricular intervals that satisfy rate criteria. Each method tolerates slow intervals in the VF zone. However, Boston Scientific tolerates more slow intervals (40%) than Medtronic (25%) or Biotronik (33%); yet only Boston Scientific ICDs have been tested with a slowest detection rate of 200 beats per minute and only for durations less than about 5 s. Patient 3 was programmed to 200 beats per minute using Medtronic counting for a longer duration (30/40 intervals) that was tested for slower rates of 182 or 188 beats per minute. Therapy would have been delivered with a threshold of 182 beats per minute. Without a monitoring zone, we cannot determine whether therapy would have occurred with a threshold of 188 beats per minute. Similarly, we cannot determine whether validated programming would have resulted in prompt therapy in patients 4 and 5.

In addition, counting methods for the VT zone vary among manufacturers. Medtronic ICDs count consecutively intervals. During VF in patient 6, the VT count was repeatedly reset to 0 by intermittent, device-measured intervals slower than the VT interval, which occurred because of undersensing or entrance block. Biotronik ICDs use up/down counting. In patient 7, VF with undersensing had a measured rate of 217 beats per minute (276 ms) in the VT2 zone. This constituted a problem because unvalidated, manufacturer-preferred programming of the Stability discriminator ≤231 beats per minute (260 ms) prevented detection of VF; Stability discriminators are of little value ≥200 beats per minute.

Episode Termination Rules
ICD-defined VT/VF episodes continue until the rhythm is classified as normal (sinus) based on (slow) rate and duration. Therapy is not delivered if the episode terminates prematurely. St. Jude Medical ICDs have the most sensitive episode termination rule. Cases 1 and 2 show how it interacts with fast detection rates and occasional undersensing to withhold therapy after VF has been detected.

Enhancements to Minimize T-Wave Oversensing
St. Jude Medical sensing enhancements Decay Delay and Threshold Start (Figure X in the Data Supplement) increase ventricular blanking and have been associated with VF undersensing. The low-frequency attenuation filter may reduce the amplitude of VF EGMs more than the amplitude of sinus-rhythm EGMs because VF EGMs have lower frequency content than sinus-rhythm EGMs. In the St. Jude Medical PROVIDE trial of strategic programming (Programming Implantable Cardioverter Defibrillators in Patients With Primary Prevention Indication to Prolong Time to First Shock), the detection rate was 180 beats per minute; use of Decay Delay
and Threshold Start were not controlled; and most ICDs predated the low-frequency attenuation filter. Thus, the interaction of these features with a detection rate of 200 beats per minute is untested.

Additional Factors
Patients 8 to 10 illustrate known mechanisms of withholding VF therapy. In patient 8, postshock undersensing of VF occurred after repetitive shocks through an integrated bipolar lead.23 Patient 9 was considered cured of VT after ablation, so his ICD was set to primary prevention parameters; in studies of VT ablation, detection rates have not been reprogrammed after VT was rendered noninducible. Case 10 emphasizes the importance of reprogramming the detection rate when antiarrhythmic drugs are added.7

Role of Preceding Monomorphic VT in Withholding VF Therapy
Untreated monomorphic VT initiated polymorphic VT/VF in 7 of the 8 patients in whom we could determine the

Figure 5. Selected electrograms (EGMs) show right ventricular (RV) integrated bipolar EGM (RV Tip-RV Coil), shock EGM (Can-RV Coil), and ventricular markers.

The implantable cardioverter–defibrillator (ICD) did not record the onset of ventricular fibrillation (VF). It recorded the first device-defined, nonsustained episode (episode 1) at 03:48. A, Nonsustained episode 6 at 03:49 is the last episode recorded before the first external defibrillation. VF EGMs have a low-frequency content and do not fulfill the programmed detection criteria for either VF (18/24 intervals shorter than 300 ms) or ventricular tachycardia (VT; 40 consecutive intervals shorter than 320 ms). Intervals in the VT zone do not contribute to detection because consecutive interval counting causes each interval in the sinus zone (320 ms or greater) to reset the VT count to 0. Undetected recurrence of undetected monomorphic and polymorphic VT is shown in Figure VB in the Data Supplement. C, VF episode 9 at 03:55. Three continuous panels show polymorphic VT with cycle length 270 to 430 ms that does not satisfy interval/duration criteria for detection and requires a second external shock (Panel 2, up arrow). If the VF interval had been programmed to the clinically validated values of 320 or 330 ms, this polymorphic VT would have satisfied the programmed 18/24 intervals for detection of VF (end of dotted arrow in Panels 1 and 2). However, the Lead Integrity Alert15 was activated incorrectly during Episode 5 when both oversensing criteria were fulfilled. This alert increased the number of intervals for VF detection to 30/40 during Episode 6 and subsequent episodes. After the shock, VT recurred following the second paced beat and immediately accelerated to VF. The frequency content of EGMs was higher during this VF than during the first VF or the polymorphic VT above. The ICD detected VF rapidly and defibrillated it with a single shock (Figure VC to VC in the Data Supplement Panels 4 to 6).
Figure 6. Case 7. Electrograms (EGMs) from 2 device-defined supraventricular tachycardia (SVT) episodes (device lifetime device episodes No. 39 and 40) recorded during cardiac arrest.

Each panel shows markers, atrial EGM, right ventricular (RV) dedicated bipolar EGM, and left ventricular (LV) bipolar EGM. A, Monomorphic ventricular tachycardia (VT) with cycle length 367 to 383 ms in the VT 1 zone. The atrial EGM confirms atrioventricular (A-V) dissociation with additional far-field R waves. This VT began during maximum rate sensor-driven pacing (not shown) and had a measured Onset of 19%, less than the 20% required to be classified as VT. B, Ventricular fibrillation (VF) with intermittent undersensed EGMs (asterisks). Most undersensed EGMs results from high-amplitude EGMs after low-amplitude EGMs faster than dynamic sensitivity can adjust. Thus, the device measured a cycle length 276 ms, in the VT2 zone. The measured Stability of 148 ms exceeded both the nominal (programmed) value of 24 ms and the manufacturer recommended value of 40 ms required for classification as VT2.
Clinical Implications

VF detection algorithms must be robust against device-detected intervals slower than the rate threshold to compensate for undersensing, entrance block, or detection restrictions applied in VT zones. Both fast detection rates and enhancements that facilitate undersensing increase the fraction of such device-detected, slow intervals. When devices measure slow intervals, strict counting methods and the Stability discriminator reduce sensitivity for detecting VF in VT zones; sensitive episode termination rules reduce the likelihood that VF therapy will be delivered once VF is detected; and long detection times enhance both effects. Finally, fast detection rates may increase the likelihood that VT will not be detected until it degenerates to low-frequency VF, which may be difficult to detect.

Ideally, programming should deliver all life-saving ICD therapy but no unnecessary therapy. Practically, the programmer’s dilemma is to balance the risks of failure to treat VF with the risks of inappropriate therapies. Although evidence-based, manufacturer-specific programming may withhold necessary therapy, the absence of deaths from untreated VF in the 6414 patients in strategic programming groups of clinical trials places a low, upper bound on the likelihood of such events.

Our cases illustrate how complex and unanticipated interactions between manufacturer-specific features and generic rate thresholds can withhold therapy for VF. Programming manufacturer-preferred values enumerated in Appendix B might have prevented some, but not all, treatment failures. No patient with manufacturer-specific, programmed validated in a clinical trial failed to receive an initial, timely shock for VF. Thus indirectly, our study supports the recommendation of the Consensus Statement7 (Section 23) encouraging programming ICDs to manufacturer-specific therapies of proven benefit; we recommend such programming even if Appendix B permits programming to other values. Our study identifies risk associated with programming recommendations extrapolated from evidence obtained using another manufacturer’s ICDs with different sensing and detection features; however, we cannot provide alternative recommendations and do not advocate abandonment of any recommendations of the Consensus Statement.

Limitations

We did not compare adverse outcomes using evidence-based manufacturer-specific programming and more restrictive, generic programming. Although such generic programming accounted for 62% of adjudicated sudden deaths in ICD patients at institutions that tracked outcomes, our series of cases is too small for definitive conclusions.

Even if manufacturer-specific, evidence-based programming is available for an ICD, programming more restrictive values permitted by the Consensus Statement Appendix B may further reduce unnecessary therapies and thus further reduce morbidity beyond the reduction provided by evidence-based programming. However, the low rate of unnecessary therapy in evidence-based clinical trials places a low upper bound on the incremental benefit of such programming.

Conclusions

Given the rarity of failure to treat VF with evidence-based, manufacturer-specific programming, failures of generic programming constitute a readily preventable cause of sudden death. More data are needed to assess both the benefits and risks of applying generic programming recommendations to specific ICDs in which these recommendations have not been validated clinically.

Affiliations

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Disclosures

Dr Abedin is a consultant to St. Jude Medical. Dr Swerdlow is a consultant to Medtronic and has received speaking hono-
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raria from Medtronic and Boston Scientific. The other authors report no conflicts.

FOOTNOTES

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REFERENCES

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SUPPLEMENTAL MATERIAL

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Supplemental eTables 1 & 2: p. 4-5
Supplemental eFigures 1 to 10: p. 6-25
Supplemental – eResults Text

Deviation from Consensus Programming (Cases 9 - 10)

Case 9

A 14 year-old boy had a primary-prevention, St Jude Medical ICD. In November 2015, he had multiple, monomorphic VTs with cycle lengths 260 – 330 ms and underwent catheter ablation that rendered VT noninducible. In April 2016, VT recurred at cycle length 285 ms. His amiodarone dose was increased. In May 2016, he presented with monomorphic VT slower than the VT interval of 300 ms and became hemodynamically unstable. He was treated promptly with external cardioversion. Immediately post-cardioversion, the rhythm degenerated to VF that the ICD did not detect, and he was defibrillated externally.

Analysis: eFigure 8 shows the undersensed VF. The proprietary Decay Delay algorithm\textsuperscript{16} may contribute to undersensing. See eFigure 8 legend an eFigure 10 for details.

Case 10

A 44 year-old man underwent primary-prevention, Medtronic CRT-D implantation in February 2011. From May 2011 to September 2016, he had 8 episodes of successfully treated VT or VF (cycle lengths 220 – 270 ms) without change in programming. In July 2015, amiodarone was started for paroxysmal atrial fibrillation; in September 2016, mexiletine was added after a shock for VT at cycle length 265 ms. In October 2016, he had a witnessed, cardiac arrest. His wife performed cardiopulmonary resuscitation, and 9 min later the ICD delivered a shock. She continued resuscitation until, 13 minutes after collapse, paramedics arrived, defibrillated him and stabilized him. He recovered over weeks but suffered neurological deficits.

Analysis: As in Case 3, the arrhythmia began with monomorphic VT at cycle length 310 - 330 ms in the Monitor zone (eFigure 9). VT persisted for up to 4 min before degenerating to VF, which did not fulfill programmed detection criteria for VF or “Fast VT via VF”\textsuperscript{18} for an additional 5 min (30/40 intervals shorter
than 250 or 300 ms, respectively). The initiating VT would have been detected if the VF interval had been programmed to validated value of 330 ms (182 bpm); Stored data are insufficient to determine if detection would have occurred with an interval of 320 ms.\textsuperscript{10,12,14,15} See eFigure 9 legend for details.
## Supplemental – eTables 1 & 2

### eTable 1. Device and implant data

<table>
<thead>
<tr>
<th>Case</th>
<th>ICD</th>
<th>Implant date*</th>
<th>Company</th>
<th>ICD model</th>
<th>ICD Lead</th>
<th>Sinus R-wave (mV)</th>
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<td>St Jude Medical</td>
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<td>Medtronic S6935</td>
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<td>St Jude Medical</td>
<td>Current VR RF 1207-36</td>
<td>St Jude Medical Durata 7120</td>
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<tr>
<td>3</td>
<td>CRT-D</td>
<td>Feb 2012</td>
<td>Medtronic</td>
<td>Protecta XT D314TR6</td>
<td>Medtronic 6947</td>
<td>12.0</td>
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<td>4</td>
<td>CRT-D</td>
<td>July 2010, May 2012</td>
<td>St Jude Medical</td>
<td>Unify Quadra 3251-40</td>
<td>Medtronic 6947</td>
<td>8.4</td>
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<td>5</td>
<td>Single</td>
<td>Sept 2016</td>
<td>Medtronic</td>
<td>Evera XT DVBB1D4</td>
<td>Medtronic 6935</td>
<td>10.9</td>
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<td>6</td>
<td>CRT-D</td>
<td>Feb 2010, June 2015</td>
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<td>Viva XT DTBA1D1</td>
<td>Medtronic 6947</td>
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<tr>
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<td>Boston Scientific</td>
<td>Autogen EL D176DR</td>
<td>Boston Scientific Four-Front 0693</td>
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<td>St Jude Medical Durata 7122Q</td>
<td>&gt;12</td>
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<tr>
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<td>Feb 2011</td>
<td>Medtronic</td>
<td>Viva XT DTBA2D1</td>
<td>St Jude Medical Durata 7122</td>
<td>11.0</td>
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</tbody>
</table>

**Abbreviation:** ATP antitachycardia pacing; ICD implantable cardioverter defibrillator; SVT supraventricular tachycardia; VT ventricular tachycardia; VF ventricular fibrillation.

*The second and third dates represent the time for generator replacement.*
**Table 2. Deaths and cardiac arrests during the study period at Sites 1 and 2**

<table>
<thead>
<tr>
<th>Patients in case series (failure of timely VF therapy)</th>
<th>Site 1 (n=995)*</th>
<th>Site 2 (n=648)*</th>
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<tr>
<td>Resuscitated cardiac arrest</td>
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<td>0</td>
<td>3</td>
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<tr>
<td>Sudden death</td>
<td>3</td>
<td>2</td>
<td>5</td>
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<tr>
<td><strong>Total events (failure of timely VF therapy)</strong></td>
<td><strong>6</strong></td>
<td><strong>2</strong></td>
<td><strong>8</strong></td>
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</tbody>
</table>

<table>
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<tr>
<th>Patients not included</th>
<th>Site 1 (n=995)*</th>
<th>Site 2 (n=648)*</th>
<th>Total</th>
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<tr>
<td>Resuscitated cardiac arrest</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cardiac death</td>
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<td>(7)</td>
<td>(16)</td>
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<tr>
<td>Heart failure</td>
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<td>6</td>
<td>12</td>
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<tr>
<td>Sudden death</td>
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<td>(4)</td>
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<tr>
<td>Not due to failure of timely VF therapy†</td>
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<td>1</td>
<td>3</td>
</tr>
<tr>
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<td>0</td>
<td>1</td>
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<tr>
<td>Vascular death</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
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<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Peripheral vascular</td>
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<td>2</td>
</tr>
<tr>
<td>Non-cardiovascularal death</td>
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<td>7</td>
<td>22</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td><strong>26</strong></td>
<td><strong>15</strong></td>
<td><strong>41</strong></td>
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<tr>
<td>* Number of ICD and CRT-D patients under follow-up on January 1, 2017.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>† Two patients died of pulseless electrical activity; 1 died of VF that was sensed and detected reliably but was refractory to 6 ICD shocks because of a fractured conductor to the RV shock coil.</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
| ‡ One patient suffered a cardiac arrest and was transported to another hospital. The ICD was not interrogated, and no additional data are available.
Supplemental – eFigures 1 to 10

eFigure 1 (Case 1).

Stored EGM displayed as 4 continuous panels displays filtered atrial EGM (A Sense Amp), filtered RV sensing EGM (V Sense Amp), shock EGM (RV coil- Can, “Discrimination”), dual-chamber markers, ventricular intervals in ms, and timeline in seconds (s). Panel 1 shows ongoing monomorphic VT at cycle length of 387 – 395 ms, slower than the programmed VT detection interval of 315 ms. The rhythm becomes polymorphic at 6 s (end of Panel 1) and then degenerates to VF, which is detected at 13.4 s (beginning of Panel 3). The ICD delivers antitachycardia pacing (ATP, STIM markers, 13.4 – 14.9 s) while charging (line of small asterisks, 13.4 – 21.8 s). However, at 22.4 s (Panel 4) the ICD classifies the rhythm as “sinus,” aborting the shock and resetting VT and VF counters to 0.
(“Return to Sinus” marker). Markers denote intervals classified (“binned”) in the Sinus zone (VS), VT zone (T), or VF zone (F). Intervals are not binned (–) in any zone if zones differ for the index interval and its average with preceding 3 intervals. In St. Jude Medical ICDs, Return to Sinus occurs when a programmable number of consecutive classified (binned) intervals are slower than the slowest detection interval. In this case Return to Sinus was programmed to the nominal value of 5 intervals (range 3 – 7 intervals). Subsequently, clinical polymorphic VT/VF did not satisfy the programmed number of intervals for detection of VT (24 intervals shorter than 315 ms) or VF (12 intervals shorter than 240 ms). Undersensing of low-amplitude VF EGMs following high-amplitude VF EGMs was critical in erroneous premature termination the device-defined VF episode and aborting the shock. Downward arrows in Panel 3 denote one example in which 6 sequential VF EGMs are not sensed following a high-amplitude EGM, despite accurate sensing of signals with comparably low amplitude toward the end of Panel 2. Undersensing occurs because EGM amplitude decreases faster than dynamically-adjusting sensitivity can adapt. The critical undersensing event occurs at 21.2 s (*) following 3 sequentially undersensed EGMs with amplitude 0.91 - 1.1. mV (3 upward arrows).

Undersensing these EGMs results in a device-defined ventricular interval of 852 ms (VS marker). The subsequent EGM is sensed accurately with an interval of 332 ms (black box), resulting in the critical, fifth consecutive binned, VS interval (*) and premature episode termination. However, if VT detection had been programmed to clinically-tested VF-interval value of 333 ms, the 332 ms interval would have been unclassified (–), and premature episode termination would not have occurred. Since the ICD completed charging during the 852 ms interval (end of line of asterisks), it would have delivered the shock synchronous with the EGM ending the 254 ms interval after the † EGM (first binned VT or VF interval after charging). VS² = events sensed on the Discrimination (shock) channel.
Failure to treat VF. Stored EGMs display filtered RV dedicated-bipolar sensing EGM (V Sense Amp), ventricular markers, ventricular intervals in ms, and timeline in seconds (s). These multiple device-defined episodes were recorded during a single clinical VT/VF episode. **A. Monomorphic VT at 3:11 PM.** The 3 continuous panels show that VT begins an unknown time before the recording. The VT cycle length straddles the Sinus-VT boundary of 300 ms so that multiple intervals in Panel 2 remain unclassified. VT is detected at 15.4 s in Panel 3 (VT(ATP----...)) and ATP is delivered immediately (STIM markers). After ATP, VT slows to 318-332 ms in the Sinus zone, resulting in episode termination (“Return to Sinus”). **B. VF.** The next stored EGM recorded about a minute later shows detection of VF. It is likely that the monomorphic VT
degnerated to VF in the interval between the two recordings. Panels 1-5 panels shows stored EGMs from sequential Episodes 1 - 3 in which VF detection criteria were met (12 intervals shorter than 250 ms) but shocks were aborted due to undersensing that caused premature episode termination. Panels 1 - 3 shows Episode 1 which begins after the onset of clinical VF. The ICD charges in Panel 2; but in Panel 3, 5 consecutive binned intervals longer than the VT interval of 300 ms terminate the VF episode prematurely (“Return to Sinus”). Panels 4 and 5 show the ends of VF Episode 2 and Episode 3, respectively. Both episodes were aborted by 5 consecutive binned intervals longer than the VT interval. Panel 6 shows the end of Episode 4 in which a shock was finally delivered to terminate VF. The mV calibration marker shows that VF EGMs have relatively high base-peak amplitudes of 5 - 10 mV for larger EGMs and 1-2 mV for most undersensed EGMs. Asterisks denote selected undersensed EGMs that contributed to premature episode termination due combined effects of highly-variable EGM amplitudes, the high programmed Threshold Start of 62.5%, and the programmed Decay Delay of 60 ms. See eFigure 10.
eFigure 3 (Case 3).

EGMs and interval plot transmitted with Lead Integrity Alert™ Atrial, RV wide-band filtered sensing channel (RV Tip- RV Ring), and dual-chamber marker channel are shown. Panel 1 shows the onset of monomorphic VT at 10:02. Event storage is triggered by the 8 intervals shorter than the programmed VF
detection interval (300 ms FS markers). In Panel 2 (continuous with Panel 1) VT cycle length then slows to 290 – 330 ms in the Monitor zone. The end of the
dotted horizontal line arrows spanning Panels 1 and 2 indicates when VF would have been detected with a clinically-validated detection interval of 330 ms
(182 bpm). Panel 3 shows the interval plot for the corresponding Monitored Episode which begins simultaneously and lasts for 35 min. Rapid “nonsustained”
VT episodes were stored intermittently for 46 min until 10:48 AM. Panels 4 - 6 show representative examples during continuous monomorphic and
polymorphic VT that never fulfilled the VF detection criteria of 30/40 intervals shorter than 300 ms. Ventricular intervals are denoted VS in the Sinus or
Monitor zone, FS in the VF zone, BV for bi-ventricular paced. Atrial markers denote pacing (AP), blanking-period sensing (AB), and refractory-period sensing
(AR).
A. Surface ECGs recorded at 25 mm/s by paramedics from defibrillation electrodes during resuscitation. In Panels 1 and 2, parallel vertical lines denote 360 J external defibrillation. Panel 1 shows defibrillation of VF
to monomorphic VT. Panel 2 shows cardioversion of VT to a slower wide-complex tachycardia; ventricular pacing pulses at 130 bpm do not capture. Panel 3 was recorded about 1 min after Panel 2 without intervention. It shows atrial pacing with intact AV conduction and premature atrial and ventricular complexes. B. Continuous ICD EGMs during one of 3 episodes of monomorphic VT detected and treated by the ICD after external defibrillation and during the 70-min resuscitation. Atrial EGM, wide-band filtered left-ventricular bipolar EGM, and narrow-band filtered RV sensing EGM are shown with markers. Panel 1 begins as ongoing VT accelerates into the VT zone (faster than 300 ms). The onset of VT is not recorded. In Panel 2, detection of VT is delayed by undersensing of low-amplitude EGMs (asterisks). Note the discrepancy between mostly monomorphic LV EGMs and RV EGMs which have variable amplitude and morphology. At right of Panel 2, parallel vertical lines and “VT” denote detection of VT. In the next panel (not shown), ATP terminates VT to atrial-sensed, biventricular paced rhythm.
Selected EGMs show RV integrated bipolar EGM (RV Tip – RV Coil), shock EGM (Can - RV Coil), and ventricular markers. The ICD did not record the onset of VF. It recorded the first device-defined, nonsustained episode (Episode 1) at 03:48. A. Nonsustained Episode 6 at 03:49 is the last episode recorded.
before the first external defibrillation. VF EGMs have a low frequency content and do not fulfills the programmed detection criteria for either VF (18/24 intervals shorter than 300 ms or VT (40 consecutive intervals shorter than 320 ms). Intervals in the VT zone do not contribute to detection because consecutive-interval counting causes each interval in the sinus zone (320 ms or greater) to reset the VT count to 0. After external defibrillation, Monitored Episode 7 (03:53, not shown) displayed a regular tachycardia accelerating from 400 to 380 ms, documented to be sinus tachycardia by surface ECG. B. Nonsustained Episode 8 recorded at 03:55 AM. Monomorphic VT begins almost isorhythmic with sinus tachycardia, and then accelerates but remains slower than the VT zone. It degenerates to polymorphic VT with cycle length 310-350 ms toward the end of Panel 3. The ICD-defined episode is triggered by double counting of VT EGMs at right of Panel 3. C. VF Episode 9 at 03:58. Six continuous panels show polymorphic VT with cycle length 270 – 430 ms that does not satisfy interval/duration criteria for detection and requires a second external shock (Panel 2, up arrow). If the VF interval had been programmed to the clinically-validated values of 320 or 330 ms, this polymorphic VT would have satisfied the programmed 18/24 intervals for detection of VF (end of dotted arrow in Panels 1 and 2). However, the Lead Integrity Alert was activated incorrectly during Episode 5 when both oversensing criteria were fulfilled. This alert increased the number of intervals for VF detection to 30/40 during Episode 6 and subsequent episodes. Because the external shock intervened, we cannot determine if the ICD would have detected VF. After the shock, VT recurred following the second paced beat and immediately accelerated to VF. The frequency content of EGMs was higher during this VF than during the first VF or the polymorphic VT above. The ICD detected VF rapidly (Panel 4, “VF Rx 1 Defib”) and defibrillated it with a single shock Panel 5 (†, CD marker, 36.3 J). Although the Lead Integrity Alert extended detection duration from 18/24 to 30/40 intervals during Episode 5, it did not delay detection of polymorphic VT/VF during Episodes 5, 6, and 8 because none fulfilled the 18/24 criterion. For the VF in Episode 9, the Lead Integrity Alert’s delay was not significant (approximately 12 x 200 ms = 2.4 s).
Stored and real-time EGMs transmitted with Lead Integrity Alert.™

A. Stored EGM with same atrial and RV EGMs as Figure 2 provides a representative example of the 12 “nonsustained” episodes recorded during the clinical event.

B. Real-time EGM during the transmission showing these two EGMs and two far-field channels, shock (Can to RV Coil) and “Leadless ECG” (LECG, Can to SVC Coil). The wide-band filtered dedicated bipolar RV sensing EGM shows
multiple low amplitude, low-frequency VF EGMs that never fulfil the programmed cycle duration and length and criteria for VF (30/40 intervals shorter than 300 ms). Some larger EGMs are undersensed because they time in post-ventricular pacing blanking period. Asterisks Panel 1 of section A and Panel 3 of section B denote selected undersensed EGMs. VT was not detected despite a long VT detection interval because Medtronic ICDs use consecutive-interval counting in the VT zone: any undersensed event resulting in device-measured RR interval ≥ 400 ms resets the VT count to 0. AP = atrial pacing; VP = ventricular pacing, BP = biventricular pacing.
Post-shock undersensing of VF. Atrial EGM A. integrated bipolar sensing EGM (RV) and Can-RV Coil EGM (Shock) are shown with dual-chamber markers and intervals. Monomorphic VT persisted for an unknown interval before accelerating across the 375 ms Sinus-Monitor zone rate boundary, 13 s before Panel 1. Panel 2, continuous with Panel 1, shows monomorphic VT degenerating to VF, which was detected rapidly and shocked successfully after a 6.5 s delay (Panel 3). This initiated a repetitive sequence of recurrent VF immediately after each shock. Continuous Panel 4 shows the first recurrence. The amplitude of the sensing
EGM decreased progressively in successive post-shock recurrences of VF. After the sixth successful defibrillation, the amplitude of the VF EGMs was so low that EGMs were undersensed consistently (Panel 5) and dual-chamber pacing (AP/VP markers) continue through VF. Some VF EGMs were sensed starting a few seconds later (Panel 6), but persistent undersensing of low-amplitude EGMs prevented detection of VF. **B.** Insert shows programmer screen shot of Panel 5 with RV EGM at high gain so that low amplitude VF EGMs are clearly visible.
eFigure 8 (Case 9).

Stored nonsustained episode shows the onset of VF immediately after external cardioversion (not recorded). In each panel, the RV unipolar tip EGM is displayed on the first and third channels with the narrow-band filtered, dedicated bipolar EGM on the second channel. Markers, intervals (ms), and timeline (s) are displayed at bottom. VF begins between 7 and 8 s on Panel 2. In VF, higher-amplitude, higher-frequency fractionated signals are separated by
approximately 300 – 500 ms intervals with isoelectric baseline or low-amplitude signals. Undersensing occurs both because of low-amplitude signals and because Decay Delay does not permit sensing immediately after expiration of the sensing blanking period (125 ms). In Panel 3, asterisks denote undersensed EGMs. Despite many short intervals, too few satisfy St. Jude Medical’s interval average plus interval count criterion to be classified as VF intervals, shorter than 240 ms. No intervals are measured in the VT zone of 250 – 299 ms. The episode ends at 30 s with a total VF count of 11, seven less than the programmed value for detection. We do not know if VF would have been detected eventually because the patient was defibrillated externally approximately 5 seconds later (not shown).
Untreated monomorphic VT degenerates to untreated polymorphic VT/VF with VF detection programmed to 30/40 intervals shorter than 300 ms. Atrial, RV wide-band filtered, dedicated bipolar sensing channel (RV Tip- RV Ring), and dual-chamber marker channel are shown. A. Panel 1 shows the onset of monomorphic VT at 320 ms in the monitor zone at 10:30. The end of the dotted arrow in Panels 1 and 2 indicates where VF would have been detected if the
detection interval was programmed to the clinically validated value of 330 ms. The recording is suspended for 3 min and 50 s at end of Panel 2. The episode ends in Panel 3, likely due to transient entrance block into the region of the sensing bipole during polymorphic VT/VF. B. Within a minute of episode termination, a “nonsustained” episode is redetected at 10:34 in which relatively monomorphic VT transforms to polymorphic VT. Repetitive “nonsustained” polymorphic VT episodes were detected over the next 5 min. These represent ongoing polymorphic VT/VF that do not fulfill the programmed detection criteria. C. Continuous panels recorded at 10:39 show the end of the episode in which VF is detected and shocked (CD, 36.3 J to atrial paced (AP), biventricular-paced (BP) rhythm, probably pulseless electrical activity based on clinical data. Repetitive nonsustained episodes begin 5 min after defibrillation and continue for an additional 6 min (not shown). These likely representing recurrent VF.
St. Jude Medical sensing enhancements to minimize T-wave oversensing, modified with permission from figures provided by St. Jude Medical. A. Decay delay and Threshold Start. The R-wave signal is rectified. After a sensed event (of minimum value 1 mV and maximum value 6mV) a dynamic sensitivity decay start linearly at 3mV/s at a programmable percentage of the R-Wave (Threshold Start). Decay Delay increases the interval from the end of the blanking period (“Sensed Refractory Period) to the start of the dynamic sensitivity decay. The dotted green line show the dynamic sensitivity when Decay Delay is 0 ms instead of 60 ms and Threshold Start is 50% instead of 62.5%. Red dots denote timing at which EGM crosses
threshold and is sensed. **B. Low Frequency Attenuation Filter.** This filter decreases the amplitude of the low frequency signals such as T waves. The figure shows simulated signals including surface ECG lead II, narrow-banded filtered atrial EGM (blue), narrow-banded filtered ventricular EGM (brown), and marker channels. The filter is turned on at the dotted vertical line. With filter ON, amplitude of simulated R waves is unchanged, but the amplitude of simulated T waves is reduced. AS/VS = atrial/ventricular sensed event.