Single-chamber Cardiac Pacing with Two Forms of Respiration-controlled Rate-responsive Pacemaker*

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Ventilatory changes correlate with the heart rate response during exercise, and such changes have been used to determine an appropriate chronotropic response in the Biorate (RDP3 and MB-1) and Meta pacemakers, both of which use a thoracic impedance measurement principle. Ten patients with the Biorate and 11 patients with the Meta were studied. In both groups, significant rate response and improvement in exercise duration compared with fixed rate ventricular pacing were achieved during symptom-limited treadmill exercise tests, with good correlations between the pacing rate and estimated oxygen consumption. Motion artefacts affected the measured impedance of both pacemakers, with rate response occurring during arm movements in the absence of respiratory activity. This observation suggested that both pacemakers have the potential of activity sensing. The earlier version of the Biorate (RDP3) was limited by myopotential interference, and erosion of the auxiliary lead can be problematic in some patients.

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In patients with complete heart block with normal sinoatrial function, dual chamber pacing can maintain atrioventricular synchrony and provide for chronotropic response during exercise. However, its use can be limited in patients with sinoatrial disease, which has been reported to be associated with complete heart block in 30 to 40 percent of patients.1,2 Also, atrial sensing can predispose to the development of pacemaker-mediated tachycardia.3 Although the use of a long atrial refractory period can reduce this problem, this leads to a limitation of the upper rate response of the pacemaker. Thus, in a subset of patients, dual chamber pacing may not be the ideal pacing method.

Karlof6 has shown that during maximal exercise, cardiac output is mainly determined by an appropriate chronotropic response rather than by maintaining atrioventricular synchrony. This was subsequently substantiated by comparing the exercise tolerance with dual chamber pacing and rate-paced ventricular pacing using the method of external triggering of implanted pacemakers.5,6 In patients with already elevated left ventricular diastolic pressure, the atrial contribution to cardiac output becomes less important.7 Thus, single chamber cardiac pacing, which automatically adjusts the pacing rate during exercise, is an alternative method of physiologic pacing in such patients. The important determinant is a sensor of physiologic demand. Pacemakers sensing the QT interval8 and body vibrations during exercise9-11 already have been introduced into clinical use.

Ventilatory response during exercise parallels work-load up to 70 percent of maximum oxygen consumption.10-12 Above this anaerobic threshold,10,17 accumulation of lactic acid increases the minute ventilation at a rate in excess of oxygen uptake. The linear relationship between heart rate and oxygen consumption allows its changes during exercise to be used for determining the appropriate heart rate during submaximal exercise. Physiologic control of pacing rate by measuring respiratory change has been suggested.18-21 Recent technologic advances have made the sensing of respiration possible in two forms of the respiration-sensing, rate-responsive pacemaker. In this study, the chronotropic responses of both forms of respiratory-sensing pacemaker were compared, and the complications encountered were reported. Although the function of the Biorate pacemaker has been reported,22 critical analysis of the rate-responsive behavior and the observation of the associated complications have not been reported. The Meta pacemaker only recently has been available for clinical trial. In this article, we present our initial experience with this form of rate-responsive pacing.

Pacemaker Description

The Biorate Pacemaker

Rossi et al22 have shown that changes in the respiratory rate correlate significantly with changes in heart rate during exercise. Furthermore, the correlation is reported to hold in patients with restrictive or obstructive airway disease.23 The Biorate pacemakers (RDP3 and MB-1 [Biotec, Bologna, Italy]) sense the respiratory rate using an auxiliary electrode placed about 8 to 10 cm from the pacemaker casing (Fig 1). Impedance

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is measured with a bipolar electrode system with the pacemaker acting as the active electrode and the tip of the auxiliary lead as the passive electrode. The depth of respiration considered as a breathing rate is determined by a programmable respiratory level, and the detected respiratory rate is converted to a change in pacing rate by a slope of rate response (Table 1). The MB-1 pacemaker is a newer version of the RDF3 with programmable sensitivities and some telemetry functions.

**The Meta Pacemaker**

In the Meta pacemaker (Teleconics-Cordis, Englewood, CO), minute ventilation is estimated from changes in intracardiac impedance. This is achieved using a tripolar electrode configuration comprised of a standard bipolar electrode and the pacemaker casing. The source of electric current for impedance measurement consists of the ring electrode and pacemaker casing, and impedance is measured between the tip of the pacing electrode and the pacemaker casing (Fig 1). Low-pass filtering to detect impedance changes below 60 Hz is used to reduce the influence of stroke volume on the impedance measurement. When programmed to the minute ventilation adaptive mode, the pacemaker registers minute ventilation throughout a prolonged period (over 1 h) to form a stable baseline minute ventilation against which a change during exercise is compared. A slope of rate response can then be programmed when the pacemaker is programmed in the rate-responsive mode (Table 1).

It is the aim of this study to assess the clinical benefits and chronotropic responses of these two forms of respiratory-sensing pacemakers. The evaluation included standard exercise tests and activities simulating ordinary daily life.

**Material and Methods**

**Patients**

Ten patients with a mean age of 59 ± 2 years received Biorate pacemakers (seven, RDF3 and three, MB-1). All had complete heart block with atrial arrhythmias, and in eight of these patients the heart block was induced therapeutically with His bundle/atrioventricular nodal ablation. Two patients subsequently had their pacemakers explanted (one due to erosion of auxiliary lead and one due to symptomatic myopotential interference) and received Meta pacemakers.

Meta pacemakers were implanted in 11 patients. Their mean age was 59 ± 4 years. Ten had complete heart block with atrial arrhythmias; in four, this was induced by His bundle/atrioventricular node ablation and in two, this occurred after cardiac surgery. One patient had sinoatrial disease. In both groups of patients, the electrode was implanted in the right ventricle.

Single-chamber rate-responsive pacing was considered in these patients in preference to dual-chamber pacing because of associated atrial arrhythmias. No patient had clinical evidence of pulmonary disease. All had normal lung fields on chest radiographs. Informed consent was obtained from all patients.

**Pacemaker Programming**

In both groups of patients, the pacemaker was programmed to achieve a pacing rate of about 100 beats per minute at the end of stage 1 of the Bruce protocol. The lower rate was set at 65 to 75
beats per minute and the upper rate was programmed at 145 to 150
beats per minute.

Protocol

1. Symptom-limited treadmill exercise test.
   At one month after pacemaker implantation, two maximal
   exercise tests, performed in the constant rate (VVI) mode and
   the rate-responsive mode, were done using the Bruce protocol
   in random order. The tests were separated by at least 2 h. A
   technician determined the randomization and monitored the
   electrocardiogram, and the blood pressure was monitored by
   a research nurse. The physician supervising the test encouraged
   the patient to maximum exercise. He also received information
   about the patients’ blood pressure and any arrhythmias during
   exercise and determined the endpoint of the test. Both he and
   the patient were not informed of the pacing mode. The exercise
duration in each pacing mode was measured. In addition, the
oxygen consumption at each minute of exercise was estimated
(using the sex and weight of each patient) according to the
published results by Bruce et al. Three patients with the
Biorate pacemaker were excluded from this test for administra-
tive reasons (two patients) and erosion of the auxiliary lead (one
patient). Two patients with the Meta pacemaker also were
excluded because maximum exercise was limited by osteoar-
thritis (one patient) and angina pectoris (one patient).

2. Brief activities performed included the following:
   a. Walking on the treadmill at 0 percent gradient using two
different speeds (1.2 and 2.5 miles per hour) for 3 min each.
   b. Walking on the treadmill at two different gradients (0 and
      15 percent) at 2.5 miles per hour for 3 min each.

Figure 2. Exercise durations of patients with the Biorate and Meta pacemakers during symptom-limited
treadmill exercise using the Bruce protocol. Each error bar refers to one standard error of the mean.

Figure 3. Correlations of pacing rate with estimated oxygen consumption during treadmill exercise.
Oxygen consumption was calculated from standard values published by Bruce et al. Satisfactory
correlations were achieved with both kinds of pacemaker.
c. The test using the treadmill setting of 2.5 miles per hour at 15 percent gradient was repeated while the subject continued talking for the whole 3 min.

d. Ascending and then descending four flights of stairs.

3. Effects of respiratory interference included the following:
   a. Hyperventilation for 1 min.
   b. Continuous coughing for 1 min.
   c. Continuous talking during brief treadmill exercise as detailed previously.

4. Effects of arm swinging.
   While holding the breath, the arm on the side of the pacemaker was swung at 10 to 60 (at 10 times per minute increment) times per minute. The rate of swinging was governed by a metronome. The pacing rate achieved at the end of 45 s was recorded.

5. Myopotential interference was assessed by pressing the palms together.

6. Ambulatory recordings were performed in all patients in the rate-responsive mode using a Reynolds Tracker (Reynolds Medical Limited, Sunnyvale, CA). Rate responses observed were compared with the activities of the patient recorded with a detailed diary.

**Statistics**

Students paired t tests were used to compare exercise durations and pacing rates where appropriate. Two-way analysis of variance was applied to the pacing rates attained during arm swinging at different frequencies. Correlations were performed between the pacing rate and the estimated oxygen consumption and probability values assessed from standard tables. Results were expressed as mean ± standard error of mean. A probability value of less than 0.05 was considered statistically significant.

**RESULTS**

**Symptom-Limited Treadmill Exercise**

The exercise durations during maximal treadmill exercise tests are summarized in Figure 2. In all patients, exercise was terminated because of breathlessness or fatigue. Significant improvement in exercise duration was achieved in both groups of patients. In patients with Biorate, the improvement was from 346 ± 43 s (VVI mode) to 448 ± 44 s (rate-responsive mode) (p<0.01; 29 percent improvement). In patients with Meta, an improvement from 440 ± 41 s to 581 ± 61 s was achieved (p<0.001; 32 percent improvement).

When the estimated oxygen consumption at each minute of the treadmill exercise was compared with the pacing rate, significant correlations between the pacing rate and oxygen consumption were noted (Fig 3). The correlations were 0.81 (p<0.001) for the Biorate and 0.83 (p<0.001) for the Meta.

The rate responses during brief treadmill exercise at different speeds and gradients are shown in Figure 4. In both groups of patients, the pacing rates increased as the patients walked at faster speeds or higher gradients. Maximum pacing rates were reached during all these activities within 2 min from the onset of exercise. Ascending and descending stairs also resulted in proportional rate response (Table 2), although the maximum pacing rate was only reached after these

![Pacing rate (bpm)](image)

**FIGURE 4.** Pacing rates achieved during brief walking activities. Although the magnitude of response differed between the two pacemakers during a similar activity, the direction of rate response was appropriate to the change in workload.

brief activities. For ascending stairs, the time delay for the Biorate and Meta pacemakers was 44 ± 16 s and 68 ± 9 s, respectively, and the delay was 20 ± 15 s and 8 ± 4 s respectively when descending the stairs. The time delay was not statistically different between these two pacemakers.

**Effects of Respiratory Interference and Arm Movement**

Hyperventilation and coughing increased the pacing rates of both pacemakers (Table 2). There was no significant effect from speech in patients with the Biorate pacemaker (Table 2). On the other hand, the pacing rate response to the same exercise was significantly reduced during speech in the Meta pacemaker (Table 2). An increase in pacing rate proportional to the frequency of arm swinging was seen in patients with the Biorate. In patients with the Meta, a maximal pacing rate response occurred with the arm swinging at 30 cycles per minute.
Table 2—Rate Responses During Stair Climbing and Effect of Voluntary Interference on Pacing Rates of Biorate and Meta Pacemaker*

<table>
<thead>
<tr>
<th>Activity</th>
<th>Biorate</th>
<th>Meta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stair climbing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ascending</td>
<td>100 ± 6</td>
<td>104 ± 7</td>
</tr>
<tr>
<td>Descending</td>
<td>88 ± 5</td>
<td>77 ± 2</td>
</tr>
<tr>
<td>Hyperventilation</td>
<td>110 ± 4</td>
<td>111 ± 10</td>
</tr>
<tr>
<td>Coughing</td>
<td>4 ± 4</td>
<td>90 ± 5</td>
</tr>
<tr>
<td>Exercise (2.5 miles per hour, 15%) Performed in silence</td>
<td>122 ± 9</td>
<td>139 ± 6</td>
</tr>
<tr>
<td>Exercise (2.5 miles per hour, 15%) Performed while talking</td>
<td>125 ± 6</td>
<td>NS 96 ± 7</td>
</tr>
<tr>
<td>Arm swinging (times per minute)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>72 ± 2</td>
<td>71 ± 1</td>
</tr>
<tr>
<td>20</td>
<td>80 ± 7</td>
<td>86 ± 6</td>
</tr>
<tr>
<td>30</td>
<td>88 ± 13</td>
<td>p &lt; 0.01 103 ± 12</td>
</tr>
<tr>
<td>40</td>
<td>100 ± 12</td>
<td>90 ± 13</td>
</tr>
<tr>
<td>50</td>
<td>104 ± 13</td>
<td>87 ± 11</td>
</tr>
<tr>
<td>60</td>
<td>113 ± 15</td>
<td>76 ± 4</td>
</tr>
</tbody>
</table>

*Pacing rates expressed in beats per minute.

Effects of Myopotential Interference

All patients with RDP3 manifested myopotential interference of >5 s when the palms were pressed together. At nominal settings, no patient with MBI or Meta had myopotential interference.

Holter Recording

Rate responses were found to be related to the levels of activity. No episode of inappropriate rate acceleration was encountered in either group of patients.

Complications Observed on Follow-up

Erosion of the auxiliary lead occurred in two patients with the Biorate pacemakers, one immediately after implantation and the other after one year (Fig 5). Symptomatic myopotential interference was found in three patients. Since the RDP3 pacemaker had no programmable sensitivity, an operative approach was used. Attempts to use an insulation boot over the pacemaker did not prevent myopotential interference. All were replaced with bipolar pacemakers.

Complications observed with Meta were related to implantation. In two patients, a hematoma developed at the site of implantation but subsided spontaneously. In one patient, lead dislodgement after implantation required repositioning.

DISCUSSION

This study demonstrates that improvement in exercise capacity can be achieved with respiration-sensing rate-responsive pacing. Both respiratory rate sensing and minute ventilation sensing resulted in pacing rates which correlated significantly with the estimated oxygen consumption. Although oxygen consumption was estimated rather than directly measured, it served as a useful index of the level of exertion. In the patient with angina, the effect of rate response on the anginal threshold was not investigated in this study. However, previous studies on patients with dual chamber pacemakers have documented that rate response in the dual-chamber pacing mode during exercise did not increase the severity of angina compared with exercise in the VVI mode.

In the two patients in whom Meta pacemaker was used as a replacement unit, there was an improvement in exercise capacity when symptom-limited exercise was performed with the Meta pacemaker (Table 3). Both patients had used the Biorate pacemaker for one year prior to developing problems. Although the maximum pacing rate achieved in both patients using

Table 3—Results of Symptom-Limited Exercise Tests (Bruce Protocol) of Two Patients with Biorate Pacemakers*

<table>
<thead>
<tr>
<th>Mode</th>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum pacing rate (beats per minute)</td>
<td>75</td>
<td>70</td>
</tr>
<tr>
<td>Exercise duration (seconds)</td>
<td>530</td>
<td>630</td>
</tr>
<tr>
<td>Rate-responsive Mode</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pacing rate at stage 1 (beats per minute)</td>
<td>92</td>
<td>95</td>
</tr>
<tr>
<td>Maximum pacing rate, (beats per minute)</td>
<td>129</td>
<td>150</td>
</tr>
<tr>
<td>Exercise duration, (seconds)</td>
<td>600</td>
<td>900</td>
</tr>
</tbody>
</table>

*These two patients subsequently received a Meta pacemaker as a replacement unit. The two tests were separated by one year in each patient.

Figure 5. Erosion of auxiliary lead in a patient with RDP3.
the Meta pacemaker was higher than that achieved when originally exercised with the Biorate one year before, better rate responses seemed unlikely to be the sole cause of the improvement because the exercise duration in the VVI mode also improved. A training effect could not be excluded, although the tests had been separated by one year and the patients had been familiarized with the treadmill prior to formal testing. Long-term improvement in physical capacity by chronic rate-responsive pacing could be the factor responsible.

Few patients perform continuous treadmill exercise in everyday life. During brief activities (walking and stair climbing), the direction of rate response was found to be appropriate to the work load. The magnitude of rate responses to these activities between the two groups was not directly compared since this could be affected by different programmed settings and the pacemaker algorithm employed in these pacemakers.

In both groups of patients, a significant delay in the onset of rate response was noted during brief activities such as climbing stairs. Theoretically, at the onset of exercise, an immediate increase in ventilation occurs which is thought to be neurally mediated. The extent of this ventilatory change is not related to the level of exercise. At the pacemaker settings used, a significant delay in rate responses occurred during brief activities. This may occur because pulmonary changes were too small to be detected or related to an in-built delay in the onset of rate response to a sensed respiratory signal. There was a trend for a faster rate response in the Biorate pacemaker, presumably because of a higher propensity of this pacemaker to sense activity, as noted later on. However, in both pacemakers, the delay in rate response was unlikely to be a major limitation because the maximum pacing rate was usually reached within 2 min from the onset of an exercise.

Respiration is affected by requirements which may have no relationship to cardiac output. Thus, hyperventilation and coughing erroneously increased the pacing rate of both pacemakers. These, however, reflected usual situations and excessive rate acceleration was not encountered. Attenuation of rate response during speech was seen in patients with the Meta pacemaker. This may be related to a higher propensity of the Biorate pacemaker to sense activity which is not affected by speech.

Arm swinging is an accompaniment of many activities, such as walking. Both pacemakers responded to arm swinging during apnea. We and others have observed that arm swinging can alter the rate response of the Biorate pacemaker, presumably due to movement artefact-induced impedance changes. The bipolar electrode configuration used in the Biorate pacemaker to measure impedance was particularly prone to this interference. In addition, the rate response was related to the frequency of arm swinging (which was interpreted as a respiratory rate). Modulation of the rate response of the Meta pacemaker also can occur during arm swinging. However, in this pacemaker, the use of a tripolar electrode configuration and the presence of a low-band pass filter (set at 60 Hz) have reduced this form of interference. As each arm swing causes the pacemaker to be displaced twice in its pocket, arm swinging faster than 30 times per minute will not be sensed by this pacemaker because of this filter. One would expect arm swinging would lead to an increase in heart rate in normal individuals under similar conditions and this form of activity sensing was probably advantageous in improving the speed and magnitude of rate response. The ability to sense motion differed among the patients, since this was related to the susceptibility of the pacemaker to be displaced by arm movement.

Heart rate during exercise has been reported to correlate better with minute ventilation than respiratory rate. This is mainly due to the relatively slow change of respiratory rate at low levels of activity, when minute ventilation is mainly determined by a change in tidal volume. However, the levels of correlation between the pacing rate and estimated oxygen consumption achieved in this study were similar (0.81 with Biorate compared with 0.83 with Meta). This may be attributed to the more pronounced activity-sensing property of the Biorate pacemaker which improved its rate response at low levels of activity.

Although both forms of respiratory sensing are feasible principles for definition of the pacing rate during exercise, the relative reliability and safety of these pacemakers need to be mentioned. Technical problems have limited the earlier version (RDP3) of the Biorate pacemaker. In this pacemaker there was no programmable sensitivity, and myopotential interference was a major problem encountered in this study. It is of interest to note that although arm swinging movement can lead to a rate response of this pacemaker, isometric arm exercise reduces its pacing rate because of myopotential interference. Bipolar sensing in the Meta pacemaker has reduced the problem of myopotential interference.

The use of an auxiliary lead for respiratory sensing in the Biorate pacemaker can be problematic. Although the implantation of this lead is not complicated, there is the potential problem of lead erosion in some patients, and intrathoracic impedance in the Meta is a clear advantage.

**Conclusion**

It is concluded that the two respiratory sensing pacemakers confer hemodynamic benefits to patients with bradycardias. Both pacing algorithms showed good correlations with estimated oxygen consumption,
and the rate responses are appropriate to ordinary daily activities. Both pacemakers have the potential for activity sensing which improves their rate response, although this is more obvious with the Biorate pacemaker. Myopotential interference is a significant problem with the RDF3, and the requirement of an auxiliary lead can be problematic in some patients.

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Single-chamber Cardiac Pacing (Lau, Ward, Camm)