Morphology discrimination criterion wavelet improves rhythm discrimination in single-chamber implantable cardioverter-defibrillators: Spanish Register of morphology discrimination criterion wavelet (REMEDIO)

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Aims
Implantable cardioverter defibrillators (ICDs) are increasingly being used for treatment of ventricular tachycardia (VT)/fibrillation. Inappropriate therapy delivery remains the most frequent complication in patients with ICDs, resulting in psychological distress, proarrhythmia, and battery life reduction. We aim to determine if inappropriate therapies could be reduced by using a morphology discrimination criterion.

Methods and results
We evaluated the performance of the Wavelet™ morphology discrimination algorithm (Medtronic, Inc.) independently from other discrimination enhancements (rate onset and interval stability). A non-randomized, prospective, multicenter, and observational study was designed to determine the sensitivity and specificity of the new morphology criterion. Sensitivity and specificity in slow tachycardia with cycle length (CL) between 340 and 500 ms were analysed as a pre-specified secondary endpoint. A total of 771 spontaneous episodes in 106 patients were analysed. Five hundred and twenty-two episodes corresponded to true supraventricular tachycardia (SVT) with ventricular CL in the VT or FVT zone, of which 473 had therapy appropriately withheld. Of the 249 episodes of true VT/FVT, 21 were classified according to the Wavelet™ criteria as SVT (specificity: 90.6%; sensitivity: 91.6%). All of them were spontaneously terminated with no adverse clinical consequences. No syncopal episodes occurred. For VTs in the slowest analysed range (CL: 340–500 ms), a total of 235 episodes were studied, yielding a specificity of 95.9% and sensitivity of 83.2%.

Conclusion
Wavelet™ discrimination criteria in single-chamber ICDs as the sole discriminator can significantly reduce inappropriate therapy for SVT, not only in the range of VTs in the slowest analysed range (340–500 ms for this study) but also for faster VTs. No significant clinical consequences were found when the algorithm was used, but final data should prompt the use of the algorithm in combination with a high rate time-out feature.

Keywords
Ventricular tachycardia • Morphology discrimination criteria • Inappropriate therapy • ICD

Introduction
Implantable cardioverter defibrillators (ICDs) have been established as the therapy of choice for the prevention and treatment of sudden cardiac death. Inappropriate therapy delivery remains the most frequent complication in patients with ICDs,1 resulting in psychological distress, proarrhythmia, and battery life reduction.2,3 Incorrect interpretation by the device of sinus
tachycardia or atrial fibrillation/flutter with rapid atrioventricular (AV) conduction is a frequent cause of inadequate therapy delivery. Detection enhancement algorithms have been implemented to discriminate supraventricular tachycardia (SVT) from ventricular tachycardia (VT). Although dual-chamber discrimination algorithms are frequently based on measurements of AV association, algorithms used in single-chamber ICDs focus on frequency-related tachycardia characteristics and electrogram (EGM) morphology. For morbidity/mortality reasons and the higher complexity and cost of dual-chamber ICDs, single-chamber devices continue to be the mainstay of therapy for patients without an atrial-pacing indication.

Nowadays, most devices on the market contain some form of SVT discriminator. In single-chamber ICDs, these algorithms have historically been based on beat-to-beat interval variability (rate stability) and abruptness of tachycardia initiation (onset). A reduction of ~50% in the inappropriate ICD therapy has been attained. In spite of two decades of evolving technology, however, a perfect discrimination algorithm remains to be achieved, and a high number of episodes are still inappropriately treated by the device. More recently, a newer morphology-based algorithm (WaveletTM, Medtronic, Inc.) has been introduced. This algorithm uses the wavelet decomposition of EGM signals to compare the morphology of tachycardia complexes with a previously collected sinus rhythm template. An automatic template-collection feature continuously checks the quality of the template and updates it when changes in the intrinsic EGM are identified.

We sought to evaluate the performance of this morphology-based algorithm in a population of patients with a single-chamber ICD implantation indication following current guidelines.

Methods
Study design
The REMEDIO (Registro Español de Morfología y Estabilidad en Discriminación Observacional; Spanish Register of morphology discrimination criterion Observational) study evaluated the performance of the WaveletTM morphology discrimination algorithm (Medtronic, Inc.) independently from other discrimination enhancements (rate onset and interval stability). This prospective and multicenter register was designed to determine the sensitivity and specificity of the new morphology criterion to distinguish SVT from VT in a wide range of different cycle lengths (CLs).

Patients included in the study had to be older than 18 years with a single-chamber ICD implantation indication following current guidelines. Exclusion criteria were Brugada syndrome, idiopathic ventricular fibrillation (VF), long QT syndrome, pregnancy, pacemaker-dependent patients, or VF cardiac arrest patients with preserved left ventricular ejection fraction (≥40%). Patients with an implanted Marquis VT(TM) Medtronic Model 7230 and a dual-coil endocardial defibrillation lead were included in the study. The study protocol was approved by the local Ethics Committee of all participating centres, and all participants provided verbal and written informed consent prior to the study. The study was sponsored by Medtronic Iberica.

Study protocol
During ICD implantation or pre-discharge follow-up (<10 days post-implantation), SVT and VT inductions were recommended to check device and discrimination algorithm adequate functioning. The patient had to be monitored during the test. Previously, the intrinsic rhythm EGM template had to be stored in the device.

Recommended device programming at implantation, discharge and follow-ups is discussed later on. In order to assess discrimination with sinus tachycardia, a slight exercise was recommended during the test to reach a heart rate faster than 100 b.p.m.

All tachycardia episodes stored were reviewed, and a final diagnosis was made by an independent panel of three expert electrophysiologists.

Device and wavelet(TM)-based algorithm description
The Marquis VT(TM) Medtronic Model 7230 ICD is an implantable medical device that automatically detects and treats VT, VF, and bradyarrhythmia episodes, and able to deliver shocks up to 30 J in magnitude. The WaveletTM feature is a dynamic EGM template-matching algorithm that compares the morphology of EGMs during a tachycardia episode to that previously obtained during intrinsic rhythm. The algorithm collects six intrinsically sensed QRS complexes during the baseline rhythm and creates a template from a QRS snapshot consisting of 48 EGM samples taken at 4 ms each by using a Haar wavelet transform. The morphology transform of the template is compared in real time with transforms of the EGMs during tachycardia. This comparison is expressed as a percent-match score that describes the degree of morphological similarity between the baseline and tachycardia EGMs. Beats with match scores below a programmed threshold (nominal 70%) are classified as ventricular (Figure 1). If at least three of the last eight QRS complexes during tachycardia match the stored template, the WaveletTM algorithm withholds the therapy. Then, the rhythm is continuously monitored until tachyarrhythmia detection occurs or the fast ventricular rate ends.

After successful template collection and calculation, the template is validated every 10 s during a confirmation period of ~12 min. Afterwards, the quality of the template is verified by comparison to the actual EGM every 1000 s. Template collection is restarted if 30 of the last 100 checked EGMs do not match the template. Template collection can be done manually by the physician or automatically by the device.

Device programming
The EGM source for WaveletTM template acquisition was selected as the nominally programmed right ventricle coil (HVB) to can (HVA). According to the findings of Luthje et al., this configuration appeared to be superior to others, also showing a better performance when different postures were tested. Recommended gain setting for the Wavelet EGM was ±8 mV (nominal value), if the recorded EGM was <6 mV base-to-peak. If greater, then the recommended EGM source was V tip-right ventricle coil (HVB) with a gain setting of ±16mV in order to avoid clipping R waves. Dynamic range was adjusted to avoid saturation.

Wavelet discrimination had to be programmed ON (activated) or MONITOR, with a defined SVT frequency upper limit selected by the investigator (maximum the lower limit for the VF detection zone) and a recommended lower limit of 600 ms at device implantation. Match threshold was programmed to a nominal value of 70%. All devices were programmed with VT, fast VT (FVT), and VF detection zones, with upper and lower limits left to each investigator discretion. FVT within the VT or VF-zone was left to investigator discretion.

Onset and stability were programmed OFF (to force exclusive use of the WaveletTM EGM feature for rhythm discrimination), and the high-rate time-out feature was programmed OFF.
At follow-up visits, recommended device window programming for VT, FVT, and VF was left to investigator discretion. A monitor-only (no therapy delivered) VTs in the slowest analysed range zone was recommended to evaluate performance of the Wavelet™ criterion during sinus tachycardia.

Statistical analysis
Sensitivity was defined as the percentage of VT/FVT episodes appropriately detected \([\text{true positives}/(\text{true positives} + \text{false negatives})]\). Specificity was defined as the percentage of SVT episodes where therapy was appropriately withheld \([\text{true negatives}/(\text{true negatives} + \text{false positives})]\). VT/FVT positive predictive value was defined as the percentage of VT/FVT episodes receiving therapy that were truly VT/FVT \([\text{true positives}/(\text{true positives} + \text{false positives})]\).

Statistics were performed using the SPSS 15.0 statistical package (SPSS Inc., Chicago, IL, USA). Descriptive statistics were performed. Categorical data are presented as frequencies (%), continuous variables are presented as median (interquartile range) or mean ± SD. Two-sided \(P\)-values < 0.05 were considered significant.

Results

Patient population
A total of 106 patients with a Marquis VR ICD implanted at six participating centres were included in the study. Of these, 88.6% were male, and the mean age was 69.6 years (12.3). The mean follow-up was 10 ± 8 months (1060 cumulative follow-up months). Table 1 shows the clinical characteristics of the enrolled patients. The most frequent underlying cardiomyopathy was ischaemic heart disease, and 17.9% of the population presented with atrial fibrillation.

Spontaneous tachycardia episodes
A total of 771 spontaneous episodes in 106 patients were analysed during the study. Two hundred and seventy-seven episodes were classified as VT/VF and 494 as SVT by the device. Of these 277 VT/VF episodes, after an independent panel of three expert electrophysiologists reviewed the stored EGMs, the final diagnosis was 228 episodes of true VT/VF and 49 episodes of SVT (Table 2). FVT was mostly programmed within the VF-zone (83.3%).
The mean CL of VT was 324 (81) ms, and the mean CL of SVT was 528 (61) ms ($P < 0.05$), with a considerable area of overlap between both types of tachycardia (Figures 2 and 3). Non-sustained episodes were not included in the analysis because of the impossibility of determining whether Wavelet™ would have delivered the therapy or not.

### Spontaneous SVT episodes

A total of 522 episodes of SVT with ventricular CL in the VT or FVT zone as confirmed by the independent panel of electrophysiologists were analysed (49 SVT episodes classified as VT/FVT by the device and 473 episodes correctly classified). Of these 522 episodes of true SVT, 473 had therapy appropriately withheld. The reduction of inappropriate VT/FVT therapy was 90.6%.

The Wavelet™ criteria failed to discriminate 49 episodes of true SVT (specificity, 90.6%; sensitivity: 91.6%; negative predictive value: 95.8%) in seven patients. Detailed data of CL, duration, and type of these 49 false-positive episodes are shown in Table 3. The majority of them (39/49 SVT episodes) corresponded to sinus tachycardia with EGM morphology significantly different than the templates recorded during usual rhythm.

### Spontaneous VT/FVT episodes

Of the 249 episodes of true VT/FVT, 21 episodes in 9 patients were classified according to the Wavelet™ criteria as SVT (Table 4). Mean VT CL of these 21 episodes was 372 ms (range: 300–490) and mean VT duration 53 s (range: 6–210). It is interesting to note that 15 of 21 were slow VTs. All of them were spontaneously terminated with no adverse clinical consequences (sensitivity: 91.6%; positive predictive value: 82.3%). No syncopal episodes occurred.

### Spontaneous slow tachycardias

Sensitivity and specificity in slow tachycardia with CL between 340 and 500 ms were analysed as a pre-specified secondary endpoint. There were a total of 235 episodes in that CL range. Follow-up for this subgroup was $10 \pm 8$ months.

Of the total of 146 true SVT episodes, the Wavelet™ criteria withheld therapy in 140 (specificity: 95.9%; negative predictive value: 90.3%).

A total of 89 episodes of true VT/FVT were recorded and stored. Wavelet™ misclassified VT as SVT in 15 patients, showing a sensitivity of 83.2% and a positive predictive value of 92.5% (Figure 4). No syncopal or pre-syncopal episodes occurred, nor decompensated heart failure or any other consequence of underdetected VTs in the slowest analysed range.

### Discussion

Inappropriate therapy delivery remains the most frequent complication in patients with ICDs, resulting in pain, psychological distress, proarrhythmia, and battery life reduction, among other effects. In this study, inappropriate therapy delivery for SVT episodes was reduced by 90.6%, with a negative predictive value of 95.8%. The Wavelet™ morphology discrimination algorithm significantly reduced inappropriate detection of SVT as VT in single-chamber ICDs, whereas maintaining a high sensitivity and positive predictive value for the detection of true VT.
Apart from the Wavelet™ algorithm, three other morphology-based discrimination algorithms have been widely evaluated and are currently implemented in market-released ICDs: EGM width, morphology discrimination, and Rhythm ID. EGM width has been replaced by the Wavelet™ algorithm in new-generation devices. During spontaneous episodes, Wavelet™ has demonstrated superiority to EGM width for tachycardia discrimination.9 The specificity identified by Luthje et al.7 for SVT detection using the Wavelet™ criteria with the RV-Can source during exercise testing was similar to that reported with the morphology discrimination algorithm.10 Although including the can (HVA) as one of the electrodes for the Wavelet EGM could potentially register noise generated by pectoral muscle, this was not an issue in our registry.

Similarly to the data found in our registry, independently of ventricular CL, morphology discrimination allowed to enhance specificity differentiating VT from SVT.11,12 specially for VTs in the slowest analysed ranges, in which specificity reached a value as high as 95.9%. Rhythm ID uses a vector time and correlation analysis for tachycardia discrimination.13 Its performance is comparable to that of the Wavelet™ algorithm with a sensitivity of 100% and specificity of 92% for SVT detection in induced and spontaneous episodes.

A high sensitivity for FVT and VF detection is mandatory in ICDs because the consequences of underdetection are potentially fatal.14 For this reason, a highly sensitive algorithm is appropriate for faster tachycardias because of the high risk of underdetection. On the other hand, a highly specific algorithm is appropriate for haemodynamically stable patients with slower VTs because the risk of underdetection is low and the probability of rate-zone overlaps with VT is high. Wavelet algorithm specificity was >90% for all VTs in our registry, with the highest value for VTs in the slowest

<table>
<thead>
<tr>
<th>Patient</th>
<th>Number of episodes/patient</th>
<th>SVT CL</th>
<th>SVT duration</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>590–570</td>
<td>1440–120</td>
<td>ST</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>240</td>
<td>13</td>
<td>AT/AF</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>370–470</td>
<td>540–15</td>
<td>ST with conduction aberrancy</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>530–590</td>
<td>420–17</td>
<td>ST</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>340</td>
<td>6</td>
<td>AT/AF</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>530–540</td>
<td>3600–1260</td>
<td>ST with conduction aberrancy</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>560</td>
<td>49</td>
<td>ST</td>
</tr>
</tbody>
</table>

Absolute value is shown in case of a single episode and range in case of several. SVT CL, supraventricular tachycardia cycle length; ST, sinus tachycardia; AT/AF, atrial tachycardia/fibrillation.
Table 4 Number, ventricular tachycardia cycle length (ms), duration (s), and wavelet match scores of episodes misclassified as supraventricular tachycardia by the Wavelet criteria (false negatives)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Number of episodes/patient</th>
<th>VT CL (ms)</th>
<th>VT duration (s)</th>
<th>Wavelet percent-match score (adjust (%))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>490</td>
<td>11</td>
<td>73–88</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>430</td>
<td>10</td>
<td>67–82</td>
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<tr>
<td>3</td>
<td>1</td>
<td>420</td>
<td>12</td>
<td>64–73</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>360–440</td>
<td>7–26</td>
<td>76–79</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>340–370</td>
<td>6–10</td>
<td>82–88</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>340–360</td>
<td>8–46</td>
<td>64–75</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>340</td>
<td>27–210</td>
<td>64–73</td>
</tr>
<tr>
<td>8</td>
<td>3</td>
<td>320</td>
<td>180–210</td>
<td>76–82</td>
</tr>
<tr>
<td>9</td>
<td>3</td>
<td>300–320</td>
<td>9–27</td>
<td>67–75</td>
</tr>
</tbody>
</table>

Absolute value is shown in case of a single episode and range in case of several. VT CL, ventricular tachycardia cycle length.

An EGM morphology algorithm may be 'fooled' by VT that has morphology similar to the intrinsic rhythm template, as occurred infrequently in this study. It is interesting to note that 15 of 21 were slow VTs and each of the 21 instances of 'missed' VT terminated spontaneously with no clinical sequelae. EGM morphology algorithms may also be thwarted by aberrancy of conduction that causes EGM morphology during SVTs to be different than the templates recorded during usual rhythm. Even not frank aberrancy but morphological changes during sinus tachycardia maybe enough to fool the algorithm, as was our case in this study (significant EGM morphology variations prevented the wavelet to get an adequate template). Given that none of these episodes have a CL >500 ms, we think that this should be considered as the lower limit when programming the Wavelet algorithm. Besides, in four of these nine patients with VT misclassified as SVT the wavelet percent-match score was ≤75%. If programmed threshold would have been 75% instead of 70% (nominal value), 9 of 21 episodes would have been correctly classified as VT.

Noise or saturation of the EGM signal is another potential pitfall of the algorithm. A careful programming of gain settings and EGM configuration can potentially solve this issue. In our registry, incorrect classification of episodes was not related to poor signal quality due to noise or saturation in any case.

Future refinements in the algorithm functioning will probably increase this figure for VTs in the slowest analysed ranges, or maybe combination of different diagnostic criteria may enhance global performance in this subset of tachycardias.

Historically, when ICDs detected VT using rate criteria only, inappropriate therapy for SVT occurred at percentages as high as 45%. Dual-chamber detection algorithms improved tachycardia discrimination by analysing the relation between atrial and ventricular activity. Some investigators have found that dual-chamber detection algorithms are superior to single-chamber ICDs, but not all recent trial reports have reached this conclusion.15,16

Gronefeld et al.17 conducted a 259-patient study in which different morphology criteria were studied. A sensitivity of 77% and specificity of 71% were found when applied to tachycardia CL from 288 to 401 ms. In combination with other discrimination criteria (sudden onset), sensitivity increased to 99.5% at the expense of lower specificity (48%).

The Detect SVT trial (199 patients) combined EGM morphology, interval stability, and sudden-onset criteria applied to episodes with CL lasting between 300 and 400 ms and demonstrated an inappropriate SVT detection rate of 39.5%.18

The 1122-patient study by Klein et al.19 was a non-randomized study that used the Wavelet™ morphology discrimination criteria to classify tachycardias. Inappropriate therapies for SVT were reduced by 78% for episodes within the range for which the Wavelet™ criteria was programmed. Sensitivity for VT was 98.6%.

In the present study, sensitivity for VT discrimination was 91.6%, which is less than the one achieved in other studies. However, it is important to point out that VT episodes classified as SVT, where the lower sensitivity was identified, had a CL superior to 320 ms, 15 of 21 were <30 s long, and never led to significant clinical consequences. Even in the absence of clinical consequences, these final data should prompt the use of the algorithm in combination with a high rate time-out feature.

Limitations

This is a prospective and multicenter register. Despite excluding patients introduced the potential for study bias in the registry, since we were evaluating the performance of a morphology discrimination criterion, we excluded pathologies expected to develop polymorphic VTs or VF, quite different in morphology to the template obtained during intrinsic rhythm and easy a priori to discriminate. Our aim was to be able to check the performance of the algorithm in the worst scenario, discriminating sustained VTs from supraventricular rhythms entering the detection window.

To fully validate these results, a randomized study is necessary to compare the performance of the Wavelet™ algorithm on and
off, and to evaluate its performance in combination with other diagnostic criteria. Apart from that, the data obtained help us to know what we can expect from the algorithm in the ‘real world’.

The final rhythm or true mechanism of tachycardia episodes stored could not be established with absolute certainty in this study; nonetheless, three expert electrophysiologists validated the study data.

**Conclusion**

Wavelet™ discrimination criteria in single-chamber ICDs as the sole discriminator can significantly reduce inappropriate therapy for SVT, not only in the range of VT/FVT but also for VTs in the slowest analysed range (340–500 ms in this registry). No detrimental clinical consequences were found when the algorithm was used. Given these data, the wavelet discrimination criteria should be considered as an effective tool when used alone but, in order to maximize the benefits, a lower limit of 500 ms and the concomitant use of other discrimination criteria or combination with a high rate time-out feature should be considered.

**Conflict of interest:** J.T. and J.L.P. are currently conducting research sponsored by Medtronic, Boston and St. Jude. L.M. is currently conducting research sponsored by Medtronic, Boston, St Jude, Sorin and Biotronik.

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**References**