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REVIEW

NonPharmacologic Management of Atrial Fibrillation Using the Dynamic Atrial Overdrive Algorithm

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ABSTRACT

A concomitant condition found in many patients with atrial fibrillation (AF) commonly requires bradycardia pacing. Comparing AAI to VVI pacing, atrial pacing appears to have an apparent protective effect on the subsequent development of AF. By addressing the proposed mechanisms responsible for AF (long-short cycles, increased temporal dispersion of refractoriness, frequent atrial ectopic beats), overdrive appears to be a promising technique to postpone or even prevent entirely the development of chronic AF while reducing the incidence of paroxysmal AF. These observations led to the development of a pacing algorithm (Dynamic Atrial Overdrive-DAO) designed to provide a high percentage of atrial pacing just above the patient's own intrinsic atrial rate. The algorithm is a dynamic stimulation technique to suppress AF effectively, overdrives the atrium just enough to prevent the intrinsic rhythm from emerging while maintaining both normal diurnal variation and rate response.

Dynamic Atrial Overdrive is a unique pacemaker algorithm designed specifically for suppression of paroxysmal AF arising from either an absolute or relative bradycardia. By maintaining an atrial stimulation rate just above the intrinsic rate, the goal is to control both the atrial rate and rhythm, reducing the incidence of ectopic beats which might be a trigger, long-short cycles, or the dispersion of refractoriness from initiating AF. In addition, because the algorithm routinely searches for intrinsic atrial activity and adjusts the stimulation rate accordingly, it avoids sustained periods of rapid stimulation that may not be required. At the same time, it preserves the normal circadian rate variation in association with normal sinus function or in the presence of sinus node dysfunction if the sleep rate feature is also enabled.

KEY WORDS: *atrial fibrillation; atrial pacing; overdrive pacing; sick sinus syndrome*

ABBREVIATIONS
AF = atrial fibrillation
DAO = dynamic atrial overdrive (algorithm)

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INTRODUCTION

Atrial fibrillation (AF), the most common significant cardiac arrhythmia, affects an estimated 4 million people around the world. Its rapid and uncoordinated atrial rhythm compromises hemodynamics, decreases cardiac output, predisposes to ventricular arrhythmias, and sets the stage for thromboembolic complications. Contributing mechanisms are presumed to be the occurrence of long-short cycles, an increased temporal dispersion of refractoriness, and atrial ectopic activity. The incidence increases with age, affecting 4% of those over 60, and up to 15% of those over 70.[1,2] Although it can

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occur in the absence of concomitant structural heart disease ("lone" AF), it is most often associated with a number of complicating conditions including hypertension, organic heart disease, coronary artery disease and others.

While the natural history of AF has not been conclusively established, it appears to start with brief paroxysmal episodes that are self-terminating. The next stage is persistent characterized by more prolonged episodes that require intervention to terminate. Finally a chronic stage develops where attempts to terminate the rhythm and restore normal sinus rhythm are essentially abandoned in favor of controlling the resulting ventricular rate and managing other consequences.[3]

The health care costs associated with this arrhythmia are enormous. It has been reported to account for one-third of hospital days for all patient discharges where arrhythmia was the primary diagnosis,[4] with an estimated cost of over $1 billion annually in the United States alone.

Historically, because of the absence of truly curative interventions and the risks and costs associated with repeated cardioversion, therapy has focused on management of the arrhythmia's consequences. Primary among these have been ventricular rate control, anticoagulation therapy and, where feasible, pharmacologic maintenance of sinus rhythm. Pharmacologic therapies have been widely used with varying degrees of success. According to the American Heart Association, several drugs effectively restore and maintain sinus rhythm in patients with AF but usually in the range of 30-45%. However, to date, little data is available to confirm the superiority of one particular drug over another for this purpose except for amiodarone, which is associated with potentially significant side effects. Agents such as digitalis, verapamil, diltiazem, and beta-adrenergic blockers may be useful during AF to decrease the ventricular response that occurs by inducing atrioventricular (AV) nodal blockade but these agents rarely terminate AF.[5] The class IC and III antiarrhythmic agents have a variable success rate in restoring sinus rhythm and new agents are under active investigation. In addition, various ablative and surgical techniques have been employed to manage AF (also with varying degrees of success). These techniques continue to evolve with technologic advances facilitating their implementation.

A concomitant condition found in many patients with AF commonly requires bradycardia pacing. A considerable body of research, both retrospective and prospective, has examined the effects of pacing on this arrhythmia. Some of the early pertinent research initially focused on the long-term results of single-chamber ventricular vs. atrial or dual-chamber pacing. Sasaki[6] reported on 103 patients with sick sinus syndrome, divided into unpaced, ventricular paced and physiologically (atrial or dual chamber) paced groups. The VVI group exhibited significantly more complications overall than the physiologically paced group with the predominant complications being AF in 36% and thromboembolism in 20%. Stangl[7] reported on 222 patients with sick sinus syndrome; 110 received AAI pacing, and 112 VVI pacing. The incidence of chronic AF was over 3 times higher in the VVI group. Feuer[8] reported on 220 patients paced for sinus node disease and AV block; half were VVI-paced, and half were DDD/DDI paced. Again, AF developed more frequently in the VVI group. The authors suggested that both preservation of AV synchrony and electrical stabilization of the sinus node and atrium might account for the apparently protective effect of dual-chamber pacing. Reporting on a larger group (950 patients) of pacemaker recipients followed for up to 8 years, Hesselson[9] found chronic AF developed significantly more frequently in the VVI group than in the DDD and DVI-paced patients. These findings were reproduced by Andersen[10] who, in the first prospective randomized trial comparing AAI to VVI, confirmed the apparent protective effect of atrial pacing on the subsequent development of AF: cumulative indices of both paroxysmal AF and chronic AF were significantly lower in the atrially paced group.

As this pattern emerged, investigators examined the characteristics of atrial pacing more closely, and overdrive appeared to be the likely mechanism, particularly in the setting of an underlying bradycardia. However, even when an underlying bradycardia was not present, a beneficial effect of pacing has been suggested. Ragonese[11] examined a small group of pacemaker recipients who had surgical repair of complex congenital heart disease and atrial reentrant tachycardias unresponsive to conventional pharmacologic therapy. Pacemakers were specifically programmed to a rate 20% higher than the mean intrinsic atrial rate previously determined via Holter recording. A total of 83% of the patients were arrhythmia-free at the end of the study. Stabile[12] found that atrial pacing markedly reduced AF using DDDR pacemakers programmed to a lower rate of 75/min, with rate response parameters programmed to help assure continuous pacing by having the paced rate always faster than the underlying sinus rate. Garrigue[13] also evaluated atrial overdrive in 22 patients with DDD pacemakers, and found no atrial arrhythmias in 14, and a reduction in the number and duration of arrhythmias in the remaining 8 compared to the baseline studies.

Continuing clinical research and technological evolution have produced a variety of device-based technologies in an attempt to control AF. The atrial defibrillator[14] has been studied, as has multi-site atrial pacing[15] and bi-atrial pacing.[16] While one or more of these newer approaches may prove practical, they are problematic at present. Internal atrial defibrillation is uncomfortable for patients who are not experiencing a life-threatening arrhythmia, while multi-site pacing requires significantly more hardware, pulse generator adaptation and is far more complex than a standard implant.

By addressing the proposed mechanisms responsible for AF (long-short cycles, increased temporal dispersion of refractoriness, frequent atrial ectopic beats), overdrive appears

to be a promising technique to postpone or even prevent entirely the development of chronic AF while reducing the incidence of paroxysmal AF. Sufficiently rapid atrial pacing can eliminate the pauses following ectopic beats, overdrive and hence suppress atrial ectopy, and reduce the dispersion of refractoriness by maintaining control of both rate and rhythm. Simply pacing at a relatively fast rate from a single site, as demonstrated by Saksena[15] may be very effective. However, sustained pacing at a high base rate without allowing for the normal circadian variation and slowing in the heart rate may have adverse hemodynamic consequences as suggested by Chew and colleagues.[17]

The observations regarding the apparently beneficial effect of relatively high rate pacing led to the development of a pacing algorithm designed to provide a high percentage of atrial pacing just above the patient's own intrinsic atrial rate, while allowing the paced rate to fluctuate in accord with either sensor drive or the patient's intrinsic atrial rhythm. The goal was to maintain the normal circadian variation in the heart rate, allow the rate to slow to relatively low levels when the patient was at rest, as long as this rate was faster by a programmable number of beats than the patient's intrinsic atrial rhythm. In this manner, the algorithm would both overdrive suppress the development of paroxysmal AF while avoiding the theoretical adverse consequences of a high sustained base rate. The resultant algorithm is a dynamic stimulation technique to suppress AF effectively, overdrives the atrium just enough to prevent the intrinsic rhythm from emerging while maintaining both normal diurnal variation and rate response.

DESCRIPTION OF ALGORITHM

St. Jude Medical designed the Dynamic Atrial Overdrive (DAO) algorithm specifically to maintain an atrial stimulation rate just above the patient's intrinsic rate. It accomplishes this by continually monitoring the atrial rate, promptly increasing the stimulation rate when the intrinsic rhythm emerges defined as at least two intrinsic (sensed) P waves. While these sensed atrial events do not have to be consecutive, they should occur within 16 cycles at which time, the pacing rate is incremented in accord with the lower or upper rate overdrive value. Assuming that there is stable atrial pacing at the higher rate, this continues for a programmable number of cycles. Upon completion of the overdrive duration criteria, the algorithm begins to gradually reduce the stimulation rate to search for intrinsic atrial activity thus ensuring that the stimulation rate does not persist at an inappropriately rapid level. In essence, the DAO algorithm reflects the circadian rhythm while delivering a high percentage of atrial pacing at a rate which is only slightly above the intrinsic rhythm

The number of beats per minute increase is a programmable value from 5 to 25 bpm at lower rates and from 5 to 10 bpm at higher rates (above 150 bpm). If, despite the initial rate increase, the subsequent atrial events continue to be sensed, the algorithm continues to increase the rate in similar steps. The magnitude of the increase is programmable, with separate values (Lower Rate Overdrive or LRO and Upper Rate Overdrive or URO) controlling the degree of rate increase. Since rate variability is typically greater at lower rates, the Lower Rate Overdrive parameter allows a more aggressive rate increase than the Upper Rate Overdrive parameter. The increased rate is maintained for the selected Number of Overdrive Cycles, after which the system begins to search for the intrinsic rate by gradually extending the atrial stimulation interval. This extension is controlled by the selected DAO Rate Recovery parameter, which, like the overdrive parameter, has separate components for higher (>100 /min) and lower rate ranges. Each atrial interval is extended by the selected millisecond value until two intrinsic atrial events are detected within 16 consecutive cycles, at which point the atrial paced rate is again increased.

The DAO algorithm is CE marked and incorporated in Trilogy® DR/DAO model 2364. It is also incorporated in the multichamber Frontier™ model 5510 and 5530 pulse generators. The DAO parameters and their programmable ranges are shown in Table 1.

Although the DAO algorithm requires the continued use of the microprocessor integral to the pacemaker, it does not limit the behavior of any of the other algorithms. In fact, it may augment the behavior of those algorithms. For the patient who has an intact sinus mechanism with the expected circadian rhythm, the DAO algorithm will track it driving the effective paced rate slightly above the sinus rate but with appropriate normal diurnal variation. In the patient with severe sinus node dysfunction in addition to the paroxysmal AF, the

TABLE I.

Parameter	Values	Recommended Settings
Lower Rate Overdrive (LRO)	5, 10, 15, 20, 25-1	10
Upper Rate Overdrive (URO)	5,10-1	5
Number of Overdrive Pacing Cycles*	1 to 16 in steps of 1	12-16
Dynamic Recovery Rate (DRR)**	6:13, 6:19; 13;19; 19;25 ms/cycle	6;13

* Preliminary clinical trial data suggests that programming the number of overdrive pacing cycles between 12 to 16 provides the best results.

** The first value of the pair specifies the pacing interval extension for rates above 100 per minute and the second value specifies the milliseconds per cycle extension for rates below 100/min

rhythm will be predominantly paced in the atrium and diurnal variation can still be accomplished using the dynamic sleep rate algorithm.[18,19]

A relatively high base rate is programmed for when the patient is active. Any sensor drive associated with physical activity starts from this higher base rate. When the patient is sleeping or during protracted periods of rest as with an afternoon nap, the rate is allowed to slow to as low as the sleep rate. As there is atrial pacing at all these times, the DAO feature of the system would be on standby. However, should there be an increase in intrinsic atrial activity, whether it due to increased ectopy associated with the lower sleep rate or during a period of physical activity with even thought the paced rates are higher due to sensor drive, the detected atrial signals will cause activation of the DAO algorithm resulting in a further increase in the paced rate in accord with the DAO feature.

DEMONSTRATION OF ALGORITHM BEHAVIOR

While one can monitor the ECG as shown in Figure 1 to document the behavior of the algorithm, it is elegantly demonstrated using the one of the diagnostic event counters integral to the pacemaker. This is the Event Record which is a time based total system performance counter.[20-22] This counter can be set to monitor every event in which case it will provide an overview of the pacing system behavior for the preceding 2 hours or it can be set to monitor the system behavior every 26 seconds at which time it provides an overview covering the preceding 60 hours. Once the data pool is filled, the system continuously updates the available data by deleting the oldest information while adding the newest information concerning pacing state and pacing rate with respect to time.

To demonstrate the behavior of the algorithm, the recordings starting with Figure 1 were obtained from a dog implanted with a Frontier biventricular pacing system. For the purposes of these illustrations, the biventricular stimulation is inconsequential. The animal had a marked sinus arrhythmia and wide fluctuations of the heart rate are shown. Following activation of the algorithm, the degree of fluctuation was markedly reduced (Figure 2). In this display, the horizontal axis is the time base and is divided into 40 equal segments. If there is more than a single event in the time bin, a vertical line will be displayed. The top of the vertical line represents the peak rate while the bottom represents the minimum rate. The crossbar represents the electrical mean rate. The thin vertical line extending from top to bottom represents the programming command which, in this case was activation of the DAO algorithm. The heavy line in the middle of the printout is a centering line provided by the programmer.

The Event Record scale can be expanded to show every event. Figure 3 shows the actual transition from DAO off to DAO on. Prior to enabling DAO (top), the rhythm was atrial sensed [P] ventricular paced [V] and the marker on the printout is a P in a black box or inhibited (atrial sensed [P] ventricular sensed [R], hence PR represented by an isolated P label. There is a considerable excursion in the PV rate associated with the marked sinus arrhythmia in this animal. After a few cycles, the DAO algorithm starts AV pacing identified by an A within a box (bottom printout).

Figure 5 was retrieved as the atrial paced rate was decreasing in accord with the programmed Dynamic Recovery Rate until native P waves are again detected and the paced rate increases.

PROSPECTIVE CLINICAL STUDIES

To evaluate the clinical effectiveness of this algorithm, two prospective randomized multicenter trials have been initiated. Titled Atrial Dynamic Overdrive Pacing Trial (ADOPT), they have been further labeled A and B.

Figure 1 shows an example of the algorithm in operation.

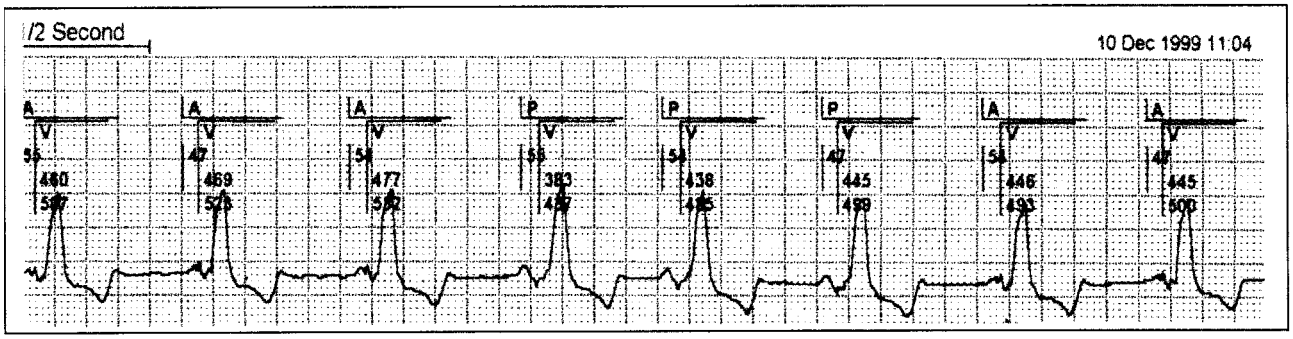

FIGURE 1. The first three cycles represent AV pacing with a progressive increment in the basic pacing interval consistent with a progressive slowing of the paced rate. Intrinsic P waves are detected at a slightly higher rate followed by an increase in the atrial paced rate. The numeric intervals are paced or sensed AV delay, atrial escape interval and "VV" or the rate interval.

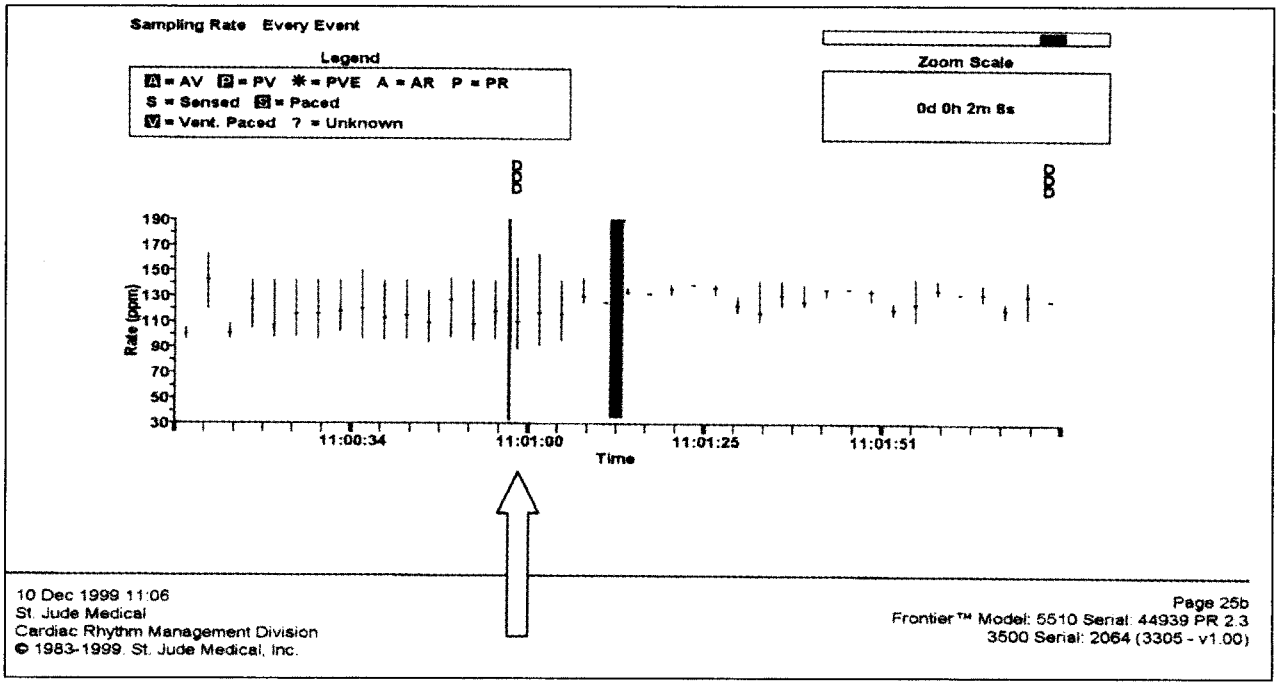

FIGURE 2. Event Record showing transition between marked sinus arrhythmia with DAO disabled followed by DAO algorithm enabled. The arrow identifies the timing of the programming command to enable DAO.

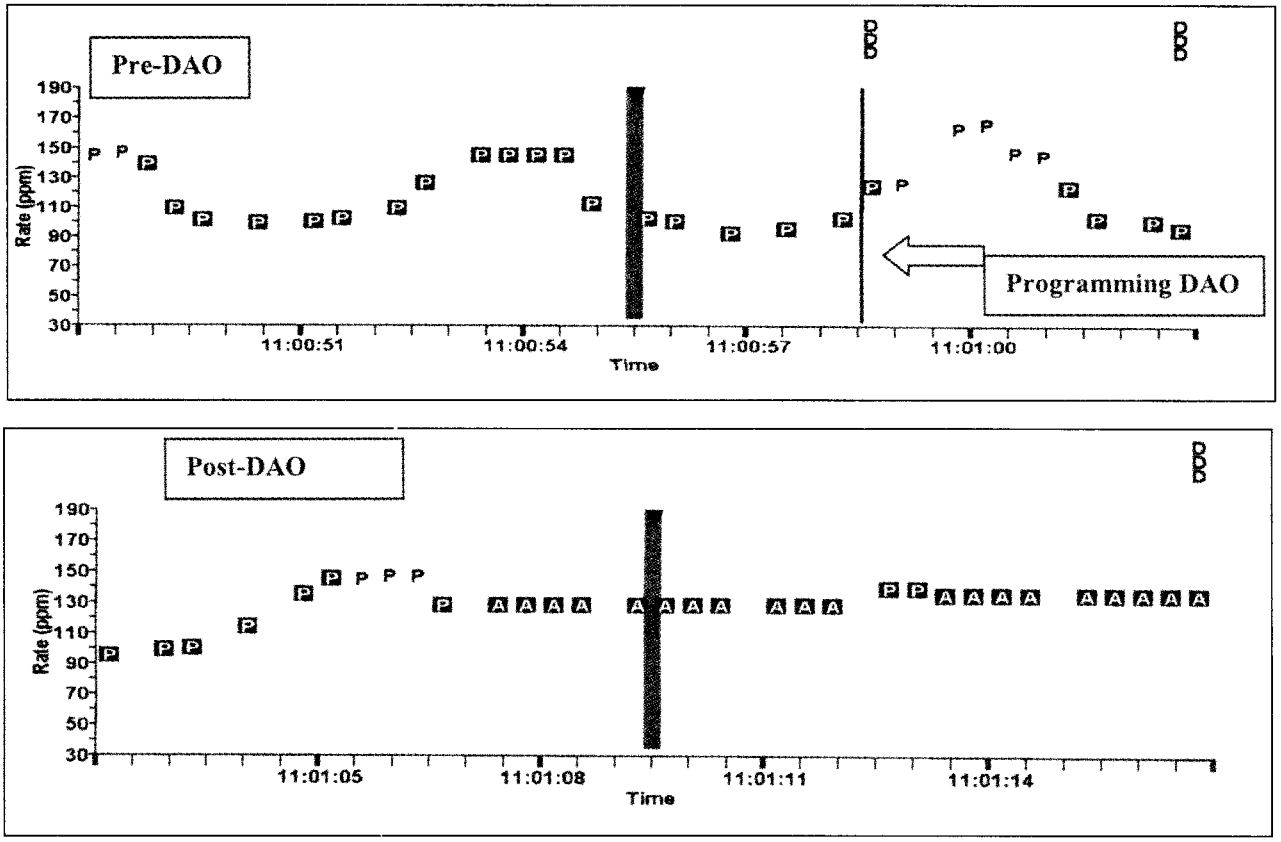

FIGURE 3. Beat-by-beat detail showing development of rate stabilization.

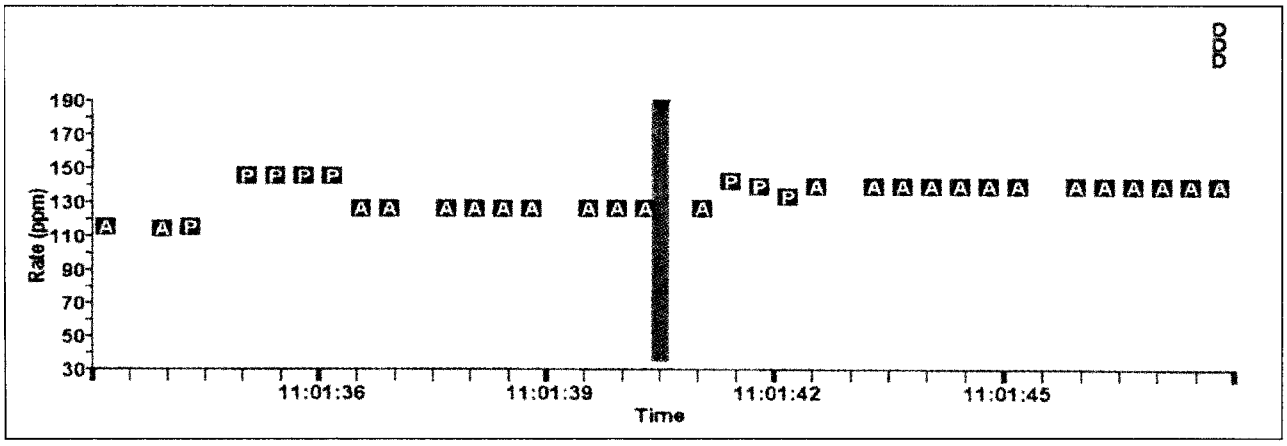

FIGURE 4. Represents the expected fluctuation in rate in the midst of the DAO algorithm. There are a few intrinsic sensed atrial events (P) at which point there is an increase in the atrial paced rate.

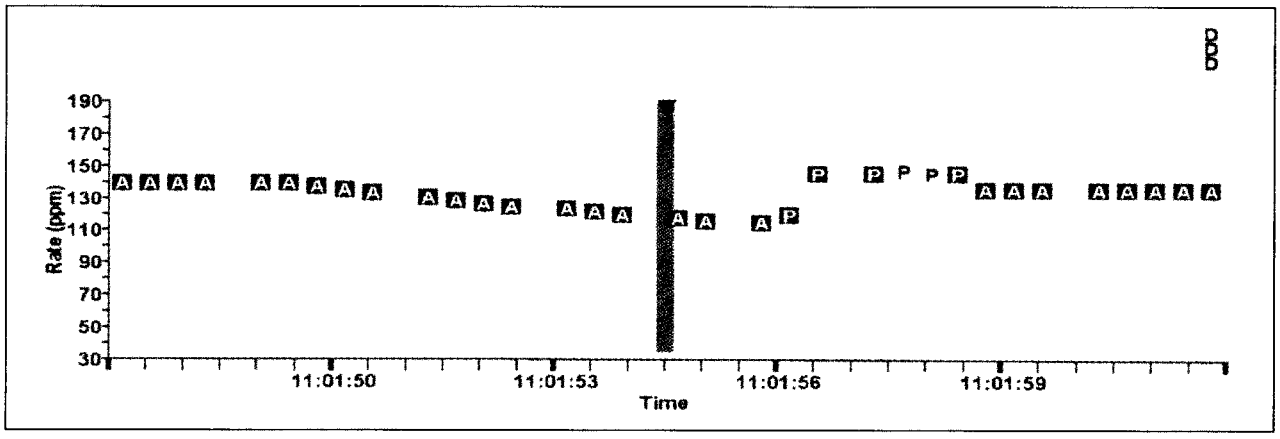

FIGURE 5. Alter a period of stable atrial pacing, the rate is progressively decreased (interval between consecutive beats is increased) until native atrial activity is again sensed as identified by the P marker. With detection of two P waves, the paced atrial rate is increased in accord with the programmed overdrive steps. If P waves are still detected, the rate is again increased until atrial pacing occurs.

ADOPT-A involves the subgroup of patients with documented bradycardia-tachycardia syndrome who would receive a pacemaker for symptomatic bradycardias. The comparison will be between the incidence of paroxysmal atrial tachyarrhythmias, most of which are likely to be AF, with standard DDDR pacing at a base rate of 70 ppm and the DAO algorithm either enabled or disabled. The number and duration of the arrhythmic episodes will be monitored using the Automatic Mode Switch Histogram integral to the pacemaker[23,24] combined with a transient arrhythmia monitor which each patient is given to capture each symptomatic episode. One of these recordings was shown in Figure 1.

The entry criterion for ADOPT-B is documented paroxysmal atrial tachyarrhythmias continuing to recur despite standard pharmacologic regimens in patients who have not been identified as having a bradycardia. There will be three arms to this trial. In one, the pacemaker will be programmed to a base rate of 45 ppm in the DDD mode with both atrial and ventricular outputs programmed to 0 volts. The pacemaker is functionally inhibited to serve as a control while the DDD mode allows the AMS algorithm to remain active so that the AMS Histogram can be used as a monitoring system for the frequency of spontaneous episodes of atrial fibrillation. In a second arm, the pacing mode will be DDD (sensor passive) at a base rate of 70 ppm while in the third arm, the mode will be DDD (sensor passive), the base rate 70 ppm and DAO will be enabled.

Neither of these trials has completed enrollment and

the cumulative data has not yet been analyzed and as such, cannot be reported at this time. Of the data that has been submitted, some patients have had a dramatic response to the DAO algorithm.

CASE STUDY

The patient is an 80 year-old man with bradycardia-tachycardia syndrome and frequent episodes of paroxysmal AF. Previous pharmacologic therapy to control the AF included a Class IC agent (propafenone) which was ineffective in stabilizing the atrium yet exacerbated the underlying sinus bradycardia. As such, the propafenone was discontinued and a DDDR pacemaker (Trilogy DR/DAO) was implanted. The patient was initially randomized to standard DDDR pacing. Despite standard pacing techniques, he continued to have frequent symptomatic episodes of paroxysmal AF with 6,240 mode switch episodes during this time interval (Figure 6A). One episode lasted between 15 to 30 hours and multiple other episodes lasted for significant although shorter periods of time. In the 3-month period following enabling of the DAO algorithm, there was a marked reduction in mode switch episodes, all other parameters in the pacemaker including the pharmacologic regimen being stable. There were only 5 mode switch episodes with no episode lasting more than 6 minutes (Figure 6B).

SUMMARY

Dynamic Atrial Overdrive is a unique pacemaker algorithm designed specifically for suppression of paroxysmal supraventricular tachycardias, most of which will be AF arising from either an absolute or relative bradycardia. In this case, relative refers to a heart rate that is slower than physiologically optimal even if it is rapid. By maintaining an atrial stimulation rate just above the intrinsic rate, the goal is to control both the atrial rate and rhythm, reducing the incidence of ectopic beats which might be a trigger, long-short cycles, or the dispersion of

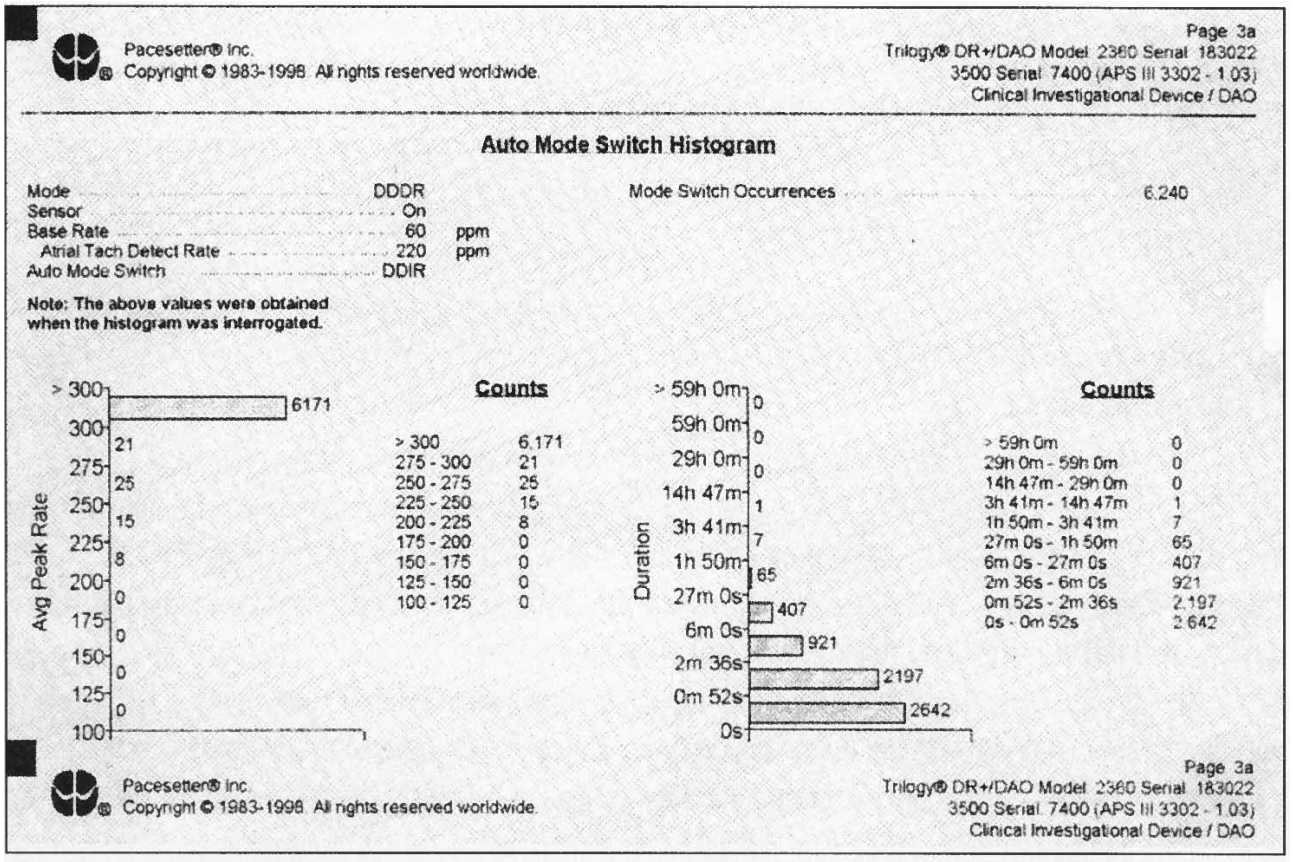

FIGURE 6A. AMS Histogram recorded at the end of a 3-month period with the pacemaker programmed to the DDDR mode but the DAO algorithm was disabled. There were 6.240 AMS episodes with 98% occurring at a filtered atrial rate above 300 bpm consistent with the patient's known paroxysmal AF.

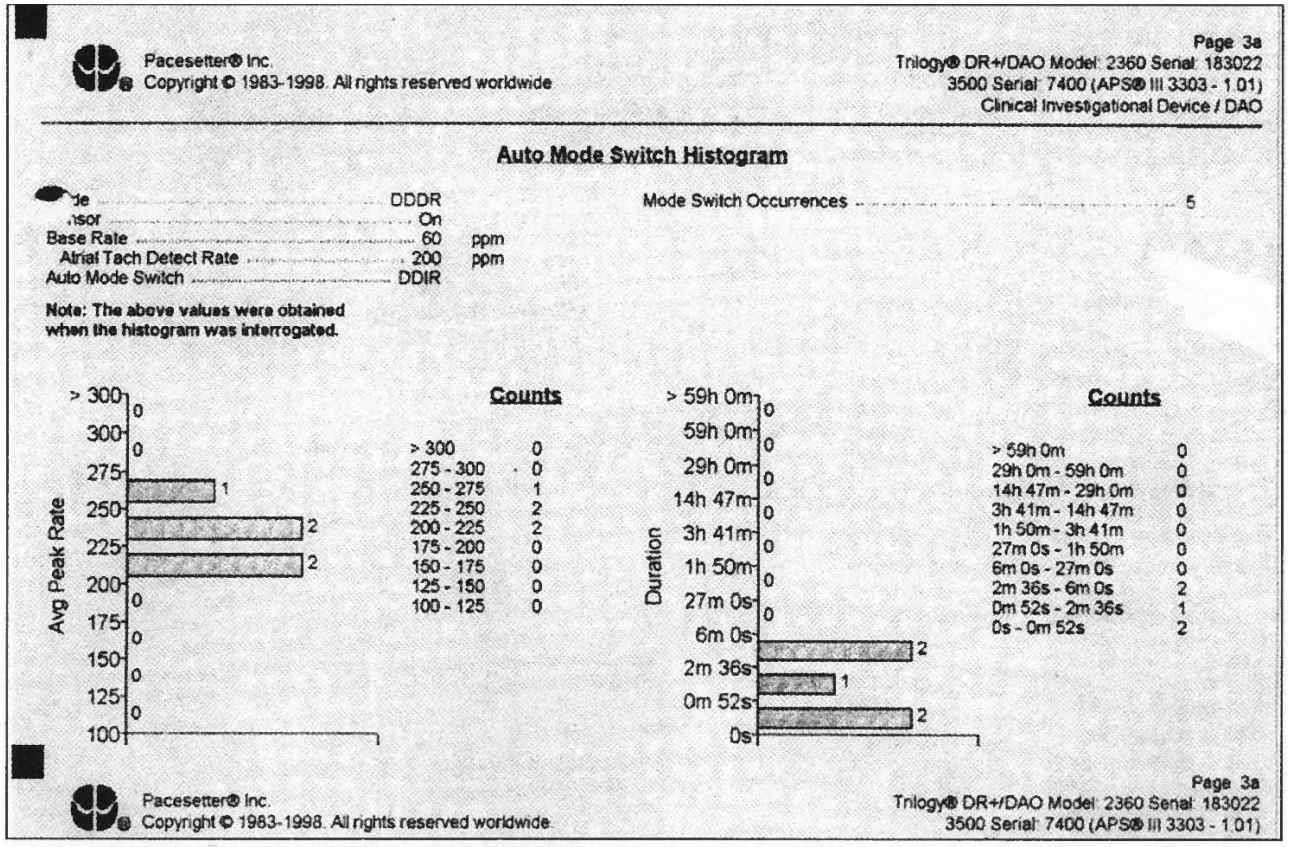

FIGURE 6B. The AMS Histogram for the 3-month period following activation of the DAO algorithm. All pacing parameters, mode switch detection parameters and medications were stable during this period of time.

refractoriness from initiating AF and other supraventricular tachyarrhythmias. In addition, because the algorithm routinely searches for intrinsic atrial activity and adjusts the stimulation rate accordingly, it avoids sustained periods of rapid stimulation that may not be required. At the same time, it preserves the normal circadian rate variation in association with normal sinus function or in the presence of sinus node dysfunction if the sleep rate feature is also enabled.

Rate modulation can be enabled with this algorithm and will initiate any rate response from the functional rate at the time of physical activity thus also preserving or supporting an appropriate chronotropic response. If sinus node function is otherwise normal, the DAO algorithm with rate modulation disabled will still overdrive the intrinsic atrial rate associated with normal chronotropic behavior. Preliminary anecdotal reports are very encouraging while the formal prospective studies continue.

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