Antitachycardia Pacing for Ventricular Tachycardia Using Implantable Cardioverter Defibrillators: Substrates, Methods, and Clinical Experience

MICHAEL O. SWEENEY
From CRM Research, Cardiac Arrhythmia Service, Brigham and Women’s Hospital and Harvard Medical School, Boston, Massachusetts

Introduction

Antitachycardia pacing (ATP) refers to the use of pacing stimulation techniques for termination of tachyarrhythmias. Such techniques can be automatically applied using implantable cardioverter defibrillators (ICDs) and offer the potential for painless termination of ventricular tachycardia (VT). Reduction in painful shocks may improve patient quality-of-life (QOL) and extend ICD pulse generator longevity. Numerous older studies have consistently demonstrated that ATP can reliably terminate ∼85%-90% of slow VT (cycle lengths [CL] < 300–320 ms) with a low risk of acceleration (1%-5%).1 More recently similar high success and low acceleration rates for fast VT (CL 320–240 ms) have been demonstrated. These observations have repositioned the ICD as primarily an ATP device with defibrillation backup only as needed.

Physiology of Pacing Termination

Tachycardias that require reentry to persist, are susceptible to termination with pacing. The sine-qua non of a reentrant arrhythmia is the ability to reproducibly initiate and terminate the tachycardia by critically timed extrastimuli.2 Therefore, the possibility of successful termination of tachycardias with pacing can be anticipated on the basis of the mechanism. It is therefore useful to consider the origin of ventricular tachycardias that are commonly encountered in the ICD patient population.

Mechanism of Sustained Monomorphic VT in Coronary Artery Disease

The pathophysiological basis for sustained monomorphic VT due to prior myocardial infarction is well understood. The mechanism of arrhythmogenesis in this setting is reentry.1–6 The anatomic substrate for reentry is the interlacing of viable myocardium and connective tissue (scar) at sites of prior myocardial infarction.7,8 This specific pathological condition is the basis for low amplitude, fractionated endocardial electrograms at the sites of origin of VT.7 Poor cellular coupling at sites where fractionated electrograms are recorded results in slow propagation of impulses necessary for initiation and maintenance of sustained VT.7,8 Such abnormalities of conduction, along with altered refractoriness, enhanced automaticity and areas of inexcitability form the electrophysiological substrates for reentry caused by prior myocardial infarction.2 The evidence for reentry obtained from electrophysiology studies includes reproducible initiation and termination of tachycardia by critically timed extrastimuli, response of the tachycardia to stimulation or drugs, and activation mapping demonstrating reentrant excitation.2 Thus, the interlacing of viable and nonviable myocardium is capable of satisfying the three conditions required for initiation and maintenance of a reentrant rhythm: (1) at least two functionally (or anatomically) distinct potential pathways that join proximally and distally to form a closed circuit of conduction; (2) unidirectional block in one of these potential pathways; (3) slow conduction down the unblocked pathway, allowing the previously blocked pathway time to recover excitability. The reentry wavefront circulates around areas of functional or anatomically fixed conduction block. Areas of fixed conduction block are most often due to inexcitable scar tissue. Occasionally, an anatomic obstacle such as the mitral annulus forms a border zone for reentry circuits in adjacent infarcted myocardium.9

The electrophysiological substrate for reentry due to prior myocardial infarction is remarkably durable. Long-term follow-up of patients who present with sustained monomorphic VT has demonstrated a 3%-5% per year incidence of recurrent VT up to 15 years after presentation.2 Sustained monomorphic ventricular tachycardias induced early after myocardial infarction among patients with spontaneous VT can be reproducibly induced up to a year later, regardless of whether the induced VT ever occurred spontaneously.10
patients with prior myocardial infarction, reduced left ventricular ejection fraction, and no history of spontaneous sustained VT is reproducibly (> 90%) inducible up to 6 years later. These studies establish that the substrate for reentry after myocardial infarction can remain anatomically persistent for many years.

Relationship Between Monomorphic VT and Ventricular Fibrillation

The underlying mechanism for ventricular fibrillation (VF) not associated with acute myocardial infarction is poorly understood. Ambulatory monitoring has clearly demonstrated that sustained monomorphic VT precedes some episodes of VF. Destabilization of monomorphic VT may be related to ischemia, left ventricular dysfunction, electrolyte imbalances, activation of the sympathetic nervous system, or other poorly understood factors. Analysis of stored electrograms retrieved from ICDs has yielded further insights regarding the initiation of VF in the setting of chronic coronary artery disease. The occurrence of spontaneous monomorphic VT was observed to be higher among patients who presented with VT (54%) versus those who presented with VF (18%) in one study. Abrupt onset VF (not preceded by monomorphic VT) was recorded in 11% of the patients who presented with VF. These observations suggest that in some patients spontaneous VF is a primary event, rather than a destabilization of monomorphic VT. An example of VF initiated by sustained VT is shown in Figure 1. The clinical importance of this observation is that termination of VT by ATP may prevent VF in some patients.

Mechanism of Sustained Monomorphic VT in Nonischemic Dilated Cardiomyopathy

Sustained monomorphic VT in nonischemic dilated cardiomyopathy (NDCMP) is less common than in ischemic cardiomyopathy. The pathophysiological basis for sustained monomorphic VT associated with NDCMP is poorly understood compared to chronic coronary artery disease, and probably more diverse.

Autopsy series have demonstrated visually evident left ventricular scars (replacement fibrosis) in patients with NDCMP. Interlacing of replacement fibrosis and viable myocardium can produce fractionated, broad, low amplitude, endocardial electrograms compatible with slow conduction zones as seen in chronic myocardial infarction. These are capable of sustaining reentry. However, most patients with NDCMP have relatively normal endocardial activation and electrograms, not significantly different than normal individuals. Only those rare patients with NDCMP and sustained monomorphic VT have fractionated endocardial electrograms.

The electrophysiological mechanisms of ventricular arrhythmia in nonischemic idiopathic dilated cardiomyopathy were studied by intraoperative mapping just prior to explantation among patients undergoing cardiac transplantation by Pogwizd et al. Zones of functional conduction delay and block were demonstrated in the epicardium and less often, in the midmyocardium and endocardium. Extensive interstitial fibrosis in continuous linear bundles extending from the endocardium to the midmyocardium was consistently found in these locations. However, ventricular premature beats and nonsustained VT induced by programmed stimulation were found to arise primarily in the subendocardium by a focal mechanism without evidence of macroreentry. These sites of initiation were consistently distant from zones of functional conduction delay and block that did not contribute to VT initiation. The investigators hypothesized that focal initiation of VT could be due to triggered activity (delayed afterdepolarizations [DADs], or early afterdepolarizations [EADs]) citing the observation that triggered activity can be initiated in the myocardium of NDCMP.

Implications of VT Substrate for Clinical Application of ATP in ICD Patients

Monomorphic VT associated with chronic ischemic heart disease is most commonly due to classic reentry and is therefore susceptible to termination by ATP. Monomorphic VT is less common due to reentry and occurs with lower frequency in NDCMP. These fundamental differences in substrate are important for interpretation of clinical trials of ATP in ICD patients since nonreentrant VT would not be expected to respond to ATP.

Termination of Reentrant VT by a Pacing Stimulus

Theoretically, any reentrant VT can be terminated by a critically timed pacing stimulus that depolarizes the excitable gap. This principle is shown schematically in Figure 2. In panel A, the head of the wave of depolarization, denoted by (1), is followed by an area of absolute refractoriness, denoted by (2), relative refractoriness, denoted by (3), and an excitable gap, denoted by (4), that is fully excitable. In panel B, the stimulus enters the excitable gap both antegradely and retrogradely. Retrogradely it collides with the head, which is extinguished. Antegrade, it “preexcites” the tail, perpetuating the reentry wavefront. Panel C shows a more premature stimulus. Termination occurs because the impulse collides retrogradely with the preceding tachycardia impulse...
Figure 1. Tracings are from a 79-year-old male with ischemic cardiomyopathy and history of cardiac arrest. The patient had a Medtronic 7271 ICD system, and the preonset electrogram storage feature was enabled. The ICD stores up to 15 seconds of electrogram prior to onset of the episode. (Panel A) Interval plot associated with episode of ventricular fibrillation. The interval plot shows each VV interval (X-axis) with its corresponding interval value in milliseconds (Y-axis). Time zero is at episode detection. Note that detection is triggered by short VV intervals with wide cycle length variability (150–320 ms) in the VF zone (< 320 ms). The VV intervals proceeding detection are stable at 400–410 ms and dissociated from the AA intervals (1,000 ms). This is consistent with stable monomorphic VT. (Panel B) Stored local bipolar atrial and far-field ventricular electrograms confirm sustained monomorphic ventricular tachycardia that degenerates to ventricular fibrillation (arrow). Had preonset electrogram storage not been enabled, the onset of VF would have been assumed to be abrupt.
and blocks antegrade owing to encroachment on the refractory period of the preceding wavefront.

Commonly, circulating reentrant VT wavefronts propagate through regions of the infarct that contain surviving myocyte bundles. This is easiest to understand by considering a simple, theoretical, single-loop reentrant circuit as shown in Figure 3. The reentry wavefront circulates around a central region of inexcitable scar tissue, or functional block, which is surrounded by viable myocardium.

However, the true configuration of reentrant VT circuits is often considerably more complex as represented in Figure 4. In each panel the gray regions are regions of conduction block, which could be due to fibrous scar or collision of excitation wavefronts. Black arrows indicate wavefronts propagating in “bystander” regions of the scar that are not in the reentry circuit. In the left hand panel, the circulating reentry wavefront propagates along the border of the infarct region. In the middle panel, most of the reentry circuit is contained within the infarct region. In the right hand panel, a portion of the reentry circuit is contained within the infarct region, but following exit of the excitation wavefronts from the infarct regions, two wavefronts travel along the border of the infarct to reach the proximal entrance to the reentry circuit path through the infarct, forming a double loop (figure-of-8) reentry circuit. The reentry circuit often contains zones of slow conduction.

Factors that Influence the Ability of Pacing to Interact with Tachycardia

In order for pacing stimuli to terminate reentrant VT they must first interact with the VT circuit. Josephson\textsuperscript{2} has summarized the major factors that influence the ability of pacing stimuli to interact with the VT circuit. These are (1) the tachycardia CL, (2) the presence and duration of an excitable gap in the VT circuit, (3) the conduction time from the stimulation site to the site of impulse formation, and (4) the refractoriness at the stimulation site and site of impulse formation. The tachycardia CL is probably most important. In general, as CL decreases the probability of termination by pacing stimuli decreases. This is because shorter CLs have a “protective” effect on the VT circuit. The duration of the excitable gap shortens with CL, therefore the “window of vulnerability” is reduced. Shorter CLs also reduce the probability that remotely delivered pacing stimuli can overcome conduction time from the stimulation site to the VT circuit before local refractoriness is reached at the stimulation site.

Factors that Influence Termination of VT by Pacing

Assuming conditions exist for pacing stimuli to interact with the VT circuit, the probability of successful termination is influenced by several factors\textsuperscript{2,23} including (1) timing of the stimulus, (2) coupling interval, rate and number of pulses in the stimulus drive train, (3) proximity of the stimulating site to the circuit (closer is better), (4) barriers (functional or anatomic) to the circuit.

Two-dimensional models of reentrant VT circuits such as shown in Figures 3 and 4 are sufficient for explaining classical resetting, entrainment, and abrupt termination (Type-I breaks) by pacing stimuli.\textsuperscript{24} However, reentrant circuits are complex three-dimensional structures with
multiple fixed barriers and pathways. Such spatial heterogeneity complicates the understanding of how pacing stimuli interact with the tachycardia circuit. Insights regarding such complexities can be gained by analyzing Type-2 breaks in response to ATP, where VT persists or changes to another VT for one or more beats before termination. Sharma et al.\textsuperscript{25} analyzed the incidence and characteristics of Type-2 breaks in response to ATP using stored EGMs from ICDs. Type-2 breaks were observed in ~32\% of patients accounting for ~10\% of episodes and were associated with a 150\% increase in VT CL variability after ATP delivery. Such oscillation in VT CL has been described in spontaneous termination of VT.\textsuperscript{26} ATP affected either VT CL or morphology, or both in 80\% of Type-2 breaks. It is possible that changes in VT CL and/or morphology during Type-2 breaks reflect modification of the reentrant path by the ATP wavefront within a complex, three-dimensional substrate. Approximately 9\% of all Type-2 episodes may be spontaneously terminating nonsustained VT since ATP did not affect these episodes in any way.

Antitachycardia Pacing Nomenclature and Modalities

A single critically timed extrastimulus may terminate reentrant VT but the efficacy is low.\textsuperscript{23} Multiple stimuli delivered in the form of pacing drive trains increase the probability of interacting with the VT circuit and the likelihood of termination. The building blocks of ATP stimulation patterns are burst and ramp pacing (Fig. 5). A burst stimulation pattern consists of a train of pacing pulses with an equal interstimulus interval. A ramp stimulation pattern consists of a train of pacing pulses with an automatically decrementing interstimulus interval. Either stimulation pattern may be applied with “rate adaptation” which means that the interval from the last sensed ventricular event during VT to the first pacing stimulus is a programmable percentage of the detected VT CL. There are an almost limitless number of variations on these themes that probably have little clinical advantages and have been reviewed elsewhere.\textsuperscript{27}

Application of ATP in ICDs

Clinical Considerations

As reviewed earlier, termination of reentrant tachycardia requires critical timing of the pacing stimulus. Success or failure of the pacing stimulus to interact with and terminate tachycardia, is influenced by several factors, some of which are specific to the pacing scheme itself. These include the timing of the stimulus, and the coupling interval, rate and number of pulses in the stimulus train. It is for this reason that different schemes may have different efficacy in terminating specific tachycardias in the individual patient. The flexibility to program different pacing schemes enables one to overcome, in part, the factors that constrain the ability of some pacing stimuli to interact with the tachycardia, such as proximity of the stimulating site to the circuit and functional or anatomic barriers to the circuit. Conventionally, ATP stimuli are delivered from the tip of an endocardial electrode positioned at the apex of the right ventricle. The pacing stimuli must capture the local myocardium and produce an excitation wavefront that propagates through the myocardium to the left ventricle, where, in the case of coronary disease, most reentrant circuits are located.

Some generalizations regarding the clinical application of ATP for terminating VT are possible. Acceleration to a faster monomorphic VT, polymorphic VT, or VF, is uncommon when ATP is applied to slow VT (CL < 300–320 ms). The lack of a consistent definition of acceleration renders comparison between studies difficult. A >10\%-25\% change in CL, or the transformation of stable VT to polymorphic VT or VF is generally accepted as acceleration. Most studies have consistently reported acceleration rates in the range of < 10\% for...
slow VT regardless of the pacing scheme. From a practical standpoint, acceleration is a variation on ATP termination failure that, in addition to invoking a painful shock, may result in hemodynamic instability due to ventricular rate, delay in definitive shock therapy, or both, and may have important clinical consequences such as syncope. The probability of ATP termination failure and acceleration increase as VT CL decreases. Early recognition of this relationship resulted in a historical hesitancy to apply ATP for fast VT (CL < 300–320 ms). This consternation has been largely resolved by recent large clinical trials and similar high success rates and low acceleration rates can be anticipated with properly applied ATP for fast VT. Additionally, ramp pacing is more likely to result in acceleration for fast VTs than burst pacing; this does not appear to be generally true for slow VTs. An example of acceleration by ATP is shown in Figure 6.

**Comparisons of ATP Modalities for VT**

As commonly occurs, the emergence of a new technology stimulates clinical research centered on application of that technology. Accordingly, when ventricular pacing capability in ICDs appeared in the late 1980s and early 1990s a series of small clinical investigations compared different ATP modalities for termination of VT. These small studies are difficult to compare due to enrollment bias, small numbers, nonrandomized treatment assignments, variable validation of treated rhythms, and differences between pacing schemes.
and substrates for VT. Nonetheless, it is instructive to selectively review some of this data as it provides a consensus on the success and limitations of ATP in a diversity of ICD patient populations.

The relative efficacy of the two most commonly applied ATP schemes, burst and ramp, has been studied (Tables I and II) for induced and spontaneous VT. In three of four studies, there was no difference in the ability of either scheme to terminate VT, which was successful in about 70%-75% of episodes.\(^28-30\) In one study, ramp pacing was significantly more effective than burst pacing, but the overall success of either scheme was significantly lower at 50%-60% than that observed in the other studies.\(^31\) There was no difference in the likelihood of pacing acceleration of induced VT using burst or ramp pacing in all four studies; the incidence ranged from 3% to 21%. Similarly, Fisher et al.\(^32\) demonstrated similar efficacy of burst and ramp pacing for induced VT, but noted that burst pacing required a significantly fewer number of attempts for termination.

The relative efficacy of burst versus ramp pacing for terminating induced VT was then compared on the basis of VT CL. Again, in two of three studies, burst and ramp pacing were equivalently effective in terminating both slower VTs, typically defined as having CLs greater than 300–330 ms, and more rapid VTs, defined as having CLs less than or equal to 300–330 ms.\(^28,29\) In contrast, one study showed that ramp pacing was more effective than burst pacing for both slower and faster VTs.\(^31\) Another important observation from these studies is that, generally, the incidence of pacing acceleration of VT is higher with shorter VT CLs, regardless of the pacing scheme. In these studies, the incidence of acceleration for slower VTs ranged from 4% to 13%, whereas the incidence of acceleration for faster VTs ranged from 0% to 55%.

As there is no reason, a priori, to believe that the response of spontaneously occurring VTs to

---

### Table I.
Comparisons of Burst vs Ramp-Pacing for Induced VT

<table>
<thead>
<tr>
<th>Reference</th>
<th>Induced VT</th>
<th>Termination (%) Burst vs Ramp</th>
<th>Acceleration (%) Burst vs Ramp</th>
</tr>
</thead>
<tbody>
<tr>
<td>(28)</td>
<td>All cycle lengths</td>
<td>76 vs 68</td>
<td>3 vs 11</td>
</tr>
<tr>
<td></td>
<td>VT CL &lt; 300 ms</td>
<td>86 vs 38*</td>
<td>0 vs 12</td>
</tr>
<tr>
<td>(29)</td>
<td>All cycle lengths</td>
<td>70 vs 72</td>
<td>21 vs 18</td>
</tr>
<tr>
<td></td>
<td>VT CL &lt; 300 ms</td>
<td>45 vs 36</td>
<td>55 vs 55</td>
</tr>
<tr>
<td></td>
<td>VT CL &lt; 300 ms</td>
<td>76 vs 80</td>
<td>13 vs 9</td>
</tr>
<tr>
<td>(30)</td>
<td>All cycle lengths</td>
<td>65 vs 72</td>
<td>4 vs 3</td>
</tr>
<tr>
<td>(31)</td>
<td>All cycle lengths</td>
<td>49 vs 75</td>
<td>11 vs 12</td>
</tr>
<tr>
<td></td>
<td>VT CL &lt; 330 ms</td>
<td>55 vs 28*</td>
<td>14 vs 7*</td>
</tr>
<tr>
<td></td>
<td>VT CL &gt; 330 ms</td>
<td>57 vs 39*</td>
<td>9 vs 6</td>
</tr>
</tbody>
</table>

*significant difference.

---

### Table II.
Comparisons of Burst vs Ramp-Pacing Spontaneous VT

<table>
<thead>
<tr>
<th>Reference</th>
<th>Spontaneous VT</th>
<th>Termination (%) Burst vs Ramp</th>
<th>Acceleration (%) Burst vs Ramp</th>
</tr>
</thead>
<tbody>
<tr>
<td>(28)</td>
<td>All cycle lengths</td>
<td>96 vs 93</td>
<td>0.02 vs 0.01</td>
</tr>
<tr>
<td></td>
<td>VT CL &lt; 300 ms</td>
<td>86 vs 38*</td>
<td>0 vs 12</td>
</tr>
<tr>
<td></td>
<td>VT CL &gt; 300 ms</td>
<td>71 vs 77</td>
<td>4 vs 10</td>
</tr>
<tr>
<td>(33)</td>
<td>All cycle lengths</td>
<td>85 vs 90</td>
<td>8 vs 3</td>
</tr>
<tr>
<td>(34)</td>
<td>All cycle lengths</td>
<td>88 vs 94*</td>
<td>4 vs 3</td>
</tr>
<tr>
<td></td>
<td>VT CL &lt; 300 ms</td>
<td>86 vs 77*</td>
<td>7 vs 18*</td>
</tr>
<tr>
<td></td>
<td>VT CL &gt; 300 ms</td>
<td>88 vs 96*</td>
<td>3 vs 2</td>
</tr>
</tbody>
</table>

*significant difference
than ramp pacing.\textsuperscript{28} In one study, ramp pacing was more successful but the difference was small.\textsuperscript{34} As was observed for induced VTs, there was no significant difference in the incidence of acceleration of spontaneous VT for either burst or ramp pacing.

The relative efficacy of burst versus ramp pacing for terminating spontaneous VT was then compared on the basis of VT CL in two of these studies. Interestingly, for slower VTs with CLs > 300 ms, there was no difference in efficacy between burst and ramp pacing. However, unlike induced VTs, for faster VTs with CLs < 300 ms, burst pacing was more likely to terminate spontaneous VTs than ramp pacing.\textsuperscript{28,34} This raises the intriguing question of why the response of induced versus spontaneous VT to ATP should be different. In either case, the incidence of acceleration was low, but more likely with ramp pacing for faster VTs in one study.\textsuperscript{34}

Peters et al.\textsuperscript{35} reported a reduced likelihood of ATP success and increased risk of acceleration with ramp versus burst-pacing schemes. In contradistinction, Nasir et al.\textsuperscript{35A} in 1997 observed no difference in termination success, failure, or risk of acceleration between burst or ramp pacing. These results were unchanged when ramp pacing and scanning were used in all possible combinations. Though the pacing schemes were nonrandomized, the consistent success, failure, and acceleration rates across pacing schemes suggested that there is probably no important clinical difference between the bewildering array of pacing schemes available to the clinician.

### Empiric Versus Untested Programming of ATP

An important practical question is whether ATP schemes should be tested on induced VTs prior to application for spontaneous VTs. Schaumann et al.\textsuperscript{36} in 1998 showed that there was a high level of concordance between the effectiveness of ATP tested against induced VTs in the electrophysiology laboratory and spontaneously occurring clinical VTs (Table III). Similarly, the incidence of acceleration was equivalently low in both circumstances. A single ATP scheme (three sequences of an 8–10 burst train of autodecremental ramp at 81% of VT CL) was prospectively evaluated in 200 patients. This scheme was demonstrated to be successful at terminating induced VT in 54 patients, and either unsuccessful or untested (due to noninducibility of VT) in the remaining 146 patients. During average follow-up of 20 months, > 90% of 5,165 spontaneously occurring VT episodes in both groups were successfully terminated with ATP. Acceleration rates were similarly low (2%-5%).

### Clinical Application of ATP for Fast VT

Until recently, ATP was conventionally applied to only slower, presumably hemodynamically tolerated VTs, typically with CLs > 300–320 ms. Though several of the small studies cited earlier showed that many fast VTs (CL < 300–300 ms) can reliably be terminated by ATP, concerns about loss of consciousness during pacing attempts that delay definitive shock therapy at extremely rapid ventricular rates or acceleration to an even faster VT or VF. Fast VT is therefore typically detected by ICDs as VF and terminated with painful shocks even though ATP might be successful. The PainFREE Rx studies tested the hypothesis that ATP is safe and effective for FVT and reduces shock burden in ICD patients (Table IV).

<table>
<thead>
<tr>
<th>Reference</th>
<th>Tested vs Nontested</th>
<th>Accleration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(77) 36</td>
<td>79 vs 76</td>
<td>N/A</td>
</tr>
<tr>
<td>(36)</td>
<td>95 vs 90</td>
<td>2 vs 5</td>
</tr>
</tbody>
</table>

The PainFREE Rx studies evaluated ATP at very rapid rates within the VF treatment zone. Fast VT (FVT) detection required 12/16 (PainFREE Rx I) or 18/24 (PainFREE Rx II) intervals with CL < 320 \textsuperscript{37} + last 8 consecutive intervals $\geq$240 ms. If 1 or more of the last 8 intervals was < 240 ms, the episode was detected as VF. In PainFREE Rx I, 220 patients with coronary artery disease and ICDs for standard indications received nonrandomized, empirical, standardized ATP therapy for all FVT episodes prior to shock delivery. The pacing scheme consisted of two sequences of an 8-pulse burst-pacing train at 88% of the FVT CL. ATP terminated 396 FVT episodes (89%) with an overall efficacy of 77% when adjusted for multiple episodes/patient and a 4% incidence of acceleration.

These observations were validated and extended in PainFREE Rx II, which was the first large-scale, randomized trial to compare use of ATP versus shocks to treat FVT (CL 320–240 ms).\textsuperscript{38} Six hundred thirty-seven patients were randomized to receive shocks or ATP (1 sequence of an 8-pulse burst-pacing train at 88% of the FVT CL). Fifty-six

---

**Table III.** Comparison of Specific ATP Schemes for Induced Versus Spontaneous VT

<table>
<thead>
<tr>
<th>Reference</th>
<th>Tested vs Nontested</th>
<th>Accleration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(77) 36</td>
<td>79 vs 76</td>
<td>N/A</td>
</tr>
<tr>
<td>(36)</td>
<td>95 vs 90</td>
<td>2 vs 5</td>
</tr>
</tbody>
</table>
percent of true ventricular episodes were classified as slow VT (CL > 320 ms), 34% as FVT (CL 240–320 ms), and 10% as VF (CL < 240 ms). ATP terminated 82% of FVT episodes (72% when adjusted for patients with multiple episodes). The relative reduction of shocked episodes by programming ATP for FVT was 71%. Acceleration occurred in 1.2% of episodes in the ATP group but was never associated with syncope. The PainFREE Rx studies conclusively demonstrate that ATP is highly effective for FVT and results in a > 70% relative reduction in the proportion of shocked episodes without increasing time to termination or risk of acceleration.

**Clinical Factors Affecting Successful Termination of VT with ATP**

The basic electrophysiological factors that influence the ability of pacing stimuli to interact with a reentrant VT circuit and terminate tachycardia have been extensively investigated and described previously. However, relatively little is known about clinical factors that influence the success of ATP among ambulatory ICD patients. Hamill et al. reported that lower ejection fraction, longer VT CL, and coronary artery disease were multivariate predictors of ATP success for induced VT. Fries et al. reported lowest relative ATP success and highest VT occurrence rates were observed in the morning hours (6 AM to noon). There was a trend towards highest risk of acceleration during ATP in this time period as well. Peters et al. observed that ATP was less successful in women, when there was more severe left ventricular dysfunction, and in the presence of antiarrhythmic drugs. Kouakam et al. observed that fast sinus rates immediately preceding the onset of VT, and absence of β-blocker therapy were the only independent predictors of ATP failure. A more comprehensive analysis from PainFree Rx II evaluated predictors of ATP success for FVT (CL 320–240 ms). The strongest predictor of ATP efficacy was ejection fraction (EF < 30% ATP efficacy 52% vs EF > 30%, efficacy = 72%, P = 0.01). History of sustained VT, inducible VT, New York Heart Association (NYHA) class, age, sex, history of infarction, and infarct location were not predictive of ATP success.

An interesting recent development in the clinical application of ATP is stimulation site of origin. It is important to note that the pathophysiological mechanism of reentrant VT is not dependent on, or influenced by, site of origin of the VT circuit. From a practical perspective, site of origin might be very important since the majority of VT circuits arise in the left ventricle and pacing stimuli are conventionally delivered from the right ventricular apex. Since distance and conduction time between stimulation site and site of origin affect the ability of pacing stimuli to interact with the reentrant circuit, ATP delivered from the left ventricular pacing lead, or biventricular pacing leads in cardiac resynchronization therapy/defibrillation systems (CRTD) might improve efficacy compared to right ventricular ATP.

The relative efficacy of right ventricular versus biventricular ATP was evaluated in the InSync ICD OUS (Outside United States) Study. ATP termination success was 2.4 times greater with biventricular versus right ventricular ATP and appeared to be associated with fewer accelerations for both slow VT and fast VT. A preliminary report from the VENTAK CHF/CONTAK CD Study showed that biventricular ATP was more successful in patients randomized to CRT pacing therapy. This effect was influenced by left ventricular pacing lead location (improving in lateral locations, worsening in anterior locations) and improved over time in the patients who were receiving CRT.

These data are insufficient to support definitive conclusions regarding the role of alternate site ATP for terminating VT. Due to technical limitations, the CRTD ICDs in both studies were only capable of right ventricular or biventricular stimulation, and therefore provide no insights on a possible role for isolated left ventricular stimulation. From a theoretical perspective, it is not immediately obvious that left ventricular stimulation...
should improve ATP success in coronary artery disease, since many reentrant VT circuits arise in the interventricular septum which is closer to a RV stimulation site than a left ventricular free wall stimulation site. Conduction delay out of left ventricular stimulation sites due to interposed infarction and fibrosis might modify any advantage related to proximity to site of VT origin, and this effect may be different in the right ventricle. Furthermore, a recent case report described the reproducible initiation of monomorphic VT by left ventricular pacing but not right ventricular pacing that could be reliably terminated by RV ATP but not by LV ATP. This suggests the possibility that local tissue anisotropy might affect the ability of site-specific stimulation wavefronts to interact with the reentrant VT circuit. Recent studies have shown that pacing-site dependent changes in ventricular activation sequence can alter ventricular repolarization and refractoriness. How these factors might influence the relative efficacy of left ventricular ATP is unknown.

**Effect of ATP on Quality of Life in ICD Patients**

The issue of QOL in the ICD patient population has been extensively evaluated. Although ICD therapy is generally well tolerated by most patients, approximately 30%-50% experience some degree of psychological distress following implantation. One of the principal limitations of ICD therapy is the discomfort associated with high-voltage shocks. Several studies have noted a direct correlation between poor QOL scores and the experience of ICD shocks.

Intuitively, the absence of discomfort is the principal merit of ATP from the patient’s perspective. Early nonrandomized studies showed that ATP reduced shocks for VT. However, the assumption that every episode of VT successfully treated with ATP would otherwise have necessitated a shock is erroneous and overestimates the magnitude of shock reduction. This is because ATP is delivered immediately when detection criteria are satisfied, whereas shocks are delayed due to capacitor charging. Therefore, ATP may appear to have successfully treated VT that would have terminated spontaneously. This situation was observed in PainFREE Rx II where 33% of fast VT episodes in the shock arm terminated spontaneously during capacitor charging. Accordingly, only randomized comparisons of ATP versus shocks for VT can account for this potential bias and accurately quantify shock reduction and possible effects on QOL.

PainFREE Rx II was the first randomized trial that tested the hypothesis that reduction in painful shocks by ATP would improve QOL. Among patients with at least one episode of FVT, those treated with ATP experienced significantly more improvement in physical functioning, role physical, social functioning, and vitality, as well as in overall mental health compared to patients treated with shocks.

**Programming ATP and Patient Selection**

**Patient and Rhythm Selection for ATP**

An important and unresolved issue is optimal application of ATP in different ICD patient populations. In general, secondary prevention patients have a greater frequency of spontaneous ventricular arrhythmia than primary prevention patients. However, differences in the incidence of specific ventricular rhythms (VT, fast VT, and VF), response to therapy (ATP or shocks) and susceptibility to spurious therapies due to VT are incompletely characterized. Several studies have preliminarily addressed these issues.

Wilkoff et al. analyzed the frequency and characteristics of spontaneous VT and VF between patients with a primary versus secondary prevention indication for ICD therapy in the MIRACLE ICD study of CRTD. Primary prevention patients had a lower frequency of appropriate VT and VF episodes (0.12 vs 0.53 episodes/month) at significantly faster CLs (303 ± 53 ms vs 367 ± 54 ms, P < 0.0001). Primary prevention patients also had a significantly higher percentage of device-classified VF (40% vs 14%, P < 0.0001). The absolute rate of inappropriate detections in the primary prevention group was lower but constituted a much higher proportion of all episodes for that group (32% vs 14% for the secondary prevention group). Most inappropriate detections in the primary prevention group were due to sinus tachycardia and were treated as VT.

Russo et al. examined spontaneous therapies in primary prevention patients. Over 21 ± 18 months, 23% patients had appropriate therapies and 14% had inappropriate therapies for SVT. Clinical VT rates were higher than SVT rates (211 ± 38 beats/min vs 179 ± 14 beats/min). Only 10% of the patients with appropriate therapies had VT rates < 190 beats/min. The authors concluded that although there was some overlap in VT and SVT rates, VT rates less than 190 beats/min were uncommon and avoidance of programming to nominal VF detection rates may reduce inappropriate shocks for SVT.

These early observations provoke examination of tachyarrhythmia detection and therapy programming based on indication for ICD therapy. “Overtreatment” in primary prevention patients is an important concern, potentially at the cost of spurious therapies for inappropriate ventricular detections due to SVT. Though similar
proportions of primary and secondary prevention patients have appropriate detections for potentially life-threatening VT, fast VT and VF the frequency is lower in primary prevention.

Since the relative frequency of specific ventricular rhythms is similar between primary and secondary prevention patients, an equivalent efficacy of ATP could be anticipated assuming similar arrhythmia substrate (i.e., reentrant VT). Therefore, it is reasonable to conclude that if any VT therapy is to be prescribed in either group, it should include ATP with the expectation that 70%-90% of episodes will be painlessly terminated. The more difficult issue is whether any slow VT therapy should be prescribed in primary prevention patients, particularly those in whom programmed stimulation has not been performed. Elimination of slow VT detection might reduce spurious therapies for some specific SVTs (such as sinus tachycardia) but might not be as effective for others, such as atrial fibrillation with a rapid ventricular response. The zeal for reducing the probability of spurious therapies by eliminating a slow VT detection zone must be balanced against the risk of failing to treat unanticipated VT. This issue was indirectly addressed by a retrospective study by Bansch et al. The risk of VT above the VT detection interval ranged between 2.7% and 3.5% per year during the first 4 years after ICD implantation. Fifty-four (88.5%) of the VT episodes above the VT detection interval were associated with significant symptoms and 10% of patients had to be resuscitated. Risk factors for VT above the initial VT detection interval were heart failure, lower EF, spontaneous or inducible monomorphic VT, and use of Class III antiarrhythmic drugs. The risk of recurrent VT above the VT detection interval was 11.8%, 12.5%, and 26.6% during the first, second, and third year after the first occurrence above the VT detection interval. This suggests that elimination of a slow VT zone in some patients will result in clinically consequential undertreatment of slow VT.

**Future Developments in ATP**

**Reducing Risk of Syncope During Attempts at Painless Termination of VT**

Syncope prior to termination of VT by ICD therapies remains a significant problem. The incidence of syncope during spontaneous VT in ICD patients ranges from 2%-4% at 6 months to 10%-15% at 2–3 years. Syncope, despite successful termination of potentially lethal VT, may result in bodily trauma. Syncope is also socially disabling and is the principal concern underlying driving restrictions in ICD patients.

The hemodynamic response to sustained VT is heterogeneous. Arterial pressure decreases and cardiac filling pressures increase at the onset of VT. If VT sustains, arterial pressure may partially recover. If arterial blood pressure does not recover sufficiently, reductions in cerebral blood flow and oxygen saturation result in syncope. The extent of this hemodynamic recovery is probably governed by multiple interlinked factors. These include heart rate, loss of atrioventricular (AV) synchrony, left ventricular EF, ventricular dyssynergy, ischemia, and alterations in autonomic activity. Of these, heart rate and autonomic response are probably the most important determinants of hemodynamic outcome.

The multiplicity of factors that may determine the hemodynamic response to VT likely explains the heterogeneous response observed among patients in clinical studies. Readily available clinical variables do not reliably predict likelihood of syncope during VT. Generally, the risk of syncope during VT relates to tachycardia rate, although the correlation is modest. In two studies, the likelihood of syncope during induced VT was correlated with heart rate but only when VT rate exceeded 200 beats/min. Thus, it may be that at slower VT rates, other factors play a more important role in hemodynamic outcome. Although VT duration prior to termination and severity of left ventricular dysfunction are commonly thought to relate to risk of syncope, this is not consistently supported by clinical investigation or experimental studies. Demographic, clinical and variables derived from electrophysiological study were not predictive of syncope during spontaneous device therapies. In contrast, Bansch et al. found that low baseline left ventricular EF and induction of fast VT (CL < 300 ms) conferred an increased risk of syncope during appropriate ICD therapies.

The clinical management of syncope risk in ICD patients is further confounded by several observations. First, many episodes of syncope appear to be due to failed therapies for relatively slow VT. Olatidoye et al. observed that 62% of syncopal events were due to VT acceleration by ATP or low energy cardioversion, whereas 23% were due to VT alone and 15% were due to VF. Second, some patients with syncopal VT may have other VT events not resulting in syncope. Third, some patients with nonsustained VT experience near-syncope.

These data suggest that VT rate and duration and other common clinical variables may not be sufficiently robust discriminators for the risk of syncope and hence, ICD design and programming. One potential approach to this problem is ATP during capacitor charging. Theoretically, this should
reduce the delay between ATP termination failure and definitive shock therapy. This might in turn reduce the risk of syncope in some patients. Weber et al.72 evaluated consciousness during induced rapid VTs (CL 300–240 ms) in 20 patients randomized to either immediate shock or a single ATP attempt prior to shock. ATP terminated 55% of episodes of induced rapid VTs whereas cardioversion shocks were 100% successful. No patient suffered syncope during capacitor charging for a shock or during successful or failed ATP attempt. This preliminary data suggests that a single attempt at ATP during capacitor charging would not result in syncope in the study population.

Selecting Fast Ventricular Rhythms for ATP

Current ICDs use rate-based detection that may not reliably discriminate between monomorphic fast VT (CL 320–240 ms) and VF. FVT is often detected as VF and treated with shocks even though most episodes of FVT are paceterrninal.37,38 In PainFREE Rx II, FVT detection required 18/24 intervals with CL < 320 + last 8 consecutive intervals ≥240 ms. Stored EGM analysis of 564 episodes of device detected VF revealed that 68/132 (52%) were actually FVT and 64/132 (48%) were true VF. Therefore, more than 50% of potentially pace-terminable FVTs are misclassified as VF using this rate-based detection technique. These observations suggest that alternative detection methods that consider CL variability or morphology73 are needed to discriminate FVT from true VF in order to permit broader application of ATP.

Summary

Antitachycardia pacing reliably terminates ~85%-90% of slow VT (cycle lengths [CL] < 300–320 ms) with a low risk of acceleration (1%-5%). Similar high success and low acceleration rates for fast VT (CL 320–240 ms) have recently been demonstrated. These results appear to be consistent across different substrates (ischemic vs non-ischemic dilated cardiomyopathy) and probably relate to a common mechanism (reentry) ATP-responsive VTs. These observations have repositioned the ICD as primarily an ATP device with defibrillation backup only as needed. Reduction in painful shocks may improve patient QOL and extend ICD pulse generator longevity.

Some general recommendations on programming ATP schemes are possible. For VT CL > 300–330 ms, burst and ramp pacing are equivalently effective for terminating VT and equivalently low risk for causing acceleration. For VT CL < 300–330 ms, burst pacing is more effective and less likely to result in acceleration than ramp pacing. In either case, the risk of acceleration is inversely related to the VT CL. “Less aggressive” burst stimulation (for example, 91% of VT CL vs 81% of VT CL) is more effective and causes less acceleration, especially for fast VT (CL < 320 ms).74 “Tailoring” of ATP to specific induced VTs is not necessary in most situations.

References

20. Delacretaz E, Stevenson WG, Ellison KE, et al. Mapping and radiofrequency catheter ablation of the three types of sustained


ANTITACHYCARDIA PACING IN ICDS