Percent ventricular pacing with managed ventricular pacing mode in standard pacemaker population

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Aims
Unnecessary right ventricular pacing has deleterious effects and becomes more significant when cumulative percent ventricular pacing (Cum%VP) exceeds 40% of time. The Managed Ventricular Pacing (MVP) mode has been shown to significantly reduce the percent ventricular pacing compared to the DDD/R mode. This study assessed the percent of ventricular pacing in a standard pacemaker population programmed to MVP and for which patients it is possible to achieve a Cum%VP < 40%.

Methods and results
Unselected, consecutive patients were implanted with a dual chamber pacemaker with a mean follow-up period of 76 days. The Cum%VP was calculated from device diagnostics between pre-hospital discharge (PHD) and the 1-month post implant visit. The median Cum%VP of 107 patients (age 67.2 ± 14 years; 53% male) who were programmed to MVP was 3.9%. The median Cum%VP was 1.4% in patients with sinus node disease (SND) and 28.8% in patients with AV block (AVB). Cum%VP < 40% was observed in 72% of all patients, in 50% of AVB patients, and in 86% of SND patients.

Conclusion
The MVP mode is capable of achieving a low percent of ventricular pacing in a standard pacemaker population with SND and AVB. In addition, 72% of patients in MVP mode demonstrated Cum%VP < 40%.

KEYWORDS
Managed ventricular pacing; Ventricular pacing; Pacing algorithms; Sinus node disease; Atrioventricular block

Introduction
Several ICD and pacemaker studies suggest that frequent and unnecessary right ventricular pacing may have adverse long-term effects, including reduced efficacy of myocardial contraction1,2 and an increased risk of atrial fibrillation and heart failure hospitalization.3–5 Moreover, the Dual Chamber and VVI Implantable Defibrillator (DAVID) trial showed that ventricular pacing more than 40% of time is associated with a higher risk of hospitalization for heart failure or death.6 In addition, the Mode Selection Trial (MOST) showed that every 10% increase in cumulative percent ventricular pacing (Cum%VP) (up to 40%), was associated with a 54% relative increase in risk of hospitalization for heart failure,4 stressing the importance of reducing unnecessary ventricular pacing as much as possible in each patient.

For this reason, new pacing algorithms have been developed, with the aim of reducing right ventricular pacing. The MVP® algorithm is designed to preserve intrinsic AV conduction and ventricular activation by automatically switching between AAI/R and DDD/R. MVP has been demonstrated to significantly reduce the amount of unnecessary right ventricular pacing in ICD patients7 and in patients with symptomatic bradycardia.8

The principal study aim was to determine the burden of ventricular pacing in a standard pacemaker population, programmed to MVP mode. Secondly, patient groups in which it is possible to achieve a Cum%VP ≤ 40% were defined.

Methods
Study design
The Adapta clinical study was a prospective, non-randomized, multicentre clinical study, evaluating the safety and clinical performance of the dual-chamber Adapta™ IPG (Model ADDR01, Medtronic). The study was set out to assess the percent of ventricular pacing in
a standard pacemaker population programmed to MVP and to assess for which patients it is possible to achieve a Cum%VP < 40%.

The study was conducted in seven European centres. Prior to enrolling any patients, each participating institution obtained local ethics committee approval. All patients gave written informed consent. The study complied with the Declaration of Helsinki.

Data were collected during implant, pre-hospital discharge (0–4 days post implant), 1-month post implant (25–45 days post implant), and 3-month post implant (77–122 days post implant), using case report forms and device interrogation save-to-disk files. At these visits, conduction status was evaluated during temporary atrial pacing at 90 bpm.

Patient population

Patients who had a Class I or II indication for implantation of a dual chamber pacemaker and who were geographically stable and available for follow-up at the study centre were invited to participate in the Adapta clinical study. Patients were excluded from enrolment if they had a mechanical tricuspid valve, a life expectancy less than 2 years, a Class III indication for permanent pacing, lead integrity problems (unless leads were being replaced), were enrolled (or intended to participate) in another clinical trial or met an exclusion criteria required by local law.

MVP algorithm

The MVP mode provides atrial-based pacing (AAI/R) with ventricular backup. If AV conduction fails for two out of four A–A intervals, MVP switches to DDD/R mode. Periodic checks for AV conduction in DDD/R mode occur. If AV conduction resumes, MVP switches back to AAI/R mode. During atrial tachyarrhythmia, MVP operates in the DDI/R mode. A more detailed explanation of MVP has been published by Sweeney et al.7 and Gillis et al.8

Device programming

The study was conducted in two phases. Patients enrolled in Phase I (n = 69) were required to have MVP programmed ON immediately after implant. Furthermore, patients with a history of atrial arrhythmias were required to have Atrial Preference Pacing (APP) programmed ON. APP provides consistent atrial pacing at a rate slightly faster than the intrinsic atrial rate. All other device programming was up to the physicians’ discretion.

For patients enrolled in Phase II (n = 54) device programming of all parameters was based on TherapyGuide (a patient-condition driven programming algorithm) recommendations, or not if medically justified.

Statistical analysis

The Adapta clinical study was a prospective, non-randomized, multicentre clinical study. Baseline demographic data are summarized as mean ± SD for quantitative variables and as counts (percentages) for categorical data. Medication data were compared among the sinus node disease (SND), AVB, and ‘Other’ subgroups, except for Calcium channel blockers (SND 27%; AVB 10%; Other 0%, P = 0.0493). When compared with the 1-month post implant medication usage, there was a difference in β-blocker use for the total group (18% at baseline, 32% at 1-month, P < 0.05).

For 82 patients (out of the 107 eligible patients), an AV conduction test was performed at 90 bpm at the PHD visit. No AV conduction test was performed if the patient had documented third degree AV block (n = 7) or was in atrial fibrillation (n = 8). For 10 patients, the test was not performed for other reasons (study deviations).

Results

Study population

Between 30 May 2005 and 22 July 2005, 123 patients were enrolled in the study, of which 120 were implanted with the Adapta IPG. One patient did not meet inclusion criteria; one patient withdrew participation after informed consent form was signed; and a third patient was not yet implanted at the time of enrolment completion. The mean follow-up duration for all 120 implanted patients was 76.3 days with a range of 26–119 days; the cumulative follow-up was 301 months in all patients. At the time data collection was stopped, several patients did not have their 3-month post implant visit yet. Therefore, we only present data up to the 1-month post implant visit.

Of the 120 implanted patients, 107 patients had MVP programmed ON and %VP data available (66 patients in Phase I and 41 patients in Phase II). Of the 68 patients implanted in Phase I, 2 were not programmed to MVP (study deviations). Of the 52 patients implanted in Phase II, 9 were not programmed to MVP [physicians discretion, most likely due to third degree AV block (AVB)], and 2 save-to-disk files were missing. APP was programmed ON in 62% of Phase I patients, and in 30% of Phase II patients.

These 107 patients were analysed to (i) assess the percent of ventricular pacing between PHD and the 1-month post implant visit, and (ii) to investigate for which patients it was possible to achieve Cum%VP < 40%.

Table 1 shows the characteristics for the 107 patients who were eligible for the ventricular pacing analysis between PHD and the 1-month post implant visit. Also medications at baseline are shown. There are no differences in medications among the sinus node disease (SND), AVB, and ‘Other’ subgroups, except for Calcium channel blockers (SND 27%; AVB 10%; Other 0%, P = 0.0493). When compared with the 1-month post implant medication usage, there was a difference in β-blocker use for the total group (18% at baseline, 32% at 1-month, P < 0.05).

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Percent ventricular pacing with MVP, by primary pacing indication

Table 2 shows the median Cum%VP at the 1-month post implant visit for all 107 patients, divided by primary pacing indication. The median Cum%VP for all patients was 3.9%. The median Cum%VP for patients with SND was 1.4% and for AVB patients 28.8%. Figure 1 shows the distribution of Cum%VP and Cum%AP for patients with SND and AVB.

Percent ventricular pacing with MVP, in AVB patients

The median Cum%VP divided for different types of patients with AVB is shown in Table 3. The median Cum%VP for patients with a medical history of first degree AVB was 8.6%. The median Cum%VP for patients with a medical history of second degree AVB was 6.6%. In addition, the median Cum%VP for patients with a medical history of third degree
AVB was 50.3% (11.6% in patients with episodic third degree AVB and 99.4% in patients with persistent third degree AVB).

**Cum%VP ≤ 40%**

Figure 2 shows the results for the Cum%VP ≤ 40% objective. A Cum%VP ≤ 40% was noticed in 72% of all 107 patients, in 86% of 59 SND patients, and in 50% of 42 AVB patients.

At the PHD visit, an AV conduction test was performed. A Cum%VP ≤ 40% was noticed in 92% of 65 patients with 1:1 AV conduction at PHD and in 24% of 17 patients without AV conduction at PHD.

Overall, 61% of patients had Cum%VP ≤ 10%, while 54% of patients had Cum%VP ≤ 5%, and 40% had Cum%VP ≤ 1%.

**Adverse events**

No adverse events related to MVP were reported during the entire follow-up period of 76.3 days with a range of 26–119 days. No patient died and no unanticipated serious adverse device effect occurred.

**Discussion**

In this study, we found that the median Cum%VP in unselected, consecutively enrolled patients with a conventional dual chamber pacemaker indication programmed to MVP mode at the 1-month post implant visit was 3.9%. In 54% of patients, Cum%VP was as low as ≤ 5%, and in 40% further diminished to ≤ 1%. In addition, 72% of patients achieved a Cum%VP ≤ 40%. Our results are in line with the recently published studies by Sweeney et al.\(^7,^{10}\) and Gillis et al.\(^8\), who showed a substantial reduction in percent ventricular pacing using the MVP mode, compared to the DDD/R mode. We observed that a low median Cum%VP can even be achieved in patients with AVB (8.6% and 6.6% in first and second degree AVB, respectively).

The MOST study\(^4\) showed that Cum%VP more than 40% of time was the cut point which significantly increased the risk of heart failure hospitalization. When ventricular pacing in DDD/R mode was ≥ 40%, for each 10% increase in ventricular pacing there was a 54% relative increase in risk for heart failure hospitalization, and when ventricular pacing was greater than 40% a patient’s relative risk for heart failure hospitalization remained elevated and constant. Therefore, in the present study, we focused on assessing for which patients in a standard bradycardia population it would be possible to achieve Cum%VP ≥ 40%. Our results showed that Cum%VP ≥ 40% occurred in 72% of all patients and in 86% of patients with SND. Our study shows that even in 50% of patients with AVB (8.6% and 6.6% in first and second degree AVB, respectively).

The MOST study\(^4\) also showed that the lowest rate of heart failure hospitalization occurred in patients who were paced ≤ 10% of time.\(^4\) In our study, 61% of patients are paced ≤ 10% in the MVP mode. Although these results suggest a beneficial prognosis for these patients, the clinical benefit of this effect of MVP needs to be proven and evaluated in a randomized outcome study.

Although a very low percent Cum%VP can be achieved in patients with SND as primary pacing indication, 14% of these patients show Cum%VP more than 40% of time.

### Table 1 Characteristics of the study population

<table>
<thead>
<tr>
<th>Primary pacing indication</th>
<th>Total (n = 107)</th>
<th>AVB (n = 42)</th>
<th>SND (n = 59)</th>
<th>Other (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>67 ± 14</td>
<td>63 ± 16</td>
<td>70 ± 12</td>
<td>67 ± 16</td>
</tr>
<tr>
<td>Male</td>
<td>57 (53%)</td>
<td>21 (50%)</td>
<td>33 (56%)</td>
<td>3 (50%)</td>
</tr>
<tr>
<td>NYHA class</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class I</td>
<td>17 (16%)</td>
<td>8 (19%)</td>
<td>7 (12%)</td>
<td>2 (33%)</td>
</tr>
<tr>
<td>Class II</td>
<td>29 (27%)</td>
<td>11 (26%)</td>
<td>16 (27%)</td>
<td>2 (33%)</td>
</tr>
<tr>
<td>Class III</td>
<td>9 (8%)</td>
<td>3 (7%)</td>
<td>6 (10%)</td>
<td>0</td>
</tr>
<tr>
<td>Class IV</td>
<td>1 (1%)</td>
<td>1 (2%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Does not meet NYHA</td>
<td>51 (48%)</td>
<td>19 (45%)</td>
<td>30 (51%)</td>
<td>2 (33%)</td>
</tr>
<tr>
<td>Prior IPG implant</td>
<td>22 (21%)</td>
<td>8 (19%)</td>
<td>12 (20%)</td>
<td>2 (33%)</td>
</tr>
</tbody>
</table>

### Table 2 Percent ventricular pacing in MVP mode, by primary pacing indication

<table>
<thead>
<tr>
<th>Primary pacing indication</th>
<th>n</th>
<th>Median Cum%VP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>107</td>
<td>3.9</td>
</tr>
<tr>
<td>SND</td>
<td>59</td>
<td>1.4</td>
</tr>
<tr>
<td>AVB</td>
<td>42</td>
<td>28.8</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>12.9</td>
</tr>
</tbody>
</table>
A possible explanation could be that these patients have intermittent AV block as well, which prevents reaching a low percent ventricular pacing in these patients. Similar observations were seen in the study by Sweeney et al.,7 where MVP mode in SND patients with intermittent or persistent AVB resulted in switches to DDD/R mode. The study showed that programming the mean PAV/SAV delay to 243/219 ms during DDD/R operation did not prevent ventricular pacing.

Another reason which stresses the importance of eliminating ventricular pacing as much as possible is that a recent study showed that bradycardia pacing might facilitate short–long–short cycle lengths, which might initiate ventricular tachycardia (VT) and ventricular fibrillation (VF). 11 Although the study showed that this pacing facilitated onset of VT/VF episodes occurs in all pacing modes (DDD/R, VVI/R, MVP), the occurrence in patients programmed to MVP was the lowest.

In the presence of hypokalemia or long QT syndrome, pause permitting pacemaker features in DDD/R or MVP have been associated with symptoms12 or Torsades des Pointes.13,14 In these patients, careful consideration should be given to pacemaker mode and lower rate programming.

No patients experienced Torsades des Pointes or symptoms due to non-physiologic AV intervals in this study.

**Limitations**

We only studied the effect of MVP on the burden of ventricular pacing. Clinical benefit and the effects of reduced ventricular pacing on symptoms and haemodynamics were not studied. However, it was recently shown that dual-chamber minimal ventricular pacing, when compared with conventional dual-chamber pacing, reduces the absolute risk of persistent atrial fibrillation by 4.8% in patients with SND.15 A second limitation of our study is that we only investigated the effect on percent of ventricular pacing over a period of 1-month. Therefore, no conclusion can be drawn for the longer term, although Gillis et al.15 showed that the reduced percent ventricular pacing during MVP was sustained over longer term follow-up.

Furthermore, it is difficult to relate the observed percent AP to MVP, since the atrial-overdrive feature APP was required to be programmed ON in Phase I patients with a history of atrial arrhythmias. This resulted in APP being

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**Table 3** Percent ventricular pacing in MVP mode in AV block patients

<table>
<thead>
<tr>
<th>AVB status</th>
<th>n</th>
<th>Median Cum%VP</th>
</tr>
</thead>
<tbody>
<tr>
<td>First degree AVB</td>
<td>6</td>
<td>8.6</td>
</tr>
<tr>
<td>Second degree AVB</td>
<td>23</td>
<td>6.6</td>
</tr>
<tr>
<td>Third degree AVB</td>
<td>26</td>
<td>50.3</td>
</tr>
<tr>
<td>Episodic</td>
<td>19</td>
<td>11.6</td>
</tr>
<tr>
<td>Persistent</td>
<td>7</td>
<td>99.4</td>
</tr>
</tbody>
</table>

AVB status was derived from the Medical History of patients. *Not mutually exclusive.

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**Figure 1** Distribution of Cum%VP and Cum%AP in sinus node disease and AV block patients.

**Figure 2** Percentage of patients with Cum%VP <40%.
ON in 62% of Phase I patients, and in 30% of Phase II patients (in Phase II, this decision was up to the physicians discretion). Finally, the Adapta IPG is based on the FDA approved Kappa® and EnPulse® devices, and the new features are either functionally equivalent to those in already regulatory-body-approved products (MVP and Atrial Preference Pacing), or do not represent a safety hazard (Therapy-Guide and Rate Response User Interface). Therefore, to evaluate the safety and performance of the Adapta IPG, a control group (e.g. DDD/R) was not needed. For this reason, in this study, we can only report descriptive values of percent ventricular pacing, and no reduction can be demonstrated. However, the reported low values of percent ventricular pacing with MVP in our population are in line with previous studies.7,8

Conclusion

In conclusion, the MVP mode is able to achieve a low percent of ventricular pacing in a standard pacemaker population consisting of SND and AVB patients. In addition, MVP resulted in a Cum%VP < 40% in 72% of patients after 1-month. Clinical benefits of these effects need to be investigated.

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Conflict of interest. This study was sponsored by Medtronic Inc. All authors were participants/investigators in this study. J.B. received honoraria from Medtronic, St Jude Medical, Biotronik, and Boston Scientific for speaking engagements; C.W. is a Statistician for and holds stock in Medtronic; M.H. is a Clinical Research Specialist for Medtronic.

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References


