Initial Clinical Experience With a New Automated Antitachycardia Pacing Algorithm

Feasibility and Safety in an Ambulatory Patient Cohort

See Editorial by Duncker and Veltmann

BACKGROUND: Antitachycardia pacing (ATP) in implantable cardioverter-defibrillators (ICD) decreases patient shock burden but has recognized limitations. A new automated ATP (AATP) based on electrophysiological first principles was designed. The study objective was to assess the feasibility and safety of AATP in ambulatory ICD patients.

METHODS AND RESULTS: Enrolled patients had dual chamber or cardiac resynchronization therapy ICDs, history of ≥1 ICD-treated ventricular tachycardias (VT)/ventricular fibrillation episode, or a recorded, sustained monomorphic VT. Detection was set to ventricular fibrillation number of intervals to detect=24/32, VT number of intervals to detect≥16, and a fast VT zone of 240 to 320 ms. AATP prescribed the components and delivery of successive ATP sequences in real time, using the same settings for all patients. ICD datalogs were uploaded every ≈3 months, at unscheduled visits, exit, and death. Episodes and adverse events were adjudicated by separate committees. Results were adjusted (generalized estimating equations) for multiple episodes.AATP was downloaded into the ICDs of 144 patients (121 men), aged 67.4±11.9 years, left ventricular ejection fraction 33.1±13.6% (n=137), and treated 1626 episodes in 49 patients during 14.5±5.1 months of follow-up. Datalogs permitted adjudication of 702 episodes, including 669 sustained monomorphic VT, 20 polymorphic VT, 10 supraventricular tachycardia, and 3 malsensing episodes. AATP terminated 39 of 69 (59% adjusted) sustained monomorphic VT in the fast VT zone, 509 of 590 (85% adjusted) in the VT zone, and 6 of 10 in the ventricular fibrillation zone. No supraventricular tachycardias converted to VT or ventricular fibrillation. No anomalous AATP behavior was observed.

CONCLUSIONS: The new AATP algorithm safely generated ATP sequences and controlled therapy progression in all zones without need for individualized programing.

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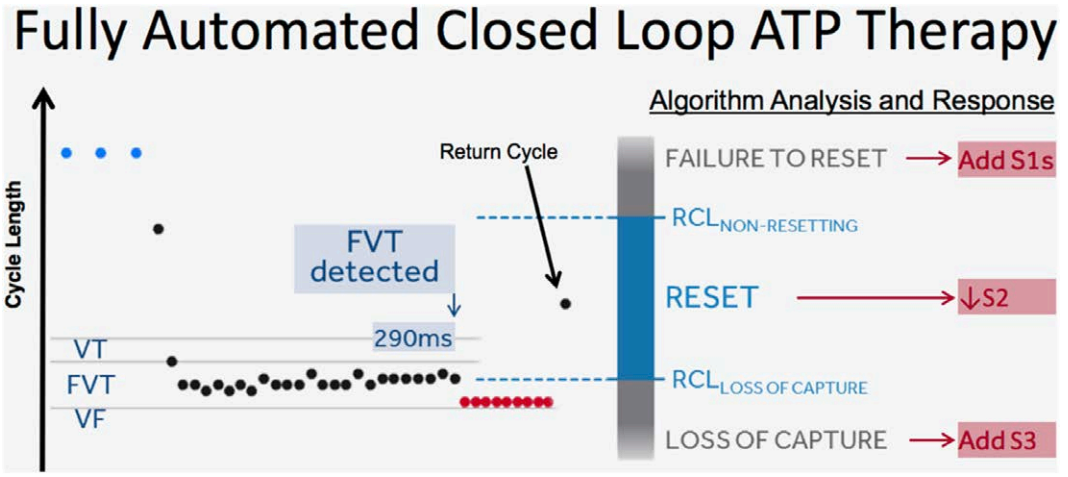

WHAT IS KNOWN

- Current implementations of antitachycardia pacing (ATP) algorithms are complex, with multiple parameters to be programed.
- The first-sequence success rate for current ATP algorithms is 70% to 75% and rises to 90% after multiple ATP sequences. However, longer detection times reduce the first-sequence ATP success rate to ≈50%.
- Aggressive ATP programing can cause acceleration of ventricular tachycardia or degeneration to ventricular fibrillation in ≤10% of episodes.

WHAT THE STUDY ADDS

- This new automatic ATP algorithm is based on electrophysiological first principles and is feasible and safe while being simpler to program.
- The efficacy of the new ATP algorithm and the low rate of acceleration of ventricular tachycardia can mitigate the effects of longer programed detection times.

Nearly a decade after the first implantable cardioverter-defibrillators (ICD) were implanted beginning in 1980, antitachycardia pacing (ATP) algorithms were incorporated to reduce reliance on shock therapy for ventricular tachycardias (VT).[1,2] Since then, most manufacturers' ATP features have incorporated similar principles and architecture.

ICDs offer much ATP programing flexibility. Typically, there are 2 VT detection zones defined by VT cycle length (VTCL) or rate. Within each zone, multiple ATP therapies consisting of one or more ATP sequences, pacing impulses (S1) per sequence, S1 cycle length (decremental or fixed), and VT rate-dependent initial S1, can be prescribed. Within shock therapy, an ATP sequence can be prescribed before or during capacitor charging. Despite this flexibility, ATP has limitations, and how it is programed varies considerably among centers.

Programing flexibility allows individual tailoring, but evidence from studies have called into question the benefits of tailored programing, whereas others have sought to establish empirical programing as standard-of-care.[3–5] The issue of empirical versus tailored programing has been further impacted by studies showing the benefit of delayed detection to avoid treating putative nonsustained VTs but at the possible expense of reduced ATP efficacy.[6–8]

Moreover, it is not clear that ATP tailoring guidelines would help because they could only be used a priori. Even carefully programed therapies progress within predetermined boundaries, yet they interact with complex pathological electrophysiology intraepisode and interepisode. Multiple VT circuits in the myocardium can lead to VT acceleration and complex progressions from monomorphic VT to polymorphic VT (PVT) and ventricular fibrillation (VF). Progressive ischemia or coronary artery disease may add VT circuits and advance VT instability. Tailoring of current ATP regimes involves guessing. Many ATP protocols have been tried historically, but even the ones that have endured, such as burst- and ramp-like protocols, do not fully exploit current knowledge concerning cardiac electrophysiological mechanisms.

This study describes the first clinical experience with a new algorithm that links therapy to fundamental electrophysiology by automatically tailoring ATP sequence-by-sequence based on real-time data from the prior failed ATP sequence(s). It uses an ATP protocol that is maximally aggressive in the excitable gap over all VTCLs and is simple to program.[3,9,10] This article reports feasibility testing in a patient cohort selected to provide a high incidence of VT.

METHODS

Study Design

This was a multicenter, prospective, single cohort study to assess the first clinical use of a new, automatic ATP (AATP) algorithm. The primary objective of this study was to assess the feasibility of the new algorithm in at least 30 ambulatory subjects with sustained monomorphic VT (SMVT). A secondary objective was to assess whether the new ATP algorithm would induce VT when it was inappropriately delivered into supraventricular tachycardia (SVT). The study was not designed to compare algorithm efficacy against any market-released ATP algorithm. The study protocol was approved by the local institutional ethics review board at each participating center.

Patient Selection

Male or female patients >18 years of age having a qualifying ICD implanted for standard primary or secondary prevention indication and having a functional atrial lead were further assessed for study eligibility. The atrial lead was considered crucial for episode adjudication. Primary prevention ICD patients were included if they had any ICD-treated VT/VF episode, any detected VT ≥10 seconds in duration, or a monitored VT episode with VTCL in the study protocol–treatment zone. Patients were excluded if enrolled in a concurrent study that might confound study results, presence of chronic atrial fibrillation, inherited channelopathies, such as long QT and Brugada syndromes, or medical conditions limiting compliance with the study protocol.

Study Protocol

Enrolled patients had an initial study visit where baseline patient demographic data and limited medical history were collected, after which the algorithm software was downloaded into the ICD. The algorithm software was restricted to download into 1 of 6 Medtronic dual chamber ICD and cardiac resynchronization therapy ICD models. A programer was used to interrogate the device, establish baseline episode counters, and clear any stored episode electrogram data from memory. Patients were provided with a syncope diary and were followed up every 3 months for at least 12 and ≤24 months. Follow-up included interrogation in the device clinic or by remote monitoring to collect stored device data concerning detected and treated events and corresponding episode electrogram data. The study was completed when the last enrolled study subject had been followed for 12 months post-enrollment.

New ATP Algorithm

The new, automated real-time algorithm called AATP was designed to reduce ICD shocks using electrophysiological first principles. In the setting of structural heart disease, SMVTs are reentrant tachycardias. For any ATP sequence to modify the SMVT, the pacing wavefronts must first propagate to and penetrate the reentrant circuit excitable gap to cause conduction block. A paced activation wavefront penetrating the excitable gap would be expected to terminate the SMVT or if not, at least reset the VT. Pacing wavefronts can also potentially alter the reentrant circuit or initiate one or more other SMVT circuits, changing the VT or its rate in a manner that remains amenable to ongoing ATP therapy, or changing the VT to a PVT/VF that requires shock therapy.

A key issue for AATP is what to do after an ATP sequence fails to terminate SMVT. Because return cycle length (RCL)—the elapsed time from the final ATP pulse to the next ventricular sensed event—contains information about propagation of wavefronts between the pacing site and the active SMVT circuit, the AATP algorithm used the RCL to assess how ATP failed to automatically design new ATP sequences in real time, in a systematic search for an efficacious sequence. The algorithm interprets the RCL measurement as evidence of one of three possible outcomes: failure to reset, reset, or loss of capture (LOC).

AATP designed all ATP therapies as S1–S2/S3 sequences in which the S2 and S3 perform a different function than the S1 pulses. The primary purpose of the S1 pulses is not to terminate SMVT but to reach the active SMVT circuit without activating other potential SMVT circuits that could result in VT acceleration or degeneration. Therefore, the algorithm always set the S1 coupling interval conservatively at 88% of VTCL, with a sufficient number of S1 pulses to reach a maximally remote, hypothetical VT circuit (assumed to have a propagation time of 150 ms from the pacing site). If the RCL indicated that the first ATP sequence failed to reset the SMVT, S1 pulses were added in subsequent ATP sequences until reset was achieved. RCL and VTCL were also used to detect whether the S1 sequence was too long (the optimal number of S1 pulses calculated as RCL-VTCL divided by VTCL-S1, rounded up, and incremented by 1), in which case the number of S1 pulses was reduced in subsequent sequences, thereby minimizing the risk of VT acceleration or VF.

The principles and operation of the S1–S2 sequence are illustrated in Figure 1. Once the S1 train results in SMVT resetting, an S2 extrastimulus should be all that is needed to terminate SMVT. Unlike the longer coupling interval used for the S1 train, the S2 should use the shortest coupling interval that does not lose capture, to maximize the probability of effecting conduction block within the VT circuit. For the initial AATP sequence, the algorithm sets the S1–S2 coupling interval slightly longer than the myocardial effective refractory period estimated from heart rate history. In subsequent ATP sequences, the algorithm decrements the S1–S2 coupling interval in 20 to 30 ms steps until VT is terminated or until the S2 causes LOC. Should S2 LOC occur, the S1–S2 coupling interval of the next sequence is increased (back to the last successful S1–S2 coupling interval that captured) to peel back the refractory period, and an S3 is added. The AATP protocol is completed when the S3 fails to capture or when a minimum S2–S3 interval limit (160 ms) is reached. By the time S3 loses capture, the shock timer will usually have expired and shocks are delivered.

If the VTCL changes by >10% or 30 ms during AATP therapy, the algorithm interprets this as initiation of a new SMVT circuit, thereby restarting the AATP algorithm. This is important because a new SMVT circuit may be farther away from the pacing site, requiring adjustment of the ATP sequence length to ensure SMVT reset is continuing and pursuit of efficacy is not interrupted.

The principles underlying this algorithm apply across all VT zones, regardless of SMVT rate or morphology, thus

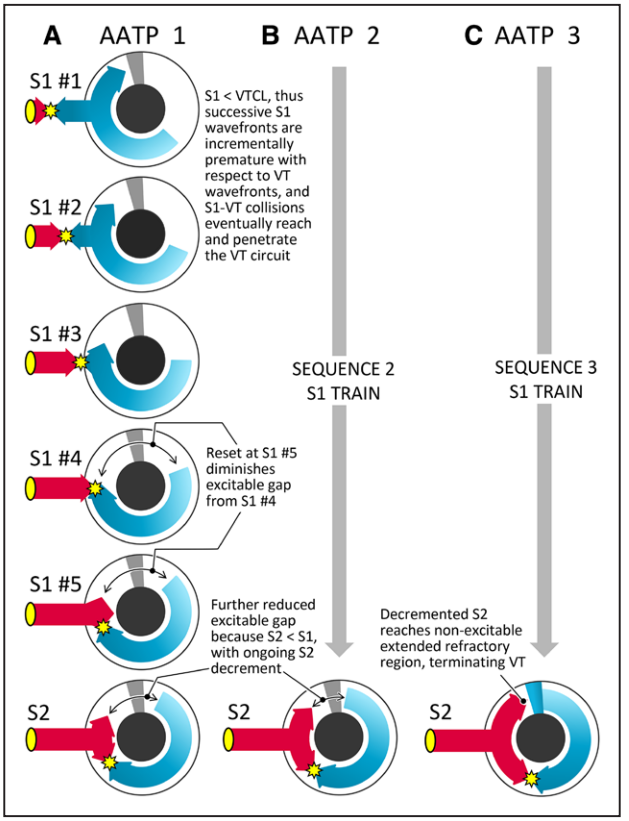

Figure 1. Schematic of antitachycardia pacing (ATP) interaction with myocardium over three successive ATP sequences (AATP 1-3) in a hypothetical sustained monomorphic ventricular tachycardia (SMVT) episode. Each VT circuit rendering shows the ATP pulse wavefront (red) when it collides with the VT wavefront (blue). The black circle is non-conducting myocardium, and the narrow area projecting radially upward is a region of extended refractoriness or slow conduction (grey, excitable; blue, non-excitable). Automatic ATP (AATP) 1 shows S1 and S2 pulse effects. All S1 pulses are 88% of VT cycle length, so AATP 2 and 3 only show S2 effects. **A**, The first four S1-VT collisions approach the VT circuit. The 5th S1 wavefront penetrates the VT circuit before a VT wavefront can exit, propagates orthodromically and antidromically, and advances the timing of the circulating VT wavefront (reset), decreasing the excitable gap. The S2 pulse further reduces the excitable gap without terminating VT. **B**, This S2 is decremented, further reducing the excitable gap, but without terminating VT. **C**, The S2 is decremented again, reaching the region of extended refractoriness when it is non-excitable, blocking VT circuit conduction, and terminating VT.

decoupling therapy selection from VT/VF detection zones and simplifying ICD programing. A patient example demonstrating several features and aspects of the AATP algorithm in operation is shown in Figure 2.

Device Programing for Shock Therapy Controller

Because patient safety was paramount, ICDs were equipped with a modified shock therapy controller that placed a time limit on AATP delivery (Figure 3). Any episode with VTCL ≤190 ms proceeded directly to shock therapy. All rhythms with VTCL >190 ms were subject to AATP therapy before shock therapy. To support shock therapy controller function, the VT, fast VT (FVT), and VF zone boundaries were set at the investigator's discretion; typical values being 400, 320, and 240 ms, respectively. At initial detection, the shock timer was set to 45/60 s (physician programable) for VT, 30 s for FVT, or 20 s for VF. At each redetection, the remaining time-to-shock could be reset, updated, or allowed to continue timing out. At timeout, shock was delivered. In general, the shock controller was designed to decrease time-to-shock as an episode progressed, but some rhythm transitions were designed to increase time-to-shock. For example, a shock timer reset to 45/60 s was allowed if a transition from a higher rate zone to the VT zone occurred. Within the VT zone, a VT break of a few slow beats between ATP therapies could also restart the shock timer to 45/60 s. The FVT zone was augmented with a rate regularity algorithm so that irregular polymorphic FVT would advance more quickly to shock than regular monomorphic FVT. SVT discriminators were applied to VTCL ≥260 ms. All post-AATP shocks were programed to maximum energy, with ATP during charging where appropriate.

Data Analysis and Definitions

Analysis focused solely on detected tachycardia episodes for which stored near- or far-field electrogram and marker channel information was retrieved. A committee of 3 scientists and 5 study investigators adjudicated all episodes treated with ATP. Three rounds of adjudication were held, with study investigators having final authority for decisions. Where differences of opinion among study investigators occurred, a discussion ensued to reach a final decision by a simple majority. Episodes were classified as SVT or VT based on commonly accepted criteria, including onset mechanism, A:V relationship, response to ATP, and far-field ventricular electrogram morphology compared with sinus rhythm. SMVT was defined as any consistent ventricular electrogram morphology and minimal cycle length variability; otherwise, it was classified as PVT or VF. AATP was judged successful when an episode terminated without delivery of shock but not if VT slowed into nontreatment zone. Although not a specific goal of the study, SMVT acceleration by AATP was also quantitated. Acceleration was defined as a decrease in the VTCL by the greater of 10% or 30 ms or conversion of SMVT to PVT/VF. Patients failed to complete syncope diaries, so syncope adverse events were collected from case report forms. Events were reviewed for relatedness to the AATP algorithm, as well as any VT or VF episode by the adverse events committee. Where indicated, proportion computations were adjusted using generalized estimating equations to account for multiple tachycardia episodes in the same patient or multiple tachycardia episodes arising from the same VT circuit. No adjustment was made for other covariates. The generalized estimating equations methodology assumed a binomial distribution with exchangeable correlation structure. Generalized estimating equations adjustments were made using SAS v9.4 statistical analysis software (SAS Institute,

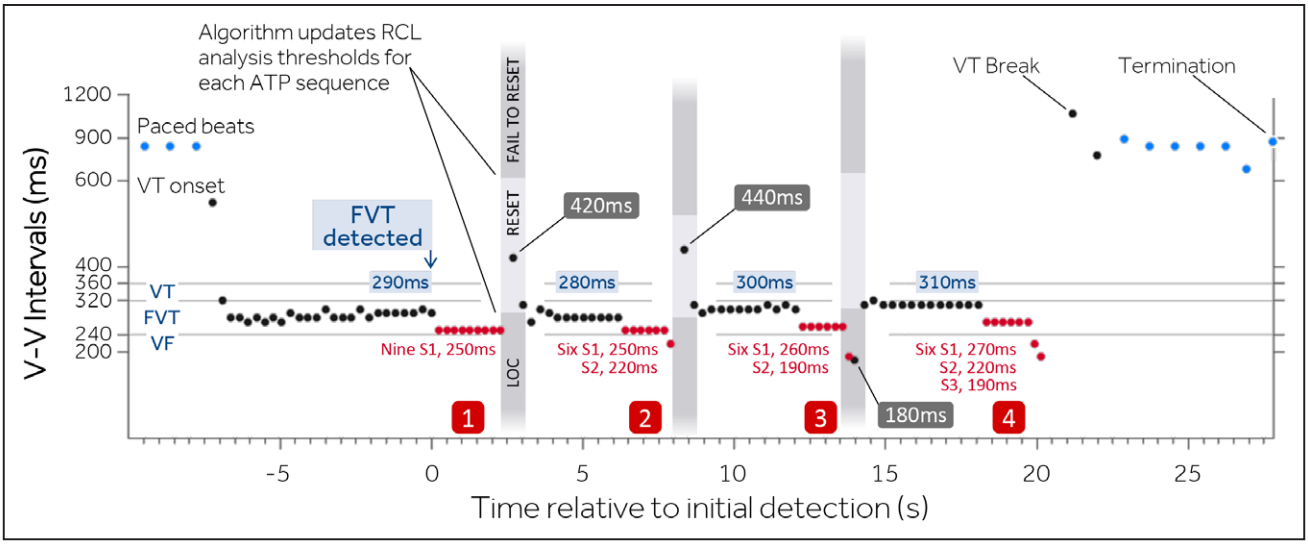

Figure 2. Plot of ventricular intervals versus time from 1 ventricular tachycardia (VT) episode (blue dot, paced; black dot, sensed; and red dot, antitachycardia pacing [ATP]).
Detection zones for VT, fast VT (FVT), and ventricular fibrillation are labeled at **left**. Detected VT cycle length values are shaded light blue, parameters of automated antitachycardia pacing sequence 1 to 4 are in red, return cycle length (RCL) values are shaded dark grey. The shaded vertical bars with 3 grey zones depict the threshold values that the algorithm applied after each failed ATP sequence to decide whether the RCL indicated loss of capture (LOC), reset, or failure to reset. The RCL analysis was used to design the next ATP sequence. ATP #1: A 9-pulse S1 train was used. No S2 was used because the algorithm predicted an S2 would fail to capture. The algorithm determined from RCL=420 ms that VT reset had occurred. ATP #2: With VT reset, propagation time to the VT circuit was computed, predicting that 7 S1 pulses would be sufficient. An S2 was added in search of efficacy. With an RCL=440 ms, ATP #2 maintained reset as predicted, but did not terminate VT. ATP #3: S2 was decremented to 190 ms in search of efficacy. The resulting RCL=180 ms indicated that S2 lost capture. ATP #4: Because ATP #3 lost capture, S2 was set to the S2 value that had most recently captured, and S3 was set to the value of S2 that had just lost capture. The resulting S2/S3 sequence captured and terminated the VT.

Inc, Cary, NC). Statistical summaries are expressed in terms of mean±1 SD.

RESULTS

A total of 150 patients consented to enter the trial, and the AATP algorithm was downloaded into the ICDs of 144 individuals (121 men) with a mean age of 67.4±11.9 years. AATP software was not downloaded in 6 patients because they were subsequently found to be ineligible for the study (4), patient noncompliance (1), and operator error (1). Left ventricular ejection fraction measurement was available in 137 patients, and the mean was 33.1±13.6%. Underlying cardiac disease etiology was ischemic cardiomyopathy or flow limiting coronary artery disease in 23.5%. (Table 1)

Data were retrieved from 1626 episodes in 49 patients treated by the AATP algorithm during a mean follow-up of 14.5±5.1 months. According to device datalogs, AATP terminated 1428 or 87.8% of episodes (79.1% adjusted). The committee adjudicated 702 episodes in 49 patients for which electrogram and marker channel data were available (Figure 4). Of the 702 treated episodes, 689 (98%) episodes were VT with 669 episodes of SMVT and 20 PVT. Ten added episodes were determined to be SVT, 1 other episode was T-wave oversensing, and 2 were caused by lead noise artifact.

AATP Algorithm Performance

Detailed analysis of all SMVT episodes found that the algorithm identified VT reset and LOC with good reliability. Detailed examination of all electrogram data showed that the first ATP sequence reset the VT circuit in 96% of episodes (95.8% adjusted). When AATP identified nonresetting after the initial ATP sequence, the number of S1s was increased and achieved reset in the subsequent sequence. The occurrence of premature ventricular contractions or pacing-provoked repetitive ventricular responses can lead to a shortened RCL value and erroneous conclusion about VT reset or LOC. This response was observed in 25 ATP sequences (2% of all ATP sequences delivered) in 23 SMVT episodes in 10 subjects. Cases of erroneous RCL analysis led primarily to wasted time in the search for efficacy with no adverse events.

Of the 669 SMVT episodes, the new ATP algorithm terminated 554 or 82.8% (80.1% adjusted) of episodes (Table 2). AATP terminated 86.3% (84.9% adjusted) of the 590 SMVT episodes and 56.5% (58.7% adjusted)

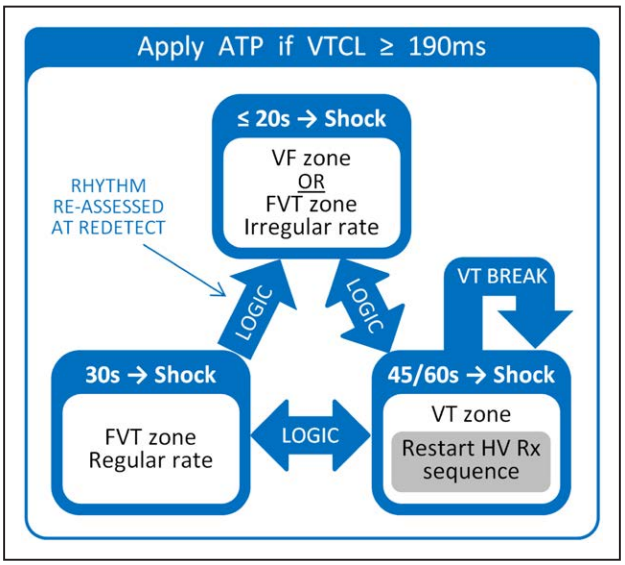

Figure 3. Schematic diagram of shock controller algorithm (logic). On initial detection, the shock timer is set to 45 or 60 s (physician programable) for ventricular tachycardia (VT), 30 s for fast VT (FVT), or 20 s for ventricular fibrillation (VF).
At each redetection, remaining time-to-shock can be reset, updated, or allowed to continue. At time expiry, shock is delivered. The shock controller timer counts down to shock as an episode progresses, but some rhythm transitions can increase time-to-shock. Reset of the shock timer back to 45/60 s was allowed if VT transitioned from a higher rate zone to the VT zone. Within the VT zone, a transient break in VT of a few slow beats between antitachycardia pacing (ATP) therapies could also restart the shock timer to 45/60 s. Within the FVT zone, transition to an irregular VT (suggesting polymorphic VT) would advance more quickly to shock than regular monomorphic FVT. VTCL indicates VT cycle length.

of FVT episodes. The cumulative success rate of AATP for all SMVT episodes was 65% after the first ATP sequence, 73% after 1 to 2 ATP sequences, and 78% after 1 to 6 ATP sequences (adjusted; Table 3). Episodes detected within the VF zone were not adjusted because of the small number of episodes.

Using its refractory period estimation function, the AATP algorithm prescribed an initial S2 at a coupling interval less than the S1 cycle length in 462 of 629 (73%) episodes. In 303 of 462 episodes (66%), the S2 terminated VT; in only 2 of 462 (0.4%) episodes did the initial S2 fail to capture. Thus, the refractory period estimation tool selected S2 for the initial ATP sequence as designed.

An S3 pulse was delivered in 91 of 1236 (7.4%) ATP sequences involving 60 of 630 (9.5%) SMVT episodes in 10 of 37 (27.0%) patients. Of these, the S3 terminated VT in 23 of 91 (25.3%) sequences in 23 of 60 (38.3%) SMVT episodes in 7 of 10 (70.0%) patients. An S3 captured but failed to terminate VT on 34 of 91 (37.4%) occasions and went on to shock therapy. Including episodes that were and were not adjudicated, 198 VT episodes in 43 patients failed to terminate with AATP and all terminated with shock therapy. The median number of shocks was 1 (interquartile range, 1–2 shocks).

Table 1. Patient Characteristics

	Total	Adjudicated Episodes
No. of Patients, N	**144**	**49**
Episodes	…	702
Age, y	67.4±11.9	68.6±14.0
Men, %	121 (84%)	42 (86%)
LVEF, %	33.1±13.6	33.7±13.8
Primary prevention	75 (52.1%)	38 (77.6%)
NYHA class 1 or 2*	62/96 (64.6%)	20/35 (57.1%)
History of documented ventricular arrhythmias†		
SMVT	37 (25.7%)	13 (26.5%)
PVT	3 (2.1%)	2 (4.1%)
VF	21 (14.6%)	10 (20.4%)
History of syncope associated with VT or VF	22 (15.3%)	9 (18.4%)

LVEF indicates left ventricular ejection fraction; NYHA, New York Heart Classification functional class; PVT, polymorphic ventricular tachycardia; SMVT, sustained monomorphic ventricular tachycardia; VF, ventricular fibrillation; and VT, ventricular tachycardia.
*NYHA class was available in only a subset of patients.
†Patients could have >1 arrhythmia.

Safety of AATP Algorithm

Table 4 lists the frequency of rate accelerations and development of PVT caused by AATP. The overall adjusted acceleration rate was 1.3% for any SMVT, including an adjusted rate of 4.2% for FVT and 1.3% for slower VT. Conversion of SMVT to PVT/VF occurred only once.

Syncope diaries were given to subjects but none were completed. However, 9 syncopal events were recorded in the study case report forms. Five syncopal events were judged to be unrelated to the new ATP algorithm, and the other 4 had an uncertain relatedness to the new ATP algorithm. Three of 9 syncopal events coincided with the dates of a VT episode, yielding an estimated arrhythmic syncope rate of 3 of 669 (0.4%) in 3 subjects. Proximate to the reported syncope, there were 5 episodes of SMVT all terminated by 1 or 2 ATP sequences and 2 episodes of PVT/VF terminated by shocks in 19.2 s after 3 ATP sequences and in 25.7 s after 4 ATP sequences.

ICD datalogs indicated that 572 SVT episodes were detected in 23 patients. Device therapy was withheld in the majority, but AATP treated 41 episodes. Only 10 episodes in 4 patients had event data, and all were

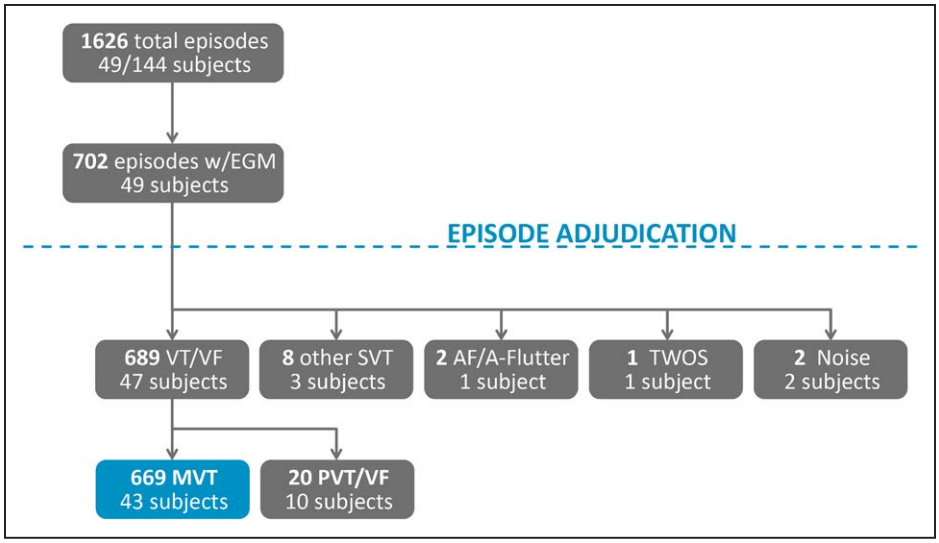

Figure 4. Detailed breakdown of responses to the new automated antitachycardia pacing algorithm as adjudicated by the events committee are shown in this chart.
A-Flutter indicates atrial flutter; AF, atrial fibrillation; MVT, monomorphic ventricular tachycardia; PVT, polymorphic ventricular tachycardia; SVT, supraventricular tachycardia; TWOS, T-wave oversensing; VF, ventricular fibrillation; VT, ventricular tachycardia; and w/EGM, with electrograms.

adjudicated as being SVT only (2 atrial fibrillation/atrial flutter and 8 other SVT). In one episode, AATP terminated the SVT, slightly increased the SVT rate in the second, and had no effect on SVT rate in the third episode. In 7 episodes, the ventricular rate slowed after AATP with 4 episodes exiting the therapy zone. AATP never converted SVT to VT/VF. No safety concerns were identified on reviewing operation of the AATP algorithm.

DISCUSSION

ATP was introduced as an enhancement to ICD therapy nearly a decade after the first ICDs were implanted as a way of reducing reliance on device shocks.[1,2] The initial recognized benefit of ICD shock avoidance was maintenance of ICD patient quality of life.[4] More recently, clinical trials have shown that appropriate shock therapy is associated with increased mortality.[11,12] Thus, there is also renewed focus on delaying time to ICD detection of ventricular arrhythmias so that therapy is avoided for self-terminating episodes and optimal programing of ATP to maximize efficacy and minimize VT acceleration or degeneration to VF.

Conventional ATP therapy has served patients well, but ATP performance is dependent on several factors. Over a wide range of VTCL, Gillis et al[13] reported 94% efficacy with 1 to 3 ATP sequences, independent of ATP protocol (burst or ramp). In contrast, Gulizia found that burst was more efficacious than ramp ATP for treatment of FVT.[10] Peinado et al[9] reported a first ATP sequence success of 72%, rising to 91% after 1 or 2 ATP sequences and showed an efficacy dependence on ATP train length and ATP cycle length. In studies focused on rapid SMVT (defined as VTCL, 250–320 ms), Anguera et al[13] reported a success rate of 83% after 2 ATP sequences, which was similar to that reported in the PainFREE Rx trial (Pacing Fast Ventricular Tachycardia Reduces Shock Therapies).[14] More recently, Anguera et al[15] reported a first ATP success rate of 73% to 77%. Subsequent ATP sequences can increase ATP efficacy to 79% to 91% but at the risk of VT acceleration, variously reported at 2% to 10%.[3,4,9,15,16] EMPIRIC (The Comparison of Empiric to Physician-Tailored Programming of Implantable Cardioverter-Defibrillators) showed that ATP success rate remained high for VT≤200 beats per minute (VTCL ≥300 ms), but other studies have suggested lower ATP success with more rapid VT rates.[5,9,17] The interaction between VT detection interval and ATP in preventing shocks was examined by Arenal et al[18] using the ADVANCE III trial (Avoid Delivering Therapies for Non-Sustained Arrhythmias in ICD Patients III) database. They reported an ATP success rate for FVT

Table 2. Automated Antitachycardia Pacing Efficacy in Adjudicated Ventricular Tachycardia Episodes

Zone(s) in Which SMVT Episodes Were Detected	SMVT Episodes Terminated Without Shock		
	X of N	%	GEE% (CI)
All	554/669	82.8	80.1 (70.9–86.9)
VT	509/590	86.3	84.9 (75.5–91.2)
FVT	39/69	56.5	58.7 (35.9–78.3)
VF	6/10	60.0	…

CI indicates confidence interval; FVT, fast ventricular tachycardia; GEE, generalize estimating equations; SMVT, sustained monomorphic ventricular tachycardia; VF, ventricular fibrillation; and VT, ventricular tachycardia.

Table 3. Cumulative Success Rate for AATP

AATP Sequence No.	Cumulative SMVT Episodes Terminated (Total=669 Episodes)		
	No. of Episodes	%	GEE% (CI)
1	438	65.5	64.7 (53.5–74.4)
2	490	73.2	73.0 (61.8–81.8)
3	502	75.0	74.1 (63.0–82.8)
4	510	76.2	75.0 (64.3–83.3)
5	527	78.8	76.8 (66.7–84.6)
6	532	79.5	78.0 (68.0–85.6)
7	533	79.7	78.1 (68.0–85.6)
8	534	79.8	78.2 (68.2–85.7)
All	554	82.8	80.1 (70.9–86.9)

AATP indicates automated antitachycardia pacing; CI, confidence intervals; GEE, generalize estimating equations; and SMVT, sustained monomorphic ventricular tachycardia.

episodes of 58%. In summary, programing of detection VTCL and delay, ATP protocol, and number of ATP sequences all affect the likelihood of shock therapy in ICD patients.

After introduction of ATP therapy, there were few guidelines on how best to program an ATP prescription for any individual patient. Some centers would tailor ATP therapy to the individual patient, whereas other centers would standardize the ATP therapy to a single, empirically derived prescription across all their patients. The EMPIRIC trial showed that a standardized ATP prescription was as effective in preventing shocks compared with individualized ATP programing tailored to each patient.[5] It has been recommended that standardized programing use ATP protocols validated in clinical trials, such as PainFREE II and PREPARE (Primary Prevention Parameters Evaluation Study).[4,7,19] Both approaches have the same limitations that are inherent to all conventional ATP therapies, however ATP is programed. (1) Optimal programing requires advance knowledge of the conduction time between the pacing site and a reentrant circuit and the excitable gap duration, and neither are available to the operator. Consequently, all conventional ATP programing, whether standardized across all patients or individually tailored, is inherently empirical. Moreover, there are multiple parameters that need to be set that affect the probability that the ATP will reach the reentrant circuit. With 2 or more VT rate zones, current ATP therapy is complex to program. (2) Patients may have >1 VT type with similar rates and they will be treated with the same programed ATP, despite different reentrant circuits being involved. An ATP, prescription may be optimal for 1 SMVT but ineffective or more likely to accelerate a different SMVT. (3) Conventional ATP algorithms do not possess any feedback mechanism that informs the ICD whether an ATP sequence was sufficient to reach the reentrant circuit or not. If an initial ATP sequences fails to terminate a VT, the inherent assumption is that subsequent ATP sequences need to be more aggressive. However, a modest increase in aggressiveness of conventional ATP sequences significantly increases the risk of VT acceleration or degeneration to PVT/VF because the entire pulse train (all S1s) is decremented with each successive ATP sequence.[9]

Table 4. Observed Rates of Acceleration by Automated Antitachycardia Pacing Algorithm

Zone(s) in Which SMVT Episodes Were Detected	Rates of SMVT Acceleration		
	X of N	%	GEE% (CI)
All	9/669	1.3	1.3 (0.8–2.3)
VT	7/590	1.2	1.3 (0.8–1.9)
FVT	2/69	2.9	4.2 (1.0–16.6)
VF	0/10	0	…

CI indicates confidence interval, FVT, fast ventricular tachycardia zone; GEE, generalize estimating equations; SMVT, sustained monomorphic ventricular tachycardia; VF, ventricular fibrillation; and VT, ventricular tachycardia.

Several mechanisms can account for ATP therapy failure. Pacing wavefronts might not reach the reentrant circuit or, if they do, they fail to do so during the excitable gap. Key determinants of the probability that the propagating ATP wavefronts will penetrate the reentrant circuit during the excitable gap include duration of the excitable gap, distance between the pacing site and reentrant circuit, and conduction velocity of the intervening myocardium.[20,21] Next, ATP may successfully penetrate the reentrant circuit and reset the VT but may be insufficiently early to engage the anterograde limb of the reentrant circuit to cause conduction block and extinguish the tachycardia. Additionally, ATP could terminate the VT, but the terminal portion of the ATP sequence could reinitiate the VT. Finally, ATP could engage a new VT circuit with or without degeneration to VF. The challenge is to further reduce shock burden by increasing ATP efficacy rate, decreasing VT acceleration/degeneration to VF, or both.

This study introduced a new automatic ATP algorithm based on electrophysiological first principles and evaluated the feasibility and safety of it in ambulatory patients. The key findings are that AATP delivered automatic ATP sequences as specified by the algorithm and functioned safely. Evaluating ATP efficacy was explicitly not a primary objective of this small initial experience, but a first ATP sequence success rate of 65% and cumulative success rate for all ATP sequences delivered of ≈80% were observed, and the incidence of VT acceleration in this small experience was low (1.3% adjusted rate).

Comparing AATP with conventional ATP used in prior trials is difficult because of variation in programed detection delay, amount of ATP programed before shock, primary indication, reduced scar size with

advancing medical therapy, and cohort demographics. The results of this early small experience are similar to conventional ATP.[4,13] The S1 train used in AATP pulse sequences was based on the PainFREE I study where the adjusted rate of ATP efficacy after 2 ATP sequences was 77%, and 90% of that success was achieved with the first sequence.[14] Other trials have similarly demonstrated incremental success in terminating SMVT by merely applying more ATP.[13,15,17] VT accelerations caused by AATP were few, comparing favorably with that reported in previous trials.[3,4,9,15,16] However, a larger study is required to determine whether the AATP algorithm increases ATP efficacy and reduces the rate of VT acceleration or degeneration to VF. Finally, the few SVT episodes subjected to the AATP algorithm were insufficient to draw any firm conclusions.

There were 4 key elements to the AATP algorithm tested in this study. First, the S1–S2/S3 pulse protocol separated ATP function into 2 components. The purpose of the S1 train is to bring the pacing wavefront to the reentrant circuit during the excitable gap (VT resetting). Once achieved, AATP only adjusts the S2 or S3 coupling interval of subsequent ATP sequences to extinguish the VT wavefront and terminate VT. This approach is consistent with that suggested by Kaiser et al[22] in their study examining the pacing pulses required to reach the reentrant circuit of a tachycardia and is consistent with earlier work by Gardner et al[23] suggesting higher efficacy with an S1–S2 protocol. Most S1 pulses in a pulse train serve only to conduct through intervening myocardium and do not interact with the VT circuit. By restricting the S1 coupling interval to 88% of VTCL, induction of another VT or VT acceleration is minimized, as was seen in the limited experience of this study. When considering ATP efficacy and safety, this early clinical experience suggests that AATP performance is as good as, if not better than, existing ATP algorithms.

A second key element in the AATP algorithm was that it estimates the effective refractory period at the pacing site and determines the initial S1–S2 coupling interval. Customizing S1–S2 in the first sequence potentially increases success by avoiding wasting valuable time on sequences with ineffectively long S2s, especially in slower VTs having longer excitable gaps. Detailed episode analysis not presented in this report indicated that the refractory period estimator performed as designed, adding S2 pulses in 73% of episodes as required by the algorithm.

As a third key element, AATP incorporates analysis of the RCL after each ATP failure as real-time feedback for prescribing subsequent ATP sequences. RCL analysis allows 3 possible AATP responses. If RCL analysis indicates failure to reset VT, more S1s are added to the subsequent sequences to facilitate reset. In this study, VT resetting occurred with the first ATP sequence in 96% of episodes (95.8% adjusted). Conversely, if RCL analysis indicates VT reset, the calculated propagation time from pacing site to VT circuit is useful in 2 ways. The algorithm immediately identifies excessively long S1 sequences and decreases the number of S1s on subsequent sequences, thereby reducing time used for AATP before the shock timer expires and possibly reducing the risk of VT termination and reinitiation. In this study, the algorithm reduced S1 sequence length on 103 of 384 occasions (27%). A second use is in cases of S2 LOC. If that occurs, the algorithm reverts to the most recent S1–S2 coupling interval that captured and appends an S3 at a coupling interval equal to the prior failed S1–S2 interval.

The final key element is AATP's ability to respond to VT acceleration or deceleration, which could reflect a new VT reentrant circuit. AATP considers any VTCL change >10% or 30 ms (whichever is the larger) to be a new VT, and it responds by readjusting the S1 train length and invoking the refractory period estimator to ensure a maximally aggressive S2.

These 4 elements ground the AATP algorithm in fundamental electrophysiological principles with the goals of making ATP more efficient in terminating SMVT while further reducing the likelihood of device shocks while also making ATP more user friendly and simpler to implement.

Limitations

This was a prospective single cohort study without a comparator group subjected to standard ATP therapy. Whether or not this new ATP algorithm is more efficacious and less likely to cause VT acceleration would require more extensive clinical experience with the algorithm. Because only VT or SVT episodes that possessed electrogram data could be evaluated, there is the potential for results bias, but this was unavoidable given that evaluation of the AATP algorithm and accurate adjudication of AATP therapy required detailed analysis of electrogram and marker channel data. Monitoring the RCL as an index of tachycardia reset also has limitations. The occurrence of over- or undersensing issues, premature ventricular contractions, or pacing stimulus provoked repetitive ventricular responses can lead to a shortened RCL measurement and erroneous conclusion about reset and LOC. Although differentiating true reset from these confounding phenomena is algorithmically challenging, its occurrence was rare in this study. Because syncope diaries were not completed by patients, no information can be drawn about the effect of AATP on syncope rates.

In conclusion, initial clinical experience with this new ATP algorithm showed that it performed as designed, delivering multiple ATP sequences and achieving reasonable success in terminating sustained monomor-

phic VT in a difficult patient cohort while not causing any obvious increase in the rate of VT acceleration. More extensive experience is warranted to evaluate ATP efficacy and safety compared with conventional ATP algorithms.

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Drs Yee, Fisher, Smith, and Canby have received honoraria as Medtronic consultants. Dr Yee holds intellectual property rights jointly with Medtronic for material unrelated to the study subject. R. Taepke, T. Jackson, and P. DeGroot are employees of Medtronic. The other authors report no conflicts.

FOOTNOTES

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Initial Clinical Experience With a New Automated Antitachycardia Pacing Algorithm: Feasibility and Safety in an Ambulatory Patient Cohort

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