Combined Atrial and Ventricular Antitachycardia Pacing as a Novel Method of Rhythm Discrimination
The Dynamic Discrimination Download Study

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Background—Inappropriate and unnecessary implantable cardioverter-defibrillator shocks continue to be highly prevalent.

Methods and Results—We prospectively evaluated a new algorithm for discriminating supraventricular (SVT) and ventricular (VT) tachycardias with 1:1 atrioventricular association that is based on the response of the arrhythmia to simultaneous or convergent dual-chamber antitachycardia pacing. Patients undergoing dual-chamber cardioverter-defibrillator implantation were randomized to the simultaneous atrioventricular and convergent atrioventricular arms with crossover at 3 months. Sixty-three patients had 1407 1:1 antitachycardia pacing sequences suitable for analysis (1381 1:1 SVT episodes in 32 patients and 26 1:1 VT episodes in 6 patients). Antitachycardia pacing terminated 66 of 1381 SVT (5%; generalized estimating equations adjusted, 23.8%) and 20 of 26 VT (77%; generalized estimating equation adjusted, 68.6%) episodes. After the exclusion of sinus tachycardia, the new software terminated 40 of 57 (70%; generalized estimating equation adjusted, 70.2%) SVT episodes. The new algorithm terminated or correctly classified 1379 of 1381 SVT sequences for an overall specificity of 99.9% (generalized estimating equation adjusted, 99.8%) and 23 of 26 VT for an overall sensitivity of 88.5% (generalized estimating equation adjusted, 82.1%). There were no statistically significant differences between the simultaneous and the convergent atrioventricular antitachycardia pacing sequences in their ability to confirm VT or reject SVT. No significant proarrhythmias were noted.

Conclusions—We describe here a new pacing algorithm in dual-chamber defibrillators that can terminate arrhythmias or discriminate between 1:1 SVT and VT if the arrhythmia persists. Testing this new algorithm in larger patient populations is warranted.


(Circulation. 2010;121:487-497.)

Key Words: antitachycardia pacing ▪ defibrillator ▪ rhythm discrimination
The DD Download Study was a multicenter, prospective, randomized, crossover clinical trial that evaluated the safety and efficacy of atrial and ventricular ATP in terminating tachyarrhythmias and discriminating between VT and SVT in those arrhythmias that were not terminated. Patients were eligible if they were older than 18 years of age, implanted with an EnTrust DR or a Virtuoso DR ICD (Medtronic Inc, Minneapolis, Minn) for approved indications, and had a history of spontaneous tachycardia with 1:1 AV association at a cycle length (CL) ≤400 ms, sustained or nonsustained VT, or inducible sustained VT. Patients were excluded if they had chronic atrial fibrillation.

Study Design

This DD Download Study was an Investigational Device Exemption trial performed at 6 centers (5 in the United States and 1 in Canada). The study protocol was approved by the institutional review boards of the respective institutions, and all of the patients provided written informed consent before enrollment. First enrollment of a patient in this protocol was on February 27, 2007. The protocol was closed to enrollment on October 24, 2008.

Eligible patients implanted with a dual-chamber ICD (EnTrust DR or Virtuoso DR ICD) were enrolled and randomized in a 1:1 ratio to the SAV or CAV arms of the study with crossover at 3 months. The DD investigational software was then downloaded to their ICDs through a user interface that runs on the 2900 programmer (Medtronic). Patients were followed up at 3-month intervals for up to 1 year from randomization. At each follow-up visit, stored electrograms and the response of arrhythmias to ATP sequences were noted and analyzed. Programmed device parameters are shown in Table 1.

The DD Algorithm

The DD algorithm uses dual-chamber ATP sequences to discriminate SVT from VT on the basis of the response of the arrhythmia to simultaneous atrial and ventricular ATP31,32 in the acute setting of the electrophysiology laboratory. In the present study, we prospectively evaluated the performance and safety of the atrial and ventricular ATP discrimination algorithm in recipients of dual-chamber ICDs by downloading the dynamic discrimination (DD) investigational software to their devices. We also compared in a randomized crossover design the performance of 2 schemes of the DD algorithm: the simultaneous (SAV) and the convergent (CAV) atrial and ventricular ATP.

Methods

Patients

The DD Download Study was a multicenter, prospective, randomized, crossover clinical trial that evaluated the safety and efficacy of atrial and ventricular ATP in terminating tachyarrhythmias and discriminating between VT and SVT in those arrhythmias that were not terminated. Patients were eligible if they were older than 18 years of age, implanted with an EnTrust DR or a Virtuoso DR ICD (Medtronic Inc, Minneapolis, Minn) for approved indications, and had a history of spontaneous tachycardia with 1:1 AV association at a cycle length (CL) ≤400 ms, sustained or nonsustained VT, or inducible sustained VT. Patients were excluded if they had chronic atrial fibrillation.

Statistical Methods

All of the measurements are reported as mean±SD. The sensitivity, specificity, positive predictive value, negative predictive value, and percent VT and SVT termination estimates were computed with SAS (version 9.2, SAS Institute Inc, Cary, NC) statistical software. When appropriate, all of the percentages were estimated with a logistic regression model and the generalized estimating equations (GEE) method with an exchangeable correlation structure to account for within-patient correlation for multiple events per patient. During estimation of percent VT termination by CAV ATP, a first-order autoregressive correlation structure was used. A value of P≤0.05 was considered statistically significant.

Results

Clinical Characteristics

Of 63 enrolled patients, 55 had a 3-month, 53 had a 6-month, and 31 had a 12-month follow-up visit for a mean follow-up duration of 9.6±3.3 months. The clinical characteristics of the enrolled patients are shown in Table 2. There were no differences between patients randomized to the 2 arms of the study in any of the baseline clinical characteristics or in follow-up rates or duration (8.3±2.0 months in the CAV group compared with 8.4±4.3 months in the SAV group).
During follow-up, 1451 DD sequences were delivered. Of those, 1407 sequences represented 1:1 SVT or VT with 1:1 retrograde conduction. These sequences were used to evaluate the safety and performance of the DD download algorithm. The remaining 44 sequences represented atrial fibrillation with rapid ventricular response. They were not included in further analysis.

Table 3 summarizes the performance of the DD download algorithm. Thirty-two patients had episodes of 1:1 SVT with a mean CL of 407±49 ms, and 6 patients had 1:1 VT with a mean CL of 317±16 ms. A total of 1407 ATP sequences (1381 1:1 SVT episodes in 32 patients and 26 1:1 VT episodes in 6 patients) were analyzed. In response to ATP, 66 of 1381 SVT (5%; GEE adjusted, 23.8%) and 20 of 26 VT (77%; GEE adjusted, 68.6%) episodes terminated. The discrepancy between the crude and the GEE-adjusted estimates of the SVT termination is caused mainly by a few patients having a large number of episodes with a relatively low SVT termination rate. Those are primarily patients with sinus tachycardia in whom ATP obviously could not terminate the rhythm. When episodes of sinus tachycardia were excluded from analysis, the termination rate of 1:1 SVT episodes by the DD ATP bursts was 40 of 57 (70%; GEE adjusted, 70.2%).

**DD Algorithm Performance**

Figure 1. The DD flowchart describing the hierarchy built into the algorithm between the DD and PR Logic algorithms. The DD software is downloaded into the Entrust and Virtuoso dual-chamber ICDs and embedded into their native detection algorithms as follows: The DD algorithm intervenes in the detection process at the time PR Logic is ready to declare either a VT or an SVT episode. If PR Logic is ready to declare the episode as either atrial fibrillation (AF) or double tachycardia, then the DD algorithm stores the PR Logic decision, delivers 1 ATP sequence, stores the DD data, and then after a subsequent initial detection allows normal PR Logic operation. When PR Logic is ready to declare an episode and the rhythm is 1:1 VT or SVT, then the DD algorithm stores the PR Logic decision, delivers 1 ATP sequence, and stores the DD data. If the DD decision is SVT, then the DD algorithm waits a designated time before allowing the initial detection process to repeat. After 3 DD sequences, the algorithm reverts to normal PR Logic behavior. During the waiting period, the software monitors for a change in rhythm or rate and proceeds to VT or ventricular fibrillation (VF) therapy if indicated. If the DD decision is VT, normal VT or ventricular fibrillation therapy is initiated. AFL indicates atrial flutter; NID Met, number of intervals for detection are met.
GEE of the sensitivity, specificity, and positive and negative predictive values and the percent arrhythmia termination for each of the CAV and SAV ATP schemes are shown in Table 4. Briefly, the DD algorithm terminated or correctly classified 1379 of 1381 SVT sequences for an overall specificity of 99.9% (GEE adjusted, 99.8%; Figures 3A and 3B) and 23 of 26 VT for an overall sensitivity of 88.5% (GEE adjusted, 82.1%; Figures 3C and 3D). There were no statistically significant differences between the SAV and CAV ATP schemes in their ability to confirm VT or reject SVT ($P_{H11022} > 0.5$). When only fast SVT episodes (CL $\leq$ 320 ms) were included in the analysis ($n = 13$), the DD algorithm terminated 8 episodes and correctly classified the other 5 episodes.

**DD Incorrect Classification of SVT**

Two sequences of SVT were misclassified as VT by the DD download algorithm of a total of 1381 1:1 SVT sequences. In 1 case, a premature ventricular contraction at the end of the ATP sequence led to the misclassification (Figure 4A). In the second case, a slow run of 5 beats of ventricular rhythm at a rate of 107 bpm was induced by the ATP sequence, as detailed in the section on proarrhythmias. In both instances, no symptoms were reported by the patient and no inappropriate therapies were delivered by the device.

**DD Incorrect Classification of VT**

There were 3 sequences of VT that were misclassified as SVT by the DD download algorithm after the first ATP sequence of a total of 26 1:1 VT sequences (Figure 4B). All 3 episodes were misclassified because of either a functional failure to capture the atrial rhythm during ATP secondary to retrograde conduction to the atria during ventricular pacing or a premature atrial contraction. This resulted in a sensed retrograde atrial event after ATP. In 1 case, the next ATP burst allowed correct classification. In the second case, the VT terminated spontaneously before a second burst of ATP was delivered. In the third case, the second ATP burst terminated the VT. There were no clinical adverse events associated with any of these episodes. In all 3 cases, unnecessary shocks were avoided.

**Proarrhythmia**

No atrial proarrhythmia was observed in any patients. There was 1 episode of ATP-induced slow ventricular rhythm. The subject was undergoing hall walk exercise to elevate his heart rate. The VT detection interval was temporarily programmed to 650 ms to maximize detection sensitivity for this exercise. Sinus rhythm was detected at 97 bpm, and CAV ATP was delivered at a pacing CL of 550 ms. This induced a 5-beat run of ventricular rhythm at a CL of 560 ms. Two previous similar sequences of CAV ATP in the same patient did not induce VT. No symptoms were reported. This instance of proarrhythmia is also reported as 1 of the 2 false-positive detections of VT by the algorithm.

**Comparison of DD to PR Logic Rhythm Classification**

The DD download software was capable of storing the PR Logic Dual-Chamber Rule decision at the time of initial
detection immediately before delivery of DD ATP. These stored results were used to provide a rough estimate of the performance of PR Logic on the same episodes used to evaluate the DD algorithm. PR Logic detected 15 of 16 VT episodes for a sensitivity of 94% (GEE adjusted, 94%) and correctly classified 763 of 819 SVT episodes for a specificity of 93% (GEE adjusted, 87%) compared with the GEE-adjusted specificity of 99.8% and sensitivity of 82.1% for the DD algorithm. Strategic use of the combined algorithms can incorporate the strengths of both algorithms.

Discussion

We report here the first clinical trial in ambulatory patients of a novel dual-chamber discrimination algorithm for 1:1 tachycardias. Unlike other algorithms currently implemented in marketed devices in the United States, it places the treatment of arrhythmias upstream of the discrimination process and uses the response to the therapy as a discriminatory test. The advantage is terminating a significant proportion of arrhythmias without a delay in therapy. The 2 prospectively tested ATP schemes were found to be equally efficacious in terminating 1:1 arrhythmias and
accurate in discriminating between their cardiac chambers of origin.

The incidence of inappropriate shock remains high despite advances in the design of discrimination algorithms to separate between VT and SVT. Both inappropriate and unnecessary shocks can result in patient discomfort and emotional distress as well as substantial expenses related to emergency department visits and hospital admissions. Repetitive shocks can lead to premature ICD battery depletion, and rare shocks can result in proarrhythmia. Furthermore, both appropriate and inappropriate shocks have been associated with excess mortality in ICD recipients, whereas ATP has not. Thus, reducing both inappropriate and unnecessary shocks is a major priority in ICD therapy.

Historically, ICD algorithms have sought to discriminate VT from SVT on the basis of passive analysis of both single-chamber and dual-chamber rhythm characteristics. Single-chamber characteristics include abruptness of onset and regularity of the ventricular rhythm and morphology of the ventricular electrogram compared with a baseline template. Dual-chamber characteristics include a relation between atrial and ventricular rates and AV association. Most such algorithms are designed to have a high sensitivity for detecting VT; however, >90% of 1:1 tachycardias are SVT. It is therefore not surprising that the performance of existing algorithms for 1:1 tachycardias has resulted in a high incidence of inappropriate therapy of SVT. Because of this a priori distribution of rhythms, an algorithm designed to discriminate 1:1 tachycardias must have a high specificity for...
rejecting SVT to be of clinical value, which highlights the importance of the present algorithm.

The dual-chamber ATP algorithm adopted in the present study uses active pacing techniques developed for rhythm discrimination in the electrophysiology laboratory in an ICD. It changes the usual ICD paradigm of “diagnose before treating” to “treat first and diagnose what is left,” using the response to the therapy as a discriminatory test. The advantage is terminating a significant proportion of arrhythmias without any delay in therapy. The “diagnose before treating” paradigm is based in part on concerns about ATP-induced proarrhythmia. The present approach was motivated in part by results of the PainFree Rx18 and PainFree Rx II19 trials, which show the safety of rate-adaptive ventricular burst ATP at 88% of the tachycardia CL as an initial treatment for regular tachycardias.

The present results for spontaneous 1:1 tachycardias in ambulatory patients expand our previous findings31,32 for 1:1 tachycardias induced in the electrophysiology laboratory. In the real-life context of the DD Download Study, almost 80% of VT episodes were terminated by the atrial plus ventricular ATP. The lower termination rate of 1:1 SVT episodes is due primarily to the fact that most were sinus tachycardia. When episodes of sinus tachycardia were excluded from analysis, the termination rate of 1:1 SVT episodes by the DD ATP bursts was high (70%). Proarrhythmia from the DD algorithm was minimal and insignificant in $>1400$ delivered ATP sequences.

The present study highlighted a few pitfalls of the DD algorithm in discriminating between VT and SVT. These were due primarily to ectopic beats induced by the ATP burst or to functional failure to capture the atrium during ATP secondary to retrograde conduction during ventricular pacing. The former problem may be overcome by having multiple ATP bursts delivered for each episode of 1:1 arrhythmia that persists after ATP, with the rhythm classification being determined by the aggregate of multiple ATP sequences (2 of 3, 3 of 5, etc). Another possible solution to this problem consists of using the DD algorithm in conjunction with other discrimination algorithms. Adjusting the blanking periods after ATP to avoid sensing ectopic beats at the end of ATP may also improve the performance of the DD algorithm. Functional lack of capture in the atrial channel may be resolved by applying established capture management protocols that identify the evoked potential after the last pacing spike in the ATP train for
both the atrial and ventricular channels. Pacing with high outputs during ATP to prevent real failure to capture the atrial and the ventricular chambers during pacing can be also implemented.

Although the benefit of this dynamic method of discrimination between VT and SVT is obvious, its future remains to be defined. Whether atrial plus ventricular ATP will replace other established discrimination algorithms or be used in conjunction with current algorithms remains unclear and will have to be tested in larger populations of patients. A significant advantage of this algorithm over other discrimination methods is the absence of delay in therapy while the discrimination process is taking place. This minimizes the incidence of symptoms such as syncope. It also eliminates the need for discrimination in a large proportion of episodes by terminating them. This is of particular importance given the high percentage (70%) of termination of non–sinus rhythm 1:1 SVT by the present ATP algorithm.

The present study has a few limitations that deserve mention. First, the total number of patients enrolled was relatively small, thus limiting the number of 1:1 VT episodes and the number of SVT episodes that were not confirmed to be sinus tachycardia. Second, because the DD algorithm could be downloaded to only 2 ICD models, no patients enrolled in this study had a cardiac resynchronization therapy ICD. Whether the efficacy and safety data extracted from the present study apply to sicker patients with biventricular pacing devices is unproven.

**Conclusions**

We describe a new “treatment-first” discrimination algorithm that can terminate a large proportion of VT and of nonsinus tachycardia SVT. This new algorithm is safe and can discriminate SVT from VT in 1:1 tachycardias with high sensitivity and specificity. The performance of this new algorithm and its potential use in conjunction with other discrimination methods merit further testing in a pivotal trial enrolling
large numbers of dual-chamber and biventricular ICD recipients.

Acknowledgments
We acknowledge all of the participating centers in the DD Download Study: Brigham and Women’s Hospital, Boston, Mass (Laurence Epstein, MD); Cedars-Sinai Medical Center, Los Angeles, Calif (Charles Swerdlow, MD); London Health Sciences Center, London, Ontario, Canada (Raymond Yee, MD); Park Nicollet Heart and Vascular Building, St Louis Park, Minn (Jay Simonson, MD); Philadelphia Heart Institute, Philadelphia, Pa (Kent Volosin, MD); and University of Pittsburgh Medical Center, Pittsburgh, Pa (Samir Saba, MD). We also acknowledge the contributions of the study manager, Jill Christensen, and statistician, Athula Abeyratne, both of Medtronic Inc.

Source of Funding
This study was sponsored by Medtronic Inc, Minneapolis, Minn.

Disclosures
Dr Saba received research grants from Medtronic Inc, Boston Scientific Inc, and St Jude Medical. He is the inventor of the patent on which the DD algorithm was based. Dr Volosin is part of the speakers’ bureau for Medtronic Inc and St Jude Medical. He has received research grants from Medtronic Inc and Biosense Webster. Dr Yee is a consultant to and is the recipient of research

Figure 4. Episodes of tachyarrhythmias misclassified by the DD algorithm. A, An episode of sinus tachycardia misclassified as VT because of a premature ventricular beat coinciding with the end of the CAV ATP burst. B, An episode of VT misclassified as SVT presumably because of lack of atrial capture during the SAV ATP burst, leading to a retrograde atrial event being sensed at the end of the ATP burst. EGM indicates electrogram.
grants from Medtronic Inc. Dr Swerdlow received research grants from Medtronic Inc. Dr Brown is an employee of Medtronic Inc.

References
We describe here the dynamic discrimination pacing algorithm in dual-chamber defibrillators that can terminate arrhythmias or discriminate between 1:1 supraventricular tachycardias and ventricular tachycardias if the arrhythmia persists. This novel algorithm considers the rhythm ventricular in origin if the first sensed event after simultaneous atrial and ventricular antitachycardia pacing is on the ventricular channel and supraventricular in origin otherwise. We tested this algorithm in 62 dual-chamber defibrillator recipients who were followed up for 9.6±3.3 months. The dynamic discrimination algorithm terminated or correctly classified 1379 of 1381 SVT sequences for an overall specificity of 99.9%.

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CLINICAL PERSPECTIVE


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Circulation. 2010;121:487-497; originally published online January 18, 2010;
doi: 10.1161/CIRCULATIONAHA.109.892570
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/121/4/487

An erratum has been published regarding this article. Please see the attached page for:
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In the article by Saba et al, “Combined Atrial and Ventricular Anti-Tachycardia Pacing As a Novel Method of Rhythm Discrimination: The Dynamic Discrimination Download Study,” which appeared in the February 2, 2010 issue of the journal (Circulation. 2010;121:487–497), the current figure 3C is not correct, and should be replaced by the following panel and figure legend:

![Figure C](image)

**Figure.** C. An episode of 1:1 VT correctly classified by a SAV ATP burst. Note that the first sensed event after the ATP burst is on the V channel.

The change has been made to the current online version of the article. The authors apologize for the error.

DOI: 10.1161/CIR.0b013e3181e6c39e