Pacemaker sensitivity to 50 Hz noise voltages

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Aims

European standards specify that pacemakers (PM) should be resistant to electromagnetic interference (EMI) up to an upper borderline voltage as a function of frequency. Electromagnetic interference fields should either remain below this upper borderline voltage level or be identified and isolated from the general population. Physicians caring for PM patients need to be aware of potential problems relating to EMI. For example, sensitivity should be programmed to avoid sensing EMI below the recommended borderline voltage level. The susceptibility of a pacemaker (PM) to 50 Hz noise is an important parameter of EMI and depends on the programmed sensitivity [sensitivity setting (SS)]. We studied SS and 50 Hz noise thresholds in a large population and determined the borderline SS, defined as the SS below which 50 Hz noise was sensed. Our results should be taken into consideration in programming the SS to protect patients from the adverse effects of EMI.

Methods and results

Measurements were performed on 189 PMs explanted after death. All PMs studied were implanted in 1998 or later. Sensitivity setting and sensing configuration (unipolar or bipolar) were left as programmed during lifetime. The ventricular SS and 50 Hz noise thresholds were measured according to the European pacemaker standard. The signal-to-noise ratios (S/N) were derived from the heart test and noise test signal thresholds. The S/N for pulsed 50 Hz noise of five manufacturers tested ranged from 0.435 to 0.59. The S/N for 50 Hz continuous noise for four manufactures other than Medtronic was higher, ranging from 0.458 to 0.623. No PM showed a ratio of 1 or better. Medtronic PMs reacted differently to 50 Hz continuous noise than the other brands. In 24 Medtronic PMs, the continuous noise threshold was evaluated with two heart test signal amplitudes: either 10 mV or threshold level. In tests at threshold amplitudes, voltages between 0.1 and 0.85 mV elicited interference proving that Medtronic PM reacted extremely sensitively to noise. At 10 mV heart test amplitude, the noise threshold was inversely proportional to the SS, i.e. higher SS resulted in lower noise thresholds. Noise immunity increases with increasing heart test signal amplitude.

Conclusion

All tested PMs reacted to pulsed 50 Hz waves as if they were heart signals and were inhibited. Continuous noise above noise threshold evoked asynchronous pacing at noise rate. All PMs had an S/N ratio < 1, indicating that the heart signals were amplified less than noise. The European Standard requires that unipolarly sensing PMs tolerate noise up to 2 mV. However, an SS of 2 mV does not guarantee a noise tolerance of 2 mV. In order to fulfil this requirement, SS in the majority of PMs must be programmed > 2 mV. In Medtronic PMs, the continuous noise threshold is paradoxical as it is higher with decreasing SS. As a good compromise in Medtronic PMs, SS should be ~ 3 mV to guarantee sufficient protection from pulsed and continuous noise, assuming ventricular heart signals of 10 mV or more.

Keywords

Cardiac pacemaker • Electromagnetic interference • Ventricular sensitivity setting • Signal-to-noise ratio • Noise immunity • Medtronic noise reaction

Introduction

Physicians assessing the potential for electromagnetic interference (EMI) with pacemakers (PM) usually consult tables listing EMI sources, potential for interference with PMs, and distance from EMI source regarded as safe to prevent EMI. This approach has three disadvantages: (i) the conditions under which the parameters are determined are undefined, (ii) not all EMI sources are listed, and (iii) the parameters may be obsolete. For example, the recommendation of PM manufacturers to maintain a distance of 15 cm...
between PMs and mobile phones is obsolete since modern PMs are all equipped with effective feed-through capacitors and the transmitting power of the mobile phones has been drastically reduced. Safety from EMI can be ensured by adherence to the recommended European standard. According to this standard, PM manufacturers should design their products to be resistant to EMI up to an upper voltage level defined by the standard as a function of frequency. Those responsible for creating EMI fields should ensure that voltages are below the standard recommended level or they should protect patients using fences and warnings. Adherence to the standard cannot prevent situations where patients touch defective electrical appliances or enter fields of older equipment. In addition, the programming physician must be aware of EMI and program sensitivity accordingly. The results of our investigation of susceptibility of PMs to interference should assist the physician in programming safe sensitivity settings (SS).

Electromagnetic interference in PMs is defined as ‘the PM is influenced by electromagnetic fields or currents so that the PM emits stimuli, though there is sufficient spontaneous activity, or inhibits stimuli, though there is a lack of spontaneous activity’. Electromagnetic interference can cause life-threatening PM malfunction if it affects the ventricular channel. If continuous 50 Hz voltages influence only the atrial channel, 97.2% of 107 DDD devices investigated switched to the VVI mode and 2.8% to the DOO mode. Pacing at the upper rate limit was not observed. Thus, we tested only ventricular systems in the present study (VVI or ventricular channel of DDD or VDD systems).

The European standard EN 45502-2-1

The European Standard EN 45502-2-1: 2003 with the title ‘Active implantable medical devices—Part 2-1: Particular requirements for active implantable medical devices intended to treat bradycardia (cardiac pacemakers)’ was prepared by the Working Group on Active Implantable Medical Devices of the ‘Comité Européen de Normalisation Electrotechnique’ (CENELEC) and came into effect in 2003. Clause 27 addresses the topic ‘Protection of the active implantable medical device from electromagnetic non-ionising radiation’ in which the requirements and test methods are stated. Subclause 27.5.1 requires the upper level of induced voltages in the low-frequency range between 16 Hz (frequency of railway systems in some European countries) and 1 kHz to be 2 mV in the unipolar and 0.3 mV in the bipolar mode. Test methods and test signals simulating heart signals for sensing threshold measurements are also described in Clause 6 of this standard.

Subclause 28.22.2 of this standard is of special interest for implanting or programming physicians. It states ‘If the implantable pulse generator permits settings more sensitive than those warranted as complying with the tests in Subclause 27.5, the manufacturer shall provide a warning that these settings may cause the implantable pulse generator to be more susceptible to electromagnetic interference, and that patients requiring such settings should be under medical direction.’ Thus, it is the responsibility of the physician to programme the SS of a PM so that it is resistant up to the recommended upper level of EMI. Otherwise, the physician is responsible for a possible malfunction due to EMI caused by a device programmed to be too sensitive. We demonstrate that it is not self-evident that programming the SS to 2 mV guarantees uninfluenced behaviour of the device up to 2 mV for 50 Hz sinusoidal waves.

**Material**

Between July 2001 and November 2004, we investigated the implanted PM system of 878 deceased PM patients in situ and determined whether the PM was providing a regular stimulation pattern. The presence of a pacing pulse was measured from the body surface. The PMs were then explanted and tested in the laboratory with respect to their function and programmed parameters.

Of the total population of 878 PMs, 254 PMs existed for which the implantation date was known to be 1998 or later. Of these, 189 were functioning and available (189/878 = 21.5%) so that noise measurements could be carried out on a relatively large population. There were five manufacturers of the tested PMs: Biotronik (BI), Guidant (GU), Medtronic (MD), St Jude Medical (SJ), and Vitatron (VI). All PMs were left as they were programmed during lifetime with respect to SS and sensing configuration (unipolar or bipolar).

**Methods**

**Evaluation of the sensitivity setting**

In all PMs the ventricular SS was measured in accordance with the test method outlined in the European Pacemaker Standard in Clause 6. The standard defines as a heart signal surrogate a triangular test signal with a 2 ms downstroke and a 13 ms upstroke that should simulate intracardiac heart signals in the following called heart test signal (see Figure 6). The heart test signal, starting from a low value, was slowly increased in amplitude until consistent inhibition was reached [sensitivity threshold = sensitivity setting (SS)]. The measurements were performed at room temperature. Earlier experiments showed that measurement at room temperature as compared with body temperature was equivalent for PM. Because not all PM manufacturers use the heart test signal as specified in the European Standard, the measured thresholds of sensitivity could differ from the SS displayed on the manufacturer’s programmer.

In Subclause 27.4 of the standard it is said that, ‘the implantable pulse generator should be set in a synchronised mode by a signal generator whose amplitude should be set at twice the value that just synchronises the implantable pulse generator under test’. We, however, deviated from this instruction because it is hard to understand physiologically that the amplitudes of ventricular heart signals should depend on SS. Our measurements have shown the amplitude of the ventricular heart signal to be ~10 mV. Thus, we chose a heart test signal of 10 mV for all sensitivity measurements if not stated otherwise.

**Measuring the noise threshold**

We chose 50 Hz voltages as a ‘noise test signal’ for two reasons: (i) PMs are most sensitive to 50 Hz signals. If a PM is uninfluenced by 50 Hz noise up to 2 mV, the PM is also uninfluenced for all other frequencies in the low-frequency range up to 1 kHz. (ii) 50 Hz noise is the most frequent interference source in Europe due to power lines, household appliances, and equipment in industry. The 50 Hz interference voltages will be called ‘noise’ or ‘noise test signal’ in the following.
**50 Hz noise, pulsed waves**
Pulsed 50 Hz packages of 100 ms duration (five full waves) and a 600 ms pause, according to the standard, were slowly increased in amplitude until continuous inhibition was observed.

**50 Hz noise, continuous waves**
All PMs were inhibited with a heart test signal whose amplitude was, as outlined above, 10 mV for all sensitivity measurements if not stated otherwise. Noise thresholds are normally the same whether the heart test signal is just above the sensing threshold or ten times higher. The 50 Hz continuous waves were slowly increased in amplitude until the PM paced asynchronously, indicating its noise mode. This criterion could not be applied to Medtronic PMs as they developed a reaction pattern depending on noise and heart test signal amplitude as well.

**Signal-to-noise ratio**
The signal-to-noise ratio (S/N) reflects the capability of a filter to distinguish a wanted signal from a noise signal. Without any filtering, this ratio must be 1 as all signals are equally attenuated or amplified by a circuit, be it a passive or an active filter. In order to determine this ratio, a wanted signal and a noise signal of equal amplitude are applied to the input of a circuit. We adjusted, however, the input signal such that the sensing threshold for both signals was reached. The quotient of both input signals at sensing threshold is the S/N (see Supplementary material online, Annex). The S/N is important to determine programming of an SS that ensures lack of interference from noise equal to or lower than a predetermined level, for example, 2 mV in the low-frequency range.

**Results**

**Pulsed and continuous interference thresholds**

*Figure 1* summarizes the interference thresholds in the form of a cumulative frequency distribution for all PMs except for Medtronic devices (for explanation see the following chapter on Medtronic PM reaction). This type of graphical presentation was chosen as it provides a good comparison of pulsed waves (PW) with continuous waves (CW). The graph depicts which percentage of a group will be influenced by a certain signal level, for instance 2 mV, and also which voltage signal causes a certain percentage, for example 50% (median value), of the group to react. The CW values of the red curve were, except in three cases out of 150, equal to or larger than the blue ones for PW. Four percent of each group showed a noise threshold of 2 mV or lower. The pulsed noise ranged between 1.4 and 8.2 mV, that for continuous noise of between 1.2 and 8.7 mV. Mean values were 3.21 and 3.34 mV, respectively.

**Signal-to-noise ratio for 50 Hz noise, pulsed waves**

Table 1 summarizes the results of pulsed noise interference for the five brands: Biotronik, Guidant, Medtronic, St. Jude Medical, and Vitatron. The PM possessed an S/N ratio of between 0.435 and 0.59. The relative standard deviation (SD) averaged over all brand was 6%, indicating that the filter characteristics, which are responsible for S/N, were intended by the manufacturer and were not by chance. The smallest S/N was 0.375, whereas the highest was 0.684.

**Signal-to-noise ratio for 50 Hz noise, continuous waves**

Table 2 summarizes the results of continuous noise interference for four brands: Biotronik, Guidant, St Jude Medical, and Vitatron. The S/N for CW was higher in all brands as compared with PW and ranged from 0.458 to 0.623. The relative SD averaged over all brands was 6%, equal to that of PW. The smallest S/N was 0.375, whereas the highest was 0.75.

*Figure 1* Cumulative frequency distribution in % (ordinate) of 50 Hz noise thresholds in mV (abscissa) in 150 pacemakers of four manufacturers. Red curve, continuous waves (CW); blue curve, pulsed waves (PW).
Reaction of Medtronic pacemakers to 50 Hz continuous noise

The Medtronic PM could not be tested with continuous noise in the same fashion as the four other brands in Table 2 for two reasons:

(i) An absolute threshold for continuous noise did not exist in Medtronic PMs. For a given heart test signal amplitude, the noise threshold depended on SS in an inverse correlation.

(ii) For a given SS, the noise threshold depended on the heart test signal amplitude in a positive correlation that was not found for the other four brands.

Therefore, the behaviour of Medtronic PMs was investigated separately. All models tested reacted in the same brand-specific manner: with the PM inhibited and increasing the amplitude of continuous noise, the first reaction was a single-pace pulse that was repeated every third or fourth heart test signal period. It was remarkable that this pulse was triggered by the heart test signal two signals prior to the pulse (see Figure 2A). If, for instance, the basic pacing rate was 64.5 bpm corresponding to a period of 930 ms and with a heart test signal period of 700 ms assumed, the pace pulse constantly appeared 230 ms after the preceding heart test signal (see Figure 2A). If this was a real intracardiac electrogram (IEG), the pace pulse could well fall into the T-wave of the preceding IEG. The next step in reaction with higher noise amplitudes was double pulses followed by a pause. We defined the Medtronic interference criterion with continuous noise as three or more pulses appearing in sequence (see Figure 2B).

Medtronic interference criterion with continuous noise as three or more pulses appearing in sequence (see Figure 2B).

Out of the 39 Medtronic PM mentioned in Table 1, 24 PMs were still functioning in 2008/2009 when the continuous noise thresholds were evaluated. Tests were conducted using heart test signals, in contrast to the procedure mentioned above (section Methods), with two amplitudes: either 10 mV or at threshold level.

Figure 3 Continuous noise thresholds in mV (ordinate) as a function of sensitivity settings in mV (abscissa) with 10 mV triangular heart test signals (24 Medtronic pulse generators). The trend line possesses a negative slope indicating that a higher sensitivity setting reduces the noise threshold (paradoxical behaviour).
noise threshold with a heart test signal of 10 mV applied. The noise threshold was lower at higher SS. When the heart test signal was reduced to threshold level, the 24 PMs reacted extremely sensitively to noise with amplitudes between 0.1 and 0.85 mV, independent of SS as is shown in Figure 4. In 21 PMs, the heart test signal amplitude was varied between threshold and 10 mV. In all PMs the noise threshold increased with increasing heart test signal amplitude. Two PMs with equal SS of 2.1 mV showed a nearly congruent linear straight line with positive slope and a correlation coefficient of $\geq 0.98$. The newest model tested (Adapta ADDR06) also possessed a linear relationship between heart test signal amplitude and noise threshold, up to a noise of 20 mV, as is demonstrated in Figure 5. Beyond 20 mV the noise threshold remained constant, probably due to overloading of the amplifier. Figure 5 also illustrates the relationship between criterion 1 (single pulse in sequence as demonstrated in Figure 2A) and criterion 2 (four pulses in sequence as shown in Figure 2B). Any noise test amplitude above the lower blue line produces a periodic pattern with between one and four pulses in sequence.

If the Medtronic PMs are tested according to the standard requirements (at twice the sensitivity threshold), then the requirement of withstanding noise voltages up to 2 mV was always fulfilled regardless of SS. However, if the heart test signal amplitude was smaller than twice the sensitivity threshold SS, the fulfilment of the requirement cannot be guaranteed as can be seen in Figure 5. With SS of 2.7 mV, the blue line in Figure 5 suggests that the heart test signal amplitude should be 5.4 mV to have a noise threshold of 2 mV. Noise amplitude, then, is $>12$ mV for the red line. Heart test signal amplitudes lower than twice SS may have noise reaction at levels $<2$ mV. This happens at heart test signal amplitudes of 5 mV for the blue line and at 3 mV for the red line.

**Discussion**

Do interference situations exist that could be dangerous for a PM patient? This question is not easy to answer because the interaction of at least five parameters will determine whether the answer is ‘yes’ or ‘no’. Important parameters of EMI effecting PM systems are:

1. position of the PM system (left or right sided, pectoral, or abdominal);
2. electrode configuration (unipolar or bipolar);
3. programmed SS;
4. sensitivity of the PM with respect to interference signals;
5. magnitude of the electromagnetic field.

We recently published a paper in which parameters (i) through (iii) were investigated and critically assessed in a German patient
population. Parameter (iv) is the topic of the present paper and should clarify the influence of EMI on PMs with respect to 50 Hz pulsed and CW.

Parameters (i) through (iii) are determined by the implanting and programming physician. For parameter (iv) the PM manufacturer and for (v) the field producer are responsible. Most patients are not in a position to contribute to the question of interference as they are laypersons who are unable to assess EMI. Therefore, it is not sufficient to teach patients ‘to avoid entrance of strong electro-magnetic fields’.

The noise thresholds for pulsed and continuous 50 Hz noise of all but Medtronic PMs showed an asymmetric distribution between 1.2 and 8.7 mV with the red curve for continuous noise nearly always to the right of the blue curve for pulsed noise in Figure 1, indicating that CW have a slightly higher noise threshold than PW. Of all PM tested only 4% possessed a noise threshold of 2 mV or lower, thus not fulfilling the requirements of the European standard for unipolar sensing. It is encouraging that 50% of all PMs tested had a noise threshold of between 2.7 and 8.7 mV. Do the other 50% really need such sensitive SS in ventricular channels or are they programmed according to tradition or under the consideration that high sensitivity ensures safety in heart signal recognition? An exaggerated sensitivity reduces safety in EMI situations. We found in the previously mentioned paper that bipolar PM systems were programmed at higher SS than unipolar PM. Thus, we can exclude bipolar PMs being predominantly programmed to <2.7 mV SS.

**Pulsed wave interference**

All tested PMs reacted to the pulsed 50 Hz waves as if they were heart signals, though the morphology of both signals differs remarkably. The heart signal has only one sharp downstroke, the so-called intrinsic deflection in the 0.5–4 ms range, followed by a slower up-stroke in the form of an asymmetric triangle, whereas one 50 Hz sinusoidal wave is symmetric, less sharp, and of a duration of 20 ms. Figure 6 shows an example of a unipolar ventricular IEG, simultaneously demonstrating that the standard heart test signal to test SS is quite close to reality.

**Signal-to-noise ratio for 50 Hz noise, pulsed waves**

The S/N for PW $S/N_{\text{pw}}$ in Table 1 was surprising: all of the tested PMs possessed a ratio $<1$, indicating that the heart test signal was less amplified than the 50 Hz noise test signal. The lowest value was 0.375, whereas the highest was 0.684. In the first case, the heart test signal must have an amplitude of 2.7 times larger than noise to reach the sensing threshold. If the European standard requires that unipolarly sensing PMs must tolerate noise voltages up to 2 mV without a change in operation, the S/N ratio gives an indication of the SS at which the borderline value of 2 mV is reached. These values were calculated by inverting Eq. (2) in the Supplementary material online, Annex, inserting 2 mV as $A_{\text{noise}}$ and solving it for the triangular test signal (see Eq. (4) in the Supplementary material online, Annex). The results are presented as ‘SS (2 mV)’ in the last column of Table 1. For the calculation the mean values of the S/N ratios minus one SD were used. According to the European standard, manufacturers should provide warnings against using SS lower than those listed in Table 1. In three brands the borderline SS is $>2$ mV showing that it is questionable whether programming SS to 2 mV guarantees uninfluenced behaviour of PMs up to 2 mV noise.

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**Figure 6** Typical intracardiac unipolar ventricular electrogram derived from a 1.2 mm² electrode in the apex of the right ventricle: the negative going peak-to-peak amplitude is 24.6 mV with a slope of 12.9 V/s. The triangular test signal was adjusted equally to an amplitude of 24.6 mV and has a slope of 12.3 V/s demonstrating that standard heart test signal is quite close to reality.

Intracardiac electrogram/mV

<table>
<thead>
<tr>
<th>Characteristics IEG:</th>
<th>Amplitude: 24.6 mV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decay time: 1.9 ms</td>
<td></td>
</tr>
<tr>
<td>Slope: 12.9 V/s</td>
<td></td>
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</tbody>
</table>

IEG characteristics

![Characteistics IEG](https://example.com/characteristics_ieg.png)

Heart test signal

![Heart test signal](https://example.com/heart_test_signal.png)
If the specific S/N of a PM is unknown, we recommend programming the SS to at least 2.5 mV to be sure that a noise test signal must be >2 mV to reach noise threshold as required by the standard for unipolar PMs.²

**Signal-to-noise ratio for 50 Hz noise, continuous waves**

In Table 2, the S/N ratios are all higher than those in Table 1, but they are all still <1, the best being 0.75 in VI PMs. The reason for higher S/N ratios with CW is that the pulsed noise voltages produce a transient response within the filters which increases the noise amplitude. Although the mean value increased for SJ, the borderline SS (2 mV) increased due to a higher SD. The differences between maximum and minimum borderline SS are due to variations in filter performance. The recommendation of programming SS to 2.5 mV or higher can also be derived from Table 2 for all brands except for Medtronic.

**Reaction of Medtronic pacemakers to continuous 50 Hz noise**

Whereas the reaction of the Medtronic PM to pulsed noise was comparable with all other brands and models, the continuous noise behaviour was completely different and rather complex. The noise threshold for continuous noise decreases in Figures 3 and 4 with increasing SS. Figure 3 shows that the noise threshold could even increase up to 17 mV with SS of 2 mV and heart test signal amplitudes of 10 mV. A remarkable feature shown in Figure 3 is the low noise threshold of only 0.5 mV for a PM with an SS of 9.6 mV. In 18 tested PMs, the noise level was 2 mV if the heart test signals were 1.52 times higher than SS (mean value). This means that the PMs in Figures 3 and 4 (right low corner) with an SS of 9.6 mV would have to reach the 2 mV level with a heart test signal of 9.6 mV times 1.52 = 14.6 mV. A ventricular heart signal with such amplitude cannot be guaranteed. This demonstrates the paradoxical feature that protection against continuous noise in Medtronic PMs was reduced with increasing SS. This feature is linked in a complex manner to an adaptive amplification found in all Medtronic PMs. The Adapta instruction manual explains with respect to SS: ‘value from which adaptive adjustment begins when nominals are programmed’. The algorithm behind this adaptive adjustment is unknown to us.

From Table 1 it can be seen that SS in Medtronic PMs should be at least 2.23 mV to fulfill the requirements of the European standard with respect to pulsed noise. However, the situation is completely different with continuous noise. With an SS of 2.7 mV and a ventricular heart signal amplitude of 10 mV assumed, the modern Adapta PM must be exposed to 6.5 mV of continuous noise to produce single pacing pulses as shown by the blue line in Figure 5. In contrast, Figure 3 shows that the noise threshold above an SS of 6 mV is <6.5 mV and decreases further with increasing SS. Therefore, protection against malfunction due to continuous noise is high with low SS assuming sufficient heart signal amplitudes, a paradox that is almost incomprehensible.

The sharply pulsed signals, as they are used for testing purposes, are rare in normal everyday life (they were invented to create a simple test procedure) but they could possibly be present in industrial environments.¹,¹¹ As a good compromise, we recommend programming SS of the ventricular channel in Medtronic PMs to 3 mV to have good protection against interference in pulsed and continuous noise situations as well. The 24 Medtronic PMs tested possessed an average SS of 4.3 mV with SD of ± 2 mV. Only four pulse generators (16.7%) were programmed to an SS around 3 mV (2.6–3.2 mV) demonstrating the importance of our investigation.

The MD noise behaviour described is problematic from a standardization viewpoint. How can a standard be applied to a system in which the unknown amplitude of a heart signal plays a deciding role in the noise threshold?

**Conclusions**

Our investigation offers a basis on which the susceptibility of pulse generators to noise can be judged. We demonstrate that an SS of 2 mV does not guarantee a noise tolerance of 2 mV, thus not fulfilling the requirement of the European standard.² An S/N ratio of <0.5 requires an SS >2 mV in three out of five PM brands in order to fulfill the standard, as is illustrated in the last columns of Tables 1 and 2. If the specific S/N of a PM is unknown, we recommend programming the SS to 2.5 mV or higher to be sure that noise must be >2 mV to influence a unipolar pulse generator. This is an absolute necessity as it is the responsibility of the implanting or programming physician to avoid EMI <2 mV in the low-frequency range in patients with unipolar PMs. As interference situations also exist where patients touch defective electrical appliances or enter fields of older equipment or of products that are not designed according to the standard (antitheft devices), it is wise to programme the ventricular SS as high as possible except in Medtronic PMs.

Medtronic PMs must be programmed differently due to their continuous noise behaviour. The ventricular SS in unipolar PMs should be 3 mV as a good compromise to guarantee sufficient protection in pulsed and continuous noise assuming a ventricular heart signal of 10 mV or higher. Sensitivity settings >3 mV reduce immunity to continuous noise.

**Supplementary material**

Supplementary material is available at Europace online.

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**References**


