Novel pacing algorithms: do they represent a beneficial proposition for patients, physicians, and the health care system?

Emmanuel N. Simantirakis, Eva G. Arkolaki, and Panos E. Vardas*

Cardiology Department, University Hospital Of Heraklion, PO Box 1352, Stavrakia, Heraklion, Crete 711 10, Greece

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Modern pacemakers are enriched with several embedded algorithms, aiming at achieving a more “physiological” pacing, at reducing pacing-related costs and at maximizing the physician’s and the patient’s convenience. Though some of these algorithms offer proven benefits, the efficacy of others is still under serious dispute. Herein are presented some of the most important algorithms integrated in modern pacemakers, together with an overview of the currently available literature concerning their efficacy and safety, as well as their impact on the economics of health care systems.

The primary aim of cardiac pacing for symptomatic bradycardia has always been to alleviate patients’ symptoms and to ensure prolongation and better quality of life. Moreover, technical issues, such as minimizing the size of the implantable device as well as increasing pulse generator longevity, are also of great importance. Artificial pacing has seen impressive progress over the past few decades. The acquired knowledge of microprocessor technology and the advances in the incorporation of artificial sensors have enabled the introduction of novel pacing strategies and new sophisticated algorithms. Consequently, the revolutionized software of the latest generation of pacemakers has led to great improvements in the quality of life of pacemaker recipients, in device economics, and doctors’ convenience. Herein are presented some of the most important novel algorithms integrated in today’s pacemakers, together with a summary of the results of several clinical studies that have evaluated their efficacy.

Minimizing ventricular pacing

According to accumulating data, ventricular pacing (VP) is associated with adverse long-term effects attributed to ventricular desynchronization, such as increased risk of atrial fibrillation (AF) and congestive heart failure (HF) when compared with atrial pacing. In clinical practice, dual-chamber pacemakers are generally preferred, even in patients with intact atrioventricular (AV) conduction, for safety reasons (episodes of paroxysmal AV block occur in 0.6–2.8% of pacemaker recipients). Usually, conventional DDD pacemakers are characterized by a high percentage of VP, even in patients with intact AV conduction, as the programmed AV interval is similar to the native PR interval. In an attempt to diminish the deleterious effects of VP in those patients, new therapeutic strategies have been developed. The initial approach was by utilizing a fixed extension of the AV interval or adaptive AV interval hysteresis features. However, these strategies have been proven to be ineffective in reducing VP in 20% of patients with intact AV conduction. They have also been associated with adverse effects, such as potential retrograde conduction, higher rates of endless loop tachycardia (ELT), and under-detection of atrial and ventricular tachyarrhythmias.

Another approach to minimize VP is by utilizing the Search AV+ (SAV+) algorithm, which operates in a DDD(R) mode with an AV interval gradually extended from a nominal value of 120 ms during atrial sensing and 150 ms during atrial pacing to maximum values of 290 and 320 ms, respectively. Every time that a ventricular event is sensed, the AV interval increases slightly and if no ventricular event is sensed the algorithm delivers a ventricular stimulus and returns to the nominal settings for 30 min. Then, an AV conduction check is performed and if a ventricular event is sensed, the search AV algorithm reactivates. Otherwise, the AV conduction check will be repeated after 1 h, then every hour up to 16 h and if no intrinsic ventricular event has been sensed by then, the algorithm will be automatically disabled. In clinical studies, the algorithm has proven to be effective, as it has achieved a substantial reduction of VP without compromising the patient’s safety (it was automatically suspended when episodes of high-grade AV block occurred).
Recently, new algorithms have been designed to promote intrinsic ventricular conduction. Two of them, embedded in current pacemakers, are: SafeR (ELA Medical, Montreouge, France) and MVP (Medtronic Inc.). SafeR is an innovative type of pacing mode, designed to combine the benefits of AAI and the safety of DDD pacing. This algorithm remains in an AAI mode in the absence of AV block or in the presence of relatively acceptable episodes of first and second degree of AV block. However, in the presence of marked AV conduction disturbances, it switches to DDD mode, automatically converting back to AAI mode when stable AV conduction is detected. SafeR does not allow gradual PR prolongation. Instead, the intervals after a sensed atrial event (P) or a paced atrial event (A) are programmed to certain values. PR > 350 ms and AR > 450 ms are unacceptable to the algorithm, which switches to a DDD mode. The exact criteria of conversion of AAI to DDD pacing and vice versa, as well as inactivation criteria, are summarized in Table 1.

It is worthy mentioning that, although this algorithm has complex rules, these rules aim to minimize deleterious hemodynamic situations, always with the benefit of the patient in mind. For example, during physical exercise, when diastolic interval shortens, the algorithm determines the maximum AV delay that can be allowed to avoid P-on-T, cannon waves and the hemodynamic consequences of the pseudo-pacemaker syndrome.

The efficacy of this novel algorithm was evaluated in 147 pacemaker recipients (Symphony DR2550 ELA Medical). In the therapy group, the percentage of VP was minimized to 9 ± 21%, compared with 95 ± 14% in the group paced in a DDD mode (AV interval at 146 ± 19 ms) and 87 ± 20% in the group paced in a DDI mode (AV interval at 152 ± 15 ms). It is also noteworthy that a marked reduction in the number of episodes of ELT was observed in the therapy group (3 ± 12 vs. 46 ± 85). Thus, the SafeR algorithm has proven to be both effective and reliable, offering a significant clinical effect and at the same time providing secure ventricular backup pacing.

Managed ventricular pacing (MVP) is a similar algorithm, designed to pace in an AAI(R) mode while simultaneously monitoring ventricular activity. When no ventricular event is sensed during an A–A interval, the algorithm delivers a ventricular stimulus (after a period equal to the A-A interval plus 80 ms). If no ventricular event is sensed for two out of four consecutive cycles, the device automatically switches to DDD(R) mode for just 1 min and then an AV conduction check is carried out: the algorithm reverts automatically to AAI(R) mode just for one cycle, searching for an intrinsic ventricular event. If no such event is sensed, the time interval for the next check will double (2 min, 4 min, etc., up to 16 h after mode switch to DDD(R)). If a ventricular event is sensed, the algorithm switches back to AAI(R) mode. In practice, the MVP algorithm was able to minimize the mean percentage of VP (94% relative reduction) when compared with conventional DDDR mode, both in patients with sinus node disease and in those with intermittent AV block, and its effect was sustained during a follow-up of 6 months post-implant. Similar outcomes were also found in the SAVE-PACE trial where the median percentage of VP was significantly decreased in the therapy group compared with controls (9.1 vs. 99%). As a result, the relative risk reduction of development of persistent AF was 40%. Although harder endpoints such as mortality were not evaluated, this reduction led to smaller numbers of invasive ablation procedures and fewer hospital admissions for HF, as well as lower risk for new-onset HF attributable to pacemaker implantation. In addition, in another study, MVP was proven to be superior to Search AV+ algorithm in minimizing VP, particularly in patients with first-degree AV block.

An unsolved issue that will be evaluated by the PreFER MVP study is to what extent the deleterious effects of right VP are reversible after pacemaker replacement with a device that incorporates an MVP algorithm. This hypothesis is based on previous studies suggesting that pacemaker recipients exposed to long periods of VP can benefit from the restoration of a physiological activation pattern.

Finally, the efficacy of the MVP algorithm to prevent AF and HF will be tested in the MIVERVA study which will evaluate the clinical benefit of conventional DDDR pacing, compared with MVP algorithms combined with preventive pacing algorithms (PPA) and antitachycardia pacing (ATP) algorithms.

Therefore, it becomes evident that incorporation of an algorithm designed to minimize VP is beneficial, as it effectively reduces unnecessary VP, development of AF and new-onset HF, as well as morbidity. As mentioned earlier, the MVP algorithm has contributed to a significant reduction in VP even in patients with second degree or intermittent third degree AV block. However, in patients with intermittent third-degree AV block, there is much scepticism as to whether the MVP algorithm should be activated, as questions of safety have emerged in light of an increased risk for pause-mediated polymorphic ventricular tachycardia/ventricular fibrillation.

### Table 1 Functional criteria of the SafeR algorithm

<table>
<thead>
<tr>
<th>SafeR algorithm</th>
<th>Conversion from AAI to DDD mode</th>
<th>Conversion from DDD to AAI mode</th>
<th>Automatical inactivation of SafeR mode</th>
</tr>
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<tbody>
<tr>
<td>More than three blocked atrial events in the last 12 cycles</td>
<td>12 consecutive R waves sensed</td>
<td>More than five switches to DDD/day over three consecutive days</td>
<td></td>
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<tr>
<td>More than two consecutive blocked atrial events</td>
<td>After 100 cycles in DDD(R) mode</td>
<td>Greater than or equal to 15 switches in 1 day</td>
<td></td>
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<tr>
<td>More than six consecutive abnormal AR/PR intervals</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>More than 3 s ventricular pause</td>
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Atrial fibrillation prevention algorithms

Atrial fibrillation represents the most common cardiac arrhythmia and is associated with increased morbidity, mortality, and impairment of quality of life. The recognition of potential triggers of AF has enabled the development of novel pacing algorithms, designed to inhibit the initiation of AF episodes. At present, several similar algorithms are integrated in pacemakers software (Table 2).

(i) The continuous atrial pacing algorithm provides permanent atrial pacing at a rate just above the intrinsic sinus rate (achieved by pacing at an interval of 50 ms shorter than any sensed, non-premature, sinus cycle).

(ii) The overdrive pacing after premature atrial contractions (PAC) algorithm increases the atrial pacing rate by 5 bpm when it detects consecutive premature PACs. Acceleration of heart rate is allowed until PAC disappearance or until a total increment of 25 bpm is reached.

(iii) The algorithm for preventing pauses after PAC, which after a premature atrial event delivers an early AV pacing sequence, or an early synchronous atrial pacing pulse when a premature ventricular event is sensed.

(iv) The overdrive pacing after AF algorithm elevates atrial pacing rate after the termination of an episode of AF and then gradually reduces it until an intrinsic atrial stimulus is sensed or the lower rate limit is reached. In this way, an early recurrence of an AF episode is suppressed.

(v) Finally, the algorithm for preventing steep rate drops after exercise provides a smooth transition between a high rate (possibly after increased physical activity) and the lower normal rate.

The AF Suppression Algorithm (based on continuous atrial pacing) was evaluated by the ADOPT trial in patients with sick sinus syndrome and paroxysmal AF (receiving a Trilogy DR+/DAO or an Integrity AFx pacemaker, St Jude Medical Cardiac Rhythm Management Division, Sylmar, CA, USA). The AF Suppression Algorithm reduced symptomatic AF burden by 25% and total atrial arrhythmia burden by 26.5%. However, this achievement was diminishing during follow-up (absolute difference in AF burden between control group and treatment group was 1.25% at 1 month and 0.36% at six months’ follow-up), while automatic mode switch was similar in both groups. A similar algorithm was evaluated recently in the APP study (in recipients of a Guidant model 1280 pacemaker, St Paul, MN, USA) and though the total duration of atrial tachyarrhythmia (AT) tended to be reduced in patients with the APP algorithm ON, the reduction failed to reach statistical significance. According to the investigators, this could be attributed to the different settings used in the design of the study (three different search-interval settings of 8 cycles, 16 cycles, 32 cycles for AF detection were used in each patient). Indeed, total duration of AT was significantly reduced when the period of APP algorithm OFF was compared with the period of the most effective search interval setting in each patient. Interestingly, the optimal setting differs from one patient to another and therefore settings should be individualized to achieve optimal
effect. On the other hand, the PIPAF trial, which evaluated the efficacy of three PPA (in Chorum 7334 or Talent DR 231 pacemaker recipients, ELA Medical) demonstrated a lower AF burden only in a subgroup of patients with preserved intrinsic AV nodal conduction and therefore a low percentage of VP. Another type of algorithm, the post-mode switch overdrive pacing algorithm (utilized by the AT500 pacemaker Medtronic Inc.) was designed to prevent new episodes of AF occurring shortly after the termination of a previous AF episode. This algorithm was evaluated by the PMOP study. Based on its results, the PMOP algorithm has proven to be quite efficient in inhibiting the initiation of AF episodes during the vulnerable period that follows the termination of an AF episode. In the AFTherapy study, (conducted in recipients of a Selection model 900 pacemaker, Vitatron, B.V., Arnhem, The Netherlands), four PPA were evaluated (pace conditioning, PAC suppression, post-PAC response, and post-exercise response). Although a 37% lower mean AF burden was demonstrated in the therapy group, this difference did not reach statistical significance. Besides AF burden, time to first AF episode and average sinus rhythm duration were also evaluated without significant differences between therapy and control groups. In the PAFS study, that followed, the efficacy of atrial overdrive and ventricular rate stabilization pacing algorithms (Selection model 900 and T70 pacemakers, Vitatron, B.V.) were evaluated in patients with AF burden 1–50%. A ventricular rate stabilization pacing algorithm regulates ventricular rate during an episode of AF and in this way diminishes the symptoms of conducted AF. During an AF episode, this algorithm is programmed to pace the ventricle just above the mean ventricular rate and if a ventricular stimulus is still sensed the pacing rate increases further, until no ventricular event is sensed. This trial demonstrated a reduction of AF episodes initiated by PAC; nevertheless, total AF burden, patients’ symptoms, and quality of life did not manifest any differences between therapy and control groups. Another study that evaluated the efficacy of six PPA was the SAFARI trial. As the authors note in their results, the AF burden was significantly reduced by 1.38 h/day (P = 0.038), but only in the subgroup of patients with a high AF burden (>6%). In the low AF burden group (<6%), activation of PPA did not result in prevention of AF episodes. Finally, the ASPECT study compared the efficacy of three PPA (atrial pacing preference, atrial rate stabilization, and post-mode switch overdrive pacing) in pacemaker recipients (AT500 pacemaker, Medtronic Inc.) randomized to septal or non-septal atrial lead placement. According to the investigators, the frequency of symptomatic AT/AF episodes was significantly lower in therapy group compared with control group only in the septal pacing recipients. One very important parameter that should be taken under consideration is that each PPA aim at specific but different AF-inducing mechanisms to achieve inhibition of an AF episode. However, the AF-onset mechanism may differ in each individual, resulting in a varying efficacy of the same algorithm. Indeed, two categories of different AF-inducing mechanisms have been identified. In the first group, several PACs are needed for an AF episode to occur (trigger group), while in the second group AF is initiated after only a single PAC, indicative of an AF-vulnerable substrate (substrate group). Logically, individuals of the first group will benefit from PAC suppression algorithms, in contrast to the second group in which overdrive pacing algorithms may be more efficacious. Based on the above, the VIP registry was designed to evaluate PAC suppression and post-PAC response algorithms in the trigger group vs. pace conditioning algorithm in the substrate group. In patients of the first group, there was a significant reduction (28%) of AF burden, while in the substrate group overdrive pacing algorithm failed to demonstrate any statistically significant improvement. Therefore, we can assume that the exact AF-onset mechanism plays a determining role in the efficacy of the algorithms utilized by pacemakers and that individuals of the trigger group are more amenable to PPA. According to the aforementioned data, novel algorithms for the prevention of AF have been evaluated in several studies, but outcomes concerning their efficacy are controversial, even though their safety is indisputable (Table 3). However, as specific patient groups demonstrate substantial benefits from certain algorithms that target the arrhythmia onset mechanism, it is of great significance to treat each case on an individual basis. Furthermore, the superiority of septal atrial pacing in patients with activated PPA needs to be further evaluated. Finally, it should be kept in mind that continuous overdrive pacing is unlike to be well-tolerated in the long term, especially during resting periods, while it may provoke tachycardia-induced cardiomyopathy.

Atrial fibrillation termination algorithms

Antitachycardia pacing algorithms have proven to be quite effective for the termination of atrial flutter and slower organized AT. The fact, however, that both atrial flutter and tachycardia usually coexist in patients with AF has led to the incorporation of these algorithms in devices implanted in patients suffering from AF. These algorithms include 50 Hz pacing sequences, as well as burst and ramp pacing. The Pitagora trial was designed to compare the efficacy of Ramp sequence (which represents an autodecremental drive of stimuli) and Burst sequence (which consists of a constant drive of pulses followed by up to two extra stimuli). According to this study, Ramp sequence has proven to be more effective in terminating AT episodes (53.1% vs. 44.3%) for an AT cycle length >240 ms. On the other hand, the 50 Hz pacing sequence is a high frequency burst of atrial pacing delivered at 50 Hz (3000 bpm for 0.5–3 s). However there is little evidence of this algorithm’s efficacy in termination of AF episodes. The ATTEST trial evaluated the efficacy of two rate-adaptive atrial ATP algorithms (burst and ramp sequences) (incorporated in the AT500 pacemaker, Medtronic Inc.). According to the outcomes of this study, ATP algorithm had an extremely high detection accuracy (up to 99.9%) while 54.4% of the episodes of AT/AF were successfully terminated by the ATP algorithm. However, the study failed to demonstrate statistically significant differences in AT/AF burden and AT/AF frequency between the groups with ATP algorithm ON and controls. Similar findings to the above were obtained by the POT study, which enrolled patients who received pacemakers (AT500, Medtronic Inc.) that incorporated three PPA (atrial pacing preference, atrial rate stabilization, and post-mode switch overdrive pacing) and two ATP algorithms...
<table>
<thead>
<tr>
<th>Trial</th>
<th>Publication</th>
<th>Pacemaker</th>
<th>No. of patients</th>
<th>F/U (months)</th>
<th>Pacemaker’s algorithm evaluated</th>
<th>Outcomes</th>
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<tr>
<td>ADOPT</td>
<td>JACC 2003</td>
<td>St Jude</td>
<td>288</td>
<td>6</td>
<td>AF suppression</td>
<td>25% reduction of AF burden; 26.5% reduction of total AT</td>
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<tr>
<td>APP</td>
<td>Circulation 2008</td>
<td>Guidant</td>
<td>42</td>
<td>5</td>
<td>Atrial pacing preference</td>
<td>No statistically significant differences</td>
</tr>
<tr>
<td>PMOP</td>
<td>Heart Rhythm 2006</td>
<td>Medtronic</td>
<td>49</td>
<td>6</td>
<td>Post-mode switch overdrive pacing</td>
<td>Effective in preventing early recurrence of AT/AF episodes</td>
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<tr>
<td>PIPAF</td>
<td>Europace 2004</td>
<td>ELA</td>
<td>55</td>
<td>12</td>
<td>SR overdrive, acceleration on PAC, post-extrasystolic pause suppression</td>
<td>Lower AF burden only in a subgroup of patients with low percentage of ventricular pacing</td>
</tr>
<tr>
<td>AFT</td>
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<td>Vitatron</td>
<td>153</td>
<td>6</td>
<td>Pace conditioning, PAC suppression, Post-PAC response, post exercise response</td>
<td>No significant differences in AF burden, time to first AF episode, average SR duration</td>
</tr>
<tr>
<td>ASPECT</td>
<td>J Cardiovasc. Electrophysiol. 2003</td>
<td>Medtronic</td>
<td>277</td>
<td>6</td>
<td>Atrial preference pacing, atrial rate stabilization, post-mode switch overdrive pacing in septal/non-septal pacing</td>
<td>Lower frequency of symptomatic AT/AF episodes On vs. Off only in the septal pacing group</td>
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<tr>
<td>PAFS</td>
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<td>Vitatron</td>
<td>79</td>
<td>4</td>
<td>Atrial overdrive, ventricular rate stabilization pacing</td>
<td>Reduction of AF episodes initiated by PAC, no differences in total AF burden, patients’ symptoms, or quality of life</td>
</tr>
<tr>
<td>VIP</td>
<td>PACE 2006</td>
<td>Vitatron</td>
<td>126</td>
<td>6</td>
<td>Pace conditioning vs. PAC suppression and post-PAC response</td>
<td>Significant reduction of AF burden in the trigger group, substrate-AF patients are less likely to respond to preventive pacing algorithms</td>
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<tr>
<td>POT</td>
<td>Europace 2008</td>
<td>Medtronic</td>
<td>85</td>
<td>11</td>
<td>Atrial preference pacing, atrial rate stabilization, post-mode switch overdrive pacing plus burst+ and ramp sequences</td>
<td>Significant reduction of AF burden with PPA, without incremental benefit with ATP</td>
</tr>
<tr>
<td>SAFARI</td>
<td>Heart Rhythm 2009</td>
<td>Vitatron</td>
<td>240</td>
<td>10</td>
<td>Pace conditioning, rate soothing, PAC suppression, post-PAC response, post exercise response, post AF response</td>
<td>Significant reduction of AF burden only in the high AF burden subgroup</td>
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<tr>
<td>ATTEST</td>
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<td>Medtronic</td>
<td>324</td>
<td>3</td>
<td>Atrial preference pacing, atrial rate stabilization, post-mode switch overdrive pacing plus burst+ and ramp sequences</td>
<td>No significant differences in AF burden and total frequency between the group with ATP algorithm ON and control group</td>
</tr>
</tbody>
</table>
(burst+ and ramp sequences) and compared the efficacy of PPA alone to PPA and ATP together. According to the results, there was a significant reduction of AF burden with PPA, but no incremental benefit was demonstrated when ATP was activated. Therefore, even though the safety and detection accuracy of these algorithms are undisputed, their efficacy needs to be proven.

**Rate-drop response algorithm**

Vasovagal syncope is considered to be a rather benign symptom, especially in younger patients. However, in selected highly symptomatic individuals, pacing may be considered as a treatment alternative. In those cases, the incorporation of a rate-drop response (RDR) algorithm is associated with a decline in syncopal episodes, since the device can identify a significant fall in heart rate suggestive of an imminent syncopal episode and can initiate high-rate pacing. This algorithm includes two detection elements that can be activated simultaneously and trigger intervention therapy independently from each other: the drop-detect method and the low-rate detect method. The drop-detect method determines whether the heart rate has fallen from a rate higher than the top rate to a rate lower than the bottom rate during the predetermined time width. The low-rate detect method is activated when lower rate pacing occurs for a selected consecutive number of paced beats. However, this detection method is not appropriate for individuals who are expected to utilize low-rate pacing support due to bradyarrhythmias. When either one of the above detection methods is activated, rapid rate pacing is initiated at either a fixed rate of 100–120 bpm or a relative rate of 70–80% of the maximum heart rate. The algorithm remains activated for a certain period of time (which is also programmable) and after that pacing rate gradually declines (usually by 5–8 bpm) until the pacemaker senses three consecutive native atrial beats or reaches the lower atrial pacing rate.

The efficacy of the RDR algorithm was evaluated by several studies, which in general demonstrated a diminished frequency of syncopal episodes. Actually, in one study, the mean syncopal burden in patients with pacemakers that incorporated these algorithms fell to 0.3 episodes/month compared with 1.2 episodes/month before implantation, while 81% of the patients reported symptomatic improvement. However, an important element that affects this algorithm’s efficacy is the parameters that define the detection window and alter its sensitivity to detect rate drop episodes. For example, a reduction in drop size (which is defined as the difference between top and bottom rate) will increase the sensitivity of the method. Finally, it is essential to clarify that optimal programming of this algorithm can be achieved only by individualizing the parameters, initially based on electrocardiography, tilt-testing, and carotid sinus massage recordings and subsequently by adjusting them during the follow-up of each patient.

**Ventricular AutoCapture and Atrial Capture Management algorithm**

Prolongation of pulse generator longevity has always been a main objective in cardiac pacing. The pulse generator longevity is determined by battery capacity and current drain (which represents both housekeeping current and pacing current). Although housekeeping current increases as the pacemaker’s electronic components become more complicated, technology has managed to suppress it to a minimum (~10 μA). Given that both battery capacity and resting current are fixed, the only parameter that could play a role in pacemaker longevity is pacing current. Pacing current is associated with pacing rate, pulse width, and pulse amplitude. Both pacing rate and pulse width are usually programmed to certain values; thus pulse amplitude represents the most crucial parameter that can affect pulse generator longevity. In clinical practice, pacemakers are manually programmed to an optimized output, maintaining a safety margin that leads to unnecessary current drain. The AutoCapture (AC) algorithm verifies ventricular capture on a beat-to-beat basis, by confirming the evoked response to the pacing stimulus, and automatically adjusts output closely to pacing threshold. The AC algorithm which was introduced for the first time in 1995 by St Jude Medical in the single-chamber Microny Pacemaker, has offered an economic, yet reliable new perspective on the pacemaker’s pulse amplitude, providing an adequate safety margin while simultaneously avoiding unnecessary current drain. In more detail, after a 15 ms blanking period, the AC algorithm has a detection window open for 47.5 ms that recognizes evoked response after each pacing stimulus. When an evoked response is verified, capture is confirmed. If not, the pacemaker delivers a high output pulse to ensure capture and the amplitude of the following stimulus is increased. When no capture is detected for two consecutive pulses, the algorithm...
redetermines the capture threshold and adjusts the pacemaker’s output to 0.25 V above the new threshold, instead of the conventional two-fold amplitude safety margin. According to accumulating data, the AC algorithm can substantially increase generator’s longevity (which is more evident in patients with a high pacing threshold ≥ 1 V) and consequently reduces the expected pacing-related costs by up to 42% over a 10-year follow-up.43 Another similar study44 that included 910 patients demonstrated a 16% increase in battery longevity in the subgroup of patients with the AC algorithm ON. Specifically, the estimated longevity was 10.3 years for the therapy group vs. 8.9 years for the control group. Moreover, manual measurement of the capture threshold confirmed the accuracy of automatically measured threshold (the mean difference between the two measurements was only 0.07 V, \( P = 0.002 \)). According to the aforementioned data, the AC algorithm represents a reliable and cost-effective feature in currently available pacemakers. However, it is worthy underlining that the results for battery longevity are based on projected and not actual measurements, since following the devices until battery drainage is both impractical and time-consuming. Furthermore, there is some discrepancy in the literature concerning the efficacy of this algorithm. As mentioned earlier, when capture is not confirmed, the pacemaker delivers a high output pulse that may consume up to 25 times more energy than a threshold stimulus. Consequently, continuous adjustment of the pacing output can lead to increased energy demand compared with conventional pacing.45 Finally, there are still some unresolved technical issues involving the accurate verification of the evoked response especially when fusion and pseudofusion beats are present.

Another algorithm available in today’s pacemakers is the Atrial Capture Management (ACM) algorithm, which enables the automatic measurement of atrial pacing threshold and appropriately adjusts pacing output. According to clinical studies, this algorithm has proven to be very accurate: automatic and manual measurements of atrial threshold had a mean deviation of only 0.01 V.46 The ACM algorithm is particularly beneficial in patients with atrial thresholds >2.5 V. In these cases, a high threshold is correctly identified and atrial output is reset at a higher safe level. In addition, the ACM algorithm reduces follow-up burden, while it may even result in prolongation of device longevity especially, when combined with the ventricular AC algorithm.47

Follow-up/remote pacemaker interrogation

After a pacemaker implantation, follow-up visits are necessary to achieve optimal pacemaker settings and adequate therapy adjustments. However, as pacemakers become more sophisticated, the follow-up is more complex and time-consuming, since various measurements need to be made and interpreted by the investigator.48 Currently available pacemakers are embedded with microprocessors aiming at facilitating device follow-up. These algorithms can summarize in the first screen all the important parameters that need to be taken under consideration: battery status, lead impedance, sensing and capture thresholds, as well as numerous other data such as rate histograms, percentage of paced and sensed beats. These refined algorithms have significantly decreased the duration of follow-up visits. Therapy advisor49, a novel feature designed to serve exactly the same purpose, was introduced by Vitatron (B.V., Arnhem, The Netherlands). This algorithm not only automatically analyses all data stored in the device, providing all the measurements required for device programming, but also offers advice in order to optimize the pacemaker settings, alerting the investigator in case-specific diagnostics need to be reappraised.

Follow-up visits may also cause patients inconvenience as well as imposing a growing burden on both physicians and healthcare systems. Nowadays, telemedicine has enabled the long-distance transmission of data stored in pacemakers. The idea of developing trans-telephonic monitoring systems (TTMs) as a means of minimizing follow-up visits was initially proposed in the 1970s.50 Trans-Telephonic monitoring system was at first used only to check battery status, as the physician was unable to download data stored in the device. Therefore, in-person interrogation of the pacemaker was necessary for other parameters to be evaluated.51 A novel approach, initially applied to ICDs, is internet-based remote device interrogation systems, which provide complete and easy access to all stored data. These systems are currently available through Medtronic CareLink Network (CareLink, Minneapolis, MN, USA), Biotronik Home Monitoring (Berlin, Germany), St Jude Housecall (St Paul, MN, USA), and Boston Scientific Latitude (St Paul, MN, USA). The PREFER trial51 is designed to evaluate the efficacy of this method in pacemaker recipients compared with the combination of conventional in-person interrogation and TTM. Another attractive alternative is a remote, wireless Home Monitoring (HM) system utilized by Biotronik (Berlin, Germany). Implantable devices (pacemakers, ICDs, and biventricular pacemakers) are equipped with an antenna that enables wireless transmission of all stored data via a cell-phone-like instrument (CardioMessenger, Biotronik), which must be within 2 m of the device recipient. The transmission, which initiates automatically, without requiring active participation of the patient, takes place once daily (usually while the patient is asleep) and all the data are transmitted encrypted to a service centre of Biotronik in Berlin. There, data are anonymously decoded, analysed, and uploaded to a secure internet platform. The patient’s physician has access to this platform through identity codes and personal passwords and can also be informed of critical events via e-mail, SMS, or fax. The complexity of this remote interrogation method (encrypted transmission, personal passwords, etc.) ensures the reliability of the method, as well as the confidentiality of the personal information being transmitted. As far as reliability of transmission is concerned, an analysis of 4200 variables that were transmitted via the HM system was in absolute concordance (100%) with the data analysed via in-person interrogation.52

It is estimated that the HM system may enable detection of a parameter needing reappraisal surprisingly soon after the last follow-up visit. In patients followed every 3 months or biannually, a detection of a critical event was made 64 and 154 days, respectively, before the next scheduled visit.53 On the other hand, in cases where no particular problem was diagnosed, the next follow-up visit was omitted. However, it is worth-mentioning that neither
Conflict of interest: undoubtedly ameliorate current pacing strategies. medical and technological evolution is impressive and will be convenient for both patients and physicians. Either way, modern pacing-related costs and would seem likely to prove more convenient.

Ventricular AutoCapture algorithm and remote pacemaker interrogation seem to promise much in effectively reducing adverse effects. Some of these algorithms (minimizing VP) are of interest.

The incorporation of new algorithms in modern pacemakers has adverse effects. Some of these algorithms (minimizing VP) are of interest. The number of scheduled visits of a similar patient population, which had a positive impact on the hospital’s finances. Based on the above, it is obvious that remote interrogation of implantable devices is both feasible and reliable. However, it is vulnerable to certain ethical and legal issues that remain to be settled.

Conclusion
The incorporation of new algorithms in modern pacemakers has altered our ability to manage patients, avoiding pacing-induced adverse effects. Some of these algorithms (minimizing VP) are of indisputable value, while others (preventive pacing and ATP algorithms) need further evaluation to determine their value. Finally, the Ventricular AutoCapture algorithm and remote pacemaker interrogation seem to promise much in effectively reducing pacing-related costs and would seem likely to prove more convenient for both patients and physicians. Either way, modern medical and technological evolution is impressive and will undoubtedly ameliorate current pacing strategies.

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References