Automatic assessment of atrial pacing threshold in current medical practice

Jean Luc Rey1, Serge Quenum1, and Marc Hero2*

1Department of Cardiology, CHU Sud, Amiens, France; and 2Medtronic France, 122 Avenue du Général Leclerc, 92514 Boulogne-Billancourt, France

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Aims
The aim of this study was to validate the ambulatory automatic atrial threshold monitoring algorithm by comparing the measurements assessed by the automatic system and those evaluated manually by the physician at discharge, 2- and 8-month follow-up sessions.

Methods and results
This is an observational multicentric prospective study of 352 patients implanted with EnPulse® DR pacemakers. Mean age was 76.3 ± 9.4 years. Indications of pacing were atrio-ventricular block (AVB) (64%) and sinus dysfunction (SD) or brady–tachy syndrome (36%). The automatic atrial threshold monitoring function was maintained at nominal programming state with daily measurement scheduled at 1:00 am. Ambulatory automatic atrial threshold assessment was possible for 91.5% of patients at discharge, 97.3% at 2 months, and 95.7% at 8 months. Causes of the unsuccessful attempts to perform automatic atrial threshold were atrial arrhythmias or permanent atrial and ventricular pacing. Feasibility is significantly better for AVB indication than SD indication due to more frequent occurrence of atrial fibrillation (AF). At each stage, there is a strict correlation between the automatic measurements and those conducted manually by the physician with a \( P < 0.001 \).

Conclusion
Feasibility of ambulatory automatic atrial threshold is good. Results of the study show excellent correlation between the two methods for atrial threshold: there is no statistical difference between manual and automatic measurements during follow-up.

Keywords
Pacing • Automatic atrial threshold

Introduction
Automatic assessment of ventricular threshold by analysis of evoked response has been used in medical practice for 10 years.1 Atrial threshold measurement by analysis of evoked response is difficult because the P wave signal is small.2 For this reason, the manufacturer Medtronic has developed a specific algorithm introducing premature atrial pacing and sensing of atrial or ventricular response according to the pacing mode to assess atrial threshold.

Results of this method have been previously published.3,4 The present study has been performed in current medical practice with a large number of patients.

Methods
Study protocol
The purpose of CASA study (Contrôle Automatique du Seuil Auriculaire = Automatic Atrial Threshold Management) was to assess automatic atrial threshold performance of EnPulse® DR implantable pacemaker (Medtronic, MN, USA). The primary objective was to evaluate correlation between automatic and manual atrial threshold measurements at different follow-up visits.

Patients with indications of dual-chamber pacing were not selected a priori for enrollment in this observational, non-randomized French multicentre study. Transvenous leads were part of the inclusion criteria, but the lead selection was unrestricted. All patients gave written informed consent to the protocol, which was approved by the French national medical council.

Three hundred and fifty-two patients were enrolled in the study over 31 French centres. Data were collected by case report forms at enrollment, hospital discharge, and visits scheduled 2 months and 8 months after implantation. A manual measurement threshold using atrial amplitude auto-decrement test with a voltage step of 0.25 V was compared with the last atrial pacing threshold assessed by ambulatory automatic capture measurement (ACM) test using the same pulse width (0.4 ms) and an amplitude auto-decrement with a 0.125 V voltage step. The physician performing the manual testing...
was aware of the automatic threshold values. The ACM test results were available in the device memory. For the other parameters and particularly for the AV delay values, programming was left to the discretion of the physician.

**Description of the automatic capture measurement algorithm**

Automatic capture measurement function operates in DDD/DDDR modes and measures atrial pacing threshold automatically, nominally every day at 1:00 am. The last atrial pacing threshold is stored in the device memory, and atrial pacing voltage is adjusted based on this measurement. The pacemaker applies the programmable amplitude safety margin to the amplitude threshold value measured at a 0.4 ms pulse width to determine the target amplitude. If the operating amplitude is above the target, the pacemaker adapts the amplitude down towards the target in one-step decrements. If the operating amplitude is below the target, the amplitude is immediately adapted to the target.

A high-threshold warning is issued if the amplitude threshold is >2.5 V; the pacemaker responds by adapting to an amplitude of 5.0 V and a pulse width of 1.0 ms.

Unlike ventricular capture management, ACM does not use evoked response sensing to determine capture. Automatic capture measurement uses two methods to automatically determine the atrial threshold: atrial chamber reset (ACR) and atrio-ventricular conduction (AVC). Before starting threshold measurement, the device evaluates the patient’s rhythm and selects the more appropriate of both the methods.

If the patient has a stable sinus rhythm, the ACR method is chosen. If the patient does not have a stable sinus rhythm but has stable AVC, the device selects the AVC method. If conditions are not favourable for either method, ACM attempts to use the AVC method or tries again after 30 min. The AVC method is tested because stable AVC may be discovered when AVC lengthens the AV interval. If both methods are attempted and none is successful, another ACM test is tried in 30 min. However, each method has a maximum limit of three attempts each day (or other physician-programmed test period).

**Atrial chamber reset method**

Atrial chamber reset runs during stable sinus rhythm. It evaluates capture by observing the response of the intrinsic rhythm to the atrial test pace. If the test pace does not capture, the sinus node is not reset, and an atrial refractory sensed event (AR) is observed after the test pace. If no AR is observed within the AV interval, ACR concludes that the test pace captured the myocardium.

**Atrio-ventricular conduction method**

Atrio-ventricular conduction method runs when stable 1:1 AVC is observed with atrial pacing. The atrial pacing rate is increased by 15 bpm (but no faster than 101 bpm) and the AV interval is lengthened to try to achieve a stable atrial pacing (AP)–VS rhythm.

Atrio-ventricular conduction evaluation captures by observing the conducted ventricular response to the atrial test pace. Each atrial test pace is followed by a backup pace-delivered 70 ms after the test pace at programmed amplitude and a 1.0 ms pulse width to maintain rhythm stability during the test. If a conducted VS event is observed at approximately the expected AP–VS interval following the atrial test pace, AVC concludes that the test pace captured the myocardium.

**Implanted leads**

Implanted atrial leads included 25 different lead models from five manufacturers, mostly bipolar with active fixation; 57% were 5076 active Medtronic lead model. The most common lead location was the right atrial appendage (67%). The other locations were atrial lateral free wall (24%), mid-septum (7%), and other (2%). The atrial leads were newly implanted in 328 patients (93%).

**Statistical analysis**

The analyses of variables were presented as the mean and standard deviation. Categorical variables were presented as the frequency and percentage of subjects in the category of interest. The two-side t test was used to compare the difference of interest between groups. Regression coefficient model was used to compare manual and automatic methods.

**Results**

**Patients**

Three hundred and fifty-two patients were enrolled in the study from 31 French centres. The patient population was 76.3 ± 9.4-year old with a majority of male (57%) patients.

Indications of pacing were AV block (64%), sinus node dysfunction or brady–tachy syndrome (36%). Twenty-eight per cent of patients had a history of atrial fibrillation (AF); 39% of patients are known or likely to be pacemaker dependent; 22% of patients had an ischaemic cardiopathy history. All 352 patients were assessed at discharge (mean 3 ± 3 days), 298 patients were assessed at 2 months (mean 63 ± 29 days), and 254 patients were assessed at 8 months (mean 240 ± 91 days). There were 14 atrial lead (4%) dislocations with repositioning or replacement during the study.

**Feasibility of manual and automatic atrial thresholds during follow-up**

Table 1 shows that ambulatory automatic atrial threshold assessment was impossible for 30 patients at discharge (8.5%, after an average monitoring period of 2 days only): 14 patients due to atrial arrhythmias (AF) and 16 patients due to permanent atrial and ventricular pacing (AP–VP). For the next follow-up sessions, automatic atrial threshold assessment was impossible for 8 patients at 2 months (2.7%) and 11 patients at 8 months (4.3%).

Manual atrial threshold was impossible for 0.3% of patients at discharge, 3.7% of patients at 2 months and 5.9% at 8 months either for AF or permanent AP–VP.

Table 2 shows the applicability of automatic atrial threshold assessment according to indication of pacing at each follow-up: applicability was significantly better for atrio-ventricular block (AVB) indication (94.7% at discharge, 98.6% at 2 months, and 97.8% at 10 months) than for sinus dysfunction (SD) (85.8, 93.8, and 91%) due to more frequent AF occurrence in SD patients precluding atrial threshold assessment.

**Chronology of last successful automatic atrial threshold with regard to manual atrial threshold assessment**

For 86% of patients, the latest successful automatic atrial threshold test was performed on the same day as the manual test, and for
12% of patients one day before the manual control date. These results demonstrate the excellent feasibility of automatic atrial threshold assessment in current medical practice with only a delay of one day between the automatic test and the manual test for 98% of patients.

Results and correlations between automatic and manual thresholds

Values of manual and automatic atrial threshold are indicated in Table 3. The difference in means of values between the two methods is 0.009 V at discharge, 0.021 V at 2 months, and 0.038 V at 8 months. The mean of differences is 0.021 V at discharge, 0.044 V at 2 months, and 0.043 V at 8 months.

Figures 1 and 2 demonstrate excellent correlation between the two methods with a correlation coefficient of 0.910 at discharge, 0.890 at 2 months, and 0.916 at 8 months follow-up.

Differences between the two methods are as follows: for 95.4% of patients at discharge, 92.9% at 2 months, and 93% at 8 months, the difference was ≤0.25 V. Difference was equal to 0.5 V for 1.9, 2.2, and 1.7% of patients at discharge, 2 months, and 8 months follow-up. No difference >0.5 V between the two methods was observed. For patients with a difference of 0.5 V between automatic and manual thresholds (six patients at discharge and at 2 months, four patients at 8 months): absolute pacing threshold was 1.2 ± 0.5 V for automatic method and 0.94 ± 0.45 V for manual method; for all these measurements, automatic threshold was greater than the manual threshold with a difference of 0.5 V.

Patients with high atrial automatic threshold

Forty-eight patients have demonstrated high atrial automatic threshold superior or equal to 1.5 V at least at one control. These patients can be classified in four groups according to the evolution of atrial threshold (Figure 3): group 1 (n = 15): progressive decreasing atrial threshold during follow-up; group 2 (n = 14): increasing atrial threshold at 2 months and decreasing at 10 months; group 3 (n = 11): high atrial threshold during follow-up and group 4 (n = 8): progressive increasing atrial threshold during follow-up. No patient experienced atrial threshold superior to 2.5 V. There was no difference in pacing impedance between patients with high atrial threshold (≥1.5 V) and other patients at each follow-up. Only seven high-impedance atrial leads were implanted and none were experienced in the high atrial threshold group.

Discussion

Feasibility of automatic atrial threshold

Ambulatory automatic atrial threshold assessment was possible for 91.5% of patients at discharge, 97.3% at 2 months, and 95.7% at 8 months. Causes of the unsuccessful attempts to perform automatic atrial threshold were atrial arrhythmias or permanent AP–VP (Table 1). In Sperzel et al.’s study, the feasibility of ambulatory automatic atrial threshold assessment was 90, 91, and 96% at 2 days, 1 week, and 1 month, which is very close to our results.
Our study demonstrates that feasibility is significantly better for AVB indication than SD due to the greater occurrence of AF and permanent AP–VP (Table 2). For SD indication, feasibility could be probably improved by programming a long AV delay in order to obtain a spontaneous AVC, which was not done in our study.

### Table 3 Results of ambulatory automatic and manual atrial threshold during follow-up.

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>No. of patients</th>
<th>No. of patients auto and manual thresholds</th>
<th>Mean of auto threshold (V)</th>
<th>P</th>
<th>Mean of manual threshold (V)</th>
<th>Difference of means (V)</th>
<th>Mean of differences (V)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discharge (3 ± 3 days)</td>
<td>352</td>
<td>322</td>
<td>0.682 ± 0.393</td>
<td>NS</td>
<td>0.673 ± 0.416</td>
<td>0.009</td>
<td>0.021 ± 0.151</td>
</tr>
<tr>
<td>2 months (63 ± 29 days)</td>
<td>298</td>
<td>281</td>
<td>0.728 ± 0.416</td>
<td>NS</td>
<td>0.707 ± 0.443</td>
<td>0.021</td>
<td>0.044 ± 0.156</td>
</tr>
<tr>
<td>8 months (240 ± 90 days)</td>
<td>254</td>
<td>231</td>
<td>0.751 ± 0.433</td>
<td>NS</td>
<td>0.713 ± 0.438</td>
<td>0.038</td>
<td>0.043 ± 0.153</td>
</tr>
</tbody>
</table>

NS, not significant.

### Correlation between automatic and manual atrial thresholds.

Correlations were excellent at the three stages of the study (Figures 1 and 2) with a P < 0.001. Difference in means of values between automatic and manual atrial threshold were 0.09 V at discharge, 0.021 V at 2 months, and 0.038 V at 8 months. In Sperzel et al.s study\(^3\) difference in means of values were 0.012 V at discharge, 0.010 V at 1 month, and 0.018 V at 6 months, but validated automatic and manual threshold were present only for 60% of patients, distributed into 111 patients at discharge, and 64 patients at 6 months.

In our study, differences between automatic and manual atrial thresholds absolute values were equal to zero in 48% of patients, 0.125 V in 32%, 0.250 V in 13%, 0.375 in 5%, and 0.5 V in 2%. In Sperzel et al.s study\(^3\) results were better with 77% of patients without difference between the two methods, 21% with a difference of 0.125 V and 1.7% with a difference of 0.250 V probably because automatic and manual atrial thresholds were assessed during the same hospital visit; moreover, correlations were established only for 55% of patients at discharge, 57% at 3 months, and 62% at 6 months (64 patients at 6 months). However, when they compare the ambulatory atrial threshold and the manual atrial threshold, the difference of the means is 0.032 V, very close to that of our study.

Excellent correlations with \(r\) coefficient between 0.715 and 0.954 were found comparing ambulatory automatic and manual thresholds during follow-up presented in four groups according to the evolution of atrial thresholds.
atrial thresholds in Biffi et al.’s study but only with 76 patients. Finally in Biffi et al.’s study, the daily variability of ambulatory automatic atrial threshold was low.

Moreover, we have to note that the voltage step decrease is different for the two methods—0.125 V for the automatic capture algorithm and 0.250 V for the manual threshold test; finally automatic atrial threshold was assessed by increasing atrial output value in contrast to manual atrial threshold, which is performed generally by decreasing atrial output value.

Twenty-six patients at discharge (7.4%), 25 patients at 2 months (8.4%), and 19 patients at 8 months (7.5%) with high atrial threshold ≥1.5 V were appropriately assessed by automatic algorithm. The maximum difference between ambulatory automatic and manual thresholds was 0.5 V for six patients at discharge and at 2 months, four patients at 8 months (automatic thresholds were always superior to manual thresholds), and for all these cases, automatic adjustment of atrial amplitude algorithm with a value of amplitude that equals twice the atrial threshold measurement with a minimum of 1.5 V, ensured safe atrial pacing. However, our follow-up lasted only 8 months and a further increase of atrial pacing threshold could occur as demonstrated by Biffi et al. for ventricular threshold in 6.8% of patients beyond 1 year. In this event, the automatic adjustment of atrial amplitude can improve safety for patients.

Potential benefit of automatic threshold assessment

In Ribeiro et al.’s study, the estimated projected longevity was significantly extended with automatic ventricular threshold assessment and adjustment of amplitude with a St. Jude autocapture system. With the same system, Biffi et al. has demonstrated during long-term follow-up, a significant increase of longevity by using automatic ventricular amplitude adjustment vs. fixed-output pacing. Moreover, safety of patients is ensured in the case of ventricular threshold rise above 2.5 V, which occurred in the long term for 3.7% of the 321 patients as demonstrated by Biffi et al.3

Automatic adjustment of atrial pacing amplitude with periodic verification of atrial threshold could increase again the longevity of the pacing system especially for patients frequently paced in the atrium. Our study shows that in the case of a rise in the atrial threshold, safety of atrial capture was always assured by automatic algorithm amplitude adjustment.

Particularity of this study

In contrast to previous studies performed in pacemaker centres, our study was performed according to current medical practice in a non-selected and important population of patients: correlations between manual and automatic atrial thresholds were assessed for 322 patients at discharge, for 281 patients at 2 months, and for 231 patients at 8 months. (Table 3).

Comparisons were performed between ambulatory automatic atrial threshold and manual atrial threshold, in order to assess the validity of automatic atrial threshold assessment in replacing the manual atrial threshold in current practice.

Study limitations

The impossibility of performing automatic atrial threshold in the case of permanent AP–VP is a limit of the method, but this concerns only three patients (1%) at 2 months and four patients (1.6%) at 8 months, and could be improved by lengthening the AV delay especially for patients with SD indication. Fifty-four patients were lost to follow-up at 2 months and 44 more patients at 8 months, but it is an observational study in current medical practice.

Conflict of interest: J.L.R. and S.Q. have nothing to declare. M.H. is employed full time by Medtronic France.

References