High Resolution Monitoring of Intracardiac Signals with a DDD-Pacemaker

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Summary

The use of bioelectric signals of the heart like the monophasic action potential (MAP) or the ventricular evoked response (VER) for therapeutic as well as diagnostic applications requires a profound analysis regarding different physiological, psychological and pharmacological influences on the waveform of the intracardiac signals. A prerequisite for these investigations is a pacemaker system which allows high resolution monitoring of cardiac potentials. In this article new pacemaker systems are presented which comply with these requirements. The pacemaker systems consist of two components: Firstly, fractally coated leads (BIOTRONIK) are used providing a high signal-to-noise ratio and a negligible polarization artifact. Secondly, two pacemakers (Physios CTM 01, Logos, BIOTRONIK) have been developed providing filter characteristics and high resolution telemetry which are adapted to the frequency spectrum of intracardiac signals. In this study the new pacemaker Physios CTM 01 is used for the analysis of the ventricular evoked response in 13 patients. The clinical results show different influences on the signal waveform providing information about the adrenergic stimulation of the myocardium. Finally, as a first clinical application of the VER an algorithm for automatic amplitude adjustment has been developed and validated with the Logos system.

Key Words

ventricular evoked response, monophasic action potential, long-term monitoring, fractally coated leads, implantable pacemaker

Introduction

The goal of the technological development in the field of pacemaker therapy is a physiological pacemaker, that besides stimulation and inhibition complies with diagnostic tasks and adapts itself to physiological circumstances and demands. To realize an „auto-diagnostic pacemaker" as it was suggested by Auerbach and Furman [1] the pacemaker needs a signal of control which on the one hand reflects the present physiological status of the myocardium and on the other hand can be monitored with justifiable technological effort. One of the intracardiac signals that complies with both demands is the ventricular evoked response (VER), which is obtained by unipolar measurement via ventricular endocardial pacemaker electrode following an stimulation pulse. Another signal is the monophasic action potential (MAP) which can be measured by a bipolar electrode between tip and ring. Both are composite signals of transmembrane potentials of single myocardial cells and therefore reflect a wealth of information about the status of the heart. While the MAP shows more local cellular effects near the electrode's tip the VER contains due to the unipolar measurement mode more global informations about the myocardium's state [2].

The use of intracardiac signals for diagnostic and therapeutic applications in the electrotherapy of the heart requires an exact analysis of these signals which are influenced by different conditions like physical or emotional stress, medication, pathological changes and so on. Therefore, a pacemaker system is necessary which allows the measurement and transmission of intracardiac signals to an external device for data processing in order to analyze the extractable information content. This means: Firstly a sensor for electrical potentials is required and secondly the implantable pacemaker has to comply with special hardware requirements concerning the input channel and telemetry system.

With respect to the sensing properties of pacing electrodes problems are solved: Fractal coatings provide a high capacity of the phase boundary between the surface of the electrode and the surrounding tissue. This results in a high signal-to-noise ratio, a negligible afterpotential allowing measurements immediately after the pacing pulse and an undisturbed transmission of the heart's potentials.

Not only the electrode but also the pacemaker must comply with new requirements to provide good transmission characteristics: Firstly, filter characteristics have to be adapted to the frequency spectrum of intracardiac signals. Of the same importance is the telemetry system which must provide a high time and amplitude resolution. Following these requirements, the pacemaker Physios CTM 01 (BIOTRONIK) has been designed allowing the analysis of intracardiac potentials. To put the developed algorithms to clinical test a pacemaker (Logos, BIOTRONIK) with a programmable CPU and an EPROM for storing the algorithm has been designed. This pacemaker allows a quick application of the results of data analysis and algorithm development. The concepts of both pacemakers as well as clinical results are presented in the following.

The DDD-Pacing System

The electrode

To date, two methods for detecting intracardiac signals immediately after the pacing pulse have been used: an automatic post pulse charge compensation technique and the use of two different electrodes for pacing and sensing. The disadvantages of both methods are obvious: A recharge pulse requires additional battery power resulting in a shortening of pacemaker lifetime whereas the use of additional sensing electrodes is not acceptable for pacemaker therapy. The new method using fractally coated pacing leads with a high Helmholtz capacity avoids both disadvantages. The idea of the fractal surface is to use self-repeating structures in order to increase the active surface area. Electrodes, fractally coated with iridium by a physical vapor deposition process, reveal Helmholtz capacities up to 50 mF/cm^2. This capacity is enlarged by more than three orders of magnitude by coating and guarantees a negligible polarization artifact. So one pair of electrodes performs as actuator and sensor as well. In combination with an autoshort circuit the ventricular evoked response is detected reliably. Furthermore, due to the low polarization losses of these leads, the stimulation threshold is lowered significantly, i.e. the life-to-size ratio of the pacemaker is improved [3].

Pacemaker requirements concerning signal analysis

Exact analysis of intracardiac signals requires the use of an implantable pacemaker system to investigate the different physiological, pharmacological or pathological influences on the signal's waveform. In addition, this system is necessary for the long-term analysis of intracardiac signals like VER or MAP. However, input channels and telemetry system of usual pacemakers are not adapted to the signal's waveform. Therefore, a pacemaker has to be developed complying with specifications, exceeding the performance of "conventional" pacemakers:

- The signal filters of the pacemaker system must not change the morphology of the intracardiac signals.
- The exact analysis of the signals requires a high resolution (in time and amplitude) of the telemetry system to transmit the measured signals.

Filter characteristics of the pacemaker

A high signal resolution requires a high pass filtering of measured signals, which has to eliminate DC- and low-frequency components that are not caused by heart activity. Such components for example are due to the use of varying materials for the different and the indifferent electrode and run up to a constant offset of 100 mV caused by electrochemical potentials. Other low-frequency changes in the signal waveform are e.g. due to respiration rhythm. An adaptation of the measurement range of the input channel to a signal range of some 100 mV, which results from high DC-potentials, would lead to a low resolution of the intracardiac signals having amplitudes up to 20 mV. So, the elimination of high DC- and low-frequency components allows the reduction of the measurement range to approximately ±20 mV and increases the resolution of the signal during telemetric transmission and digitizing.

Ordinary pacemakers have high-pass filters with a cut-off frequency of about 3 Hz. However, these filters lead to distortions of intracardiac signals. Therefore, to date, there have been significant differences in the morphology between intraoperative and postoperative measurements of the VER or MAP caused by different transmitting characteristics of the measurement systems used. Whereas the external system has low cut-off frequencies which do not distort the signals a cut-off frequency of 3 Hz changes their waveform significantly (figure 1).

According to this, filter characteristics must be adapted to the frequency spectrum of intracardiac

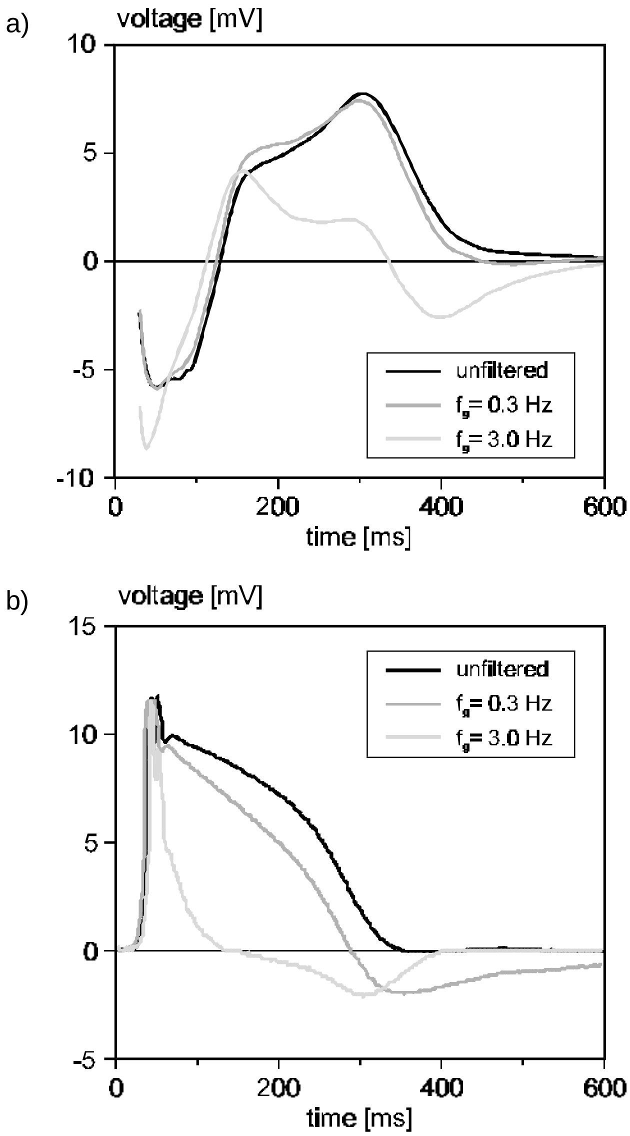

Figure 1. *Morphology of a) the ventricular evoked response and b) the monophasic action potential in relation to the high-pass filter characteristics of the telemetry system.*

signals. For transferring intracardiac signals with high accuracy the lower cut-off frequency of the telemetry system has to be as low as possible. However, to reach this goal large capacitors are necessary for a low cut-off frequency of the filter which exceed the hybrid space. In addition the build-up time τ of the filter is given by the inverse cut-off frequency f_g [4]:

$$\tau = \frac{1}{2 \cdot \pi \cdot f_g} .$$

So, a low cut-off frequency results in a large build-up time of the filters leading to settling times well above 1 s after necessary switches of the input channels. Therefore, a compromise has to be found between a distortion free measurement and an acceptable build-up time.

As figure 1 shows a cut-off frequency of 0.3 Hz provides a good compromise: The signal´s morphology shows only minor changes after passing this filter which does not disturb the analysis of VER or MAP. The settling time of the filter with a value of about 500 ms is acceptable.

The Physios CTM 01-pacemaker

For high resolution online monitoring of intracardiac signals a dual chamber pacemaker with atrial and ventricular monitoring channels has been developed. Besides this special feature the Physios CTM 01 includes all therapeutic and diagnostic options of a conventional DDD-pacemaker. The principle of the pacemaker Physios CTM 01 is shown in figure 2:

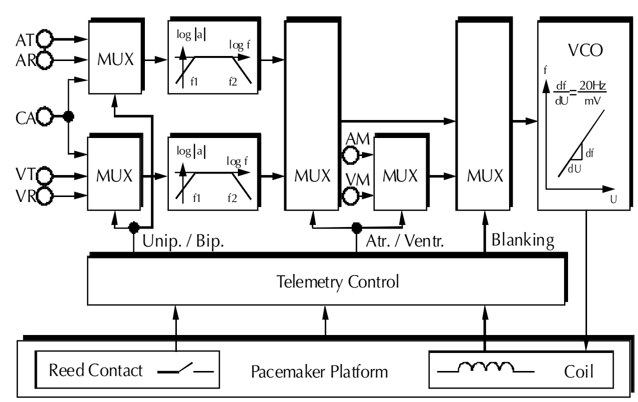

Figure 2. *Flow chart of the VER and MAP measurement within the monitoring pacemaker Physios CTM 01 (BIOTRONIK).*

The atrial lead is connected with the contacts AT (atrial tip electrode) and AR (atrial ring electrode), the ventricular lead with VT (ventricular tip electrode) and VR (ventricular ring electrode) and the pacemaker case with CA. Different telemetry functions are programmed by an external device via an extra-thoracic transmission coil and a coil on the pacemaker platform. The telemetry control allows switching between unipolar and bipolar measurements (Unip./Bip.) and between the atrial and the ventricular channel (Atr./Ventr.) corresponding to the transmitted telemetry program. Atrial and ventricular recordings are assigned with pacing markers (AM and VM) having a positive or negative amplitude of 10 mV respectively and a duration which is programmable between 0 ms and 60 ms. The bandwidth of the internal filtering with a lower cut-off frequency of 0.33 Hz and a higher cut-off frequency of 200 Hz was adapted to the frequency spectrum of the VER and the MAP. After frequency modulation performed by a VCO the measurement signals are transmitted to an external receiver via the telemetry coils. Following frequency demodulation the signals are transmitted to a computer for AD conversion, visualization, signal analysis and data storage.

As one important advantage, analogue telemetry guarantees interference-free data transfer from the implanted pacemaker to the external data storage and processing unit. The telemetry unit with a basis frequency of 1.1 kHz provides a high time resolution between 0.7 and 1.4 ms depending on the signal voltage and a high amplitude resolution of at least 0.05 mV in case of a measurement range of ± 20 mV. I.e. the pacemaker Physios CTM 01 complies with the requirements on a monitoring pacemaker for high quality measurement and analysis of electrical potentials of the heart.

The Logos-pacemaker

The aim of the data analysis with the Physios CTM 01 is the development of algorithms for diagnostic and therapeutic applications which shall improve the electrotherapy of the heart by physiological stimulation and automaticity of the pacemaker system to support the physician's diagnosis. In addition the pacemaker Logos (BIOTRONIK) – another DDD-pacemaker of the latest generation with a programmable CPU – has been designed. Algorithms can be implemented by an EPROM providing the possibility of fast algorithm validation. The input channel of this pacemaker is adapted to the frequency spectrum of intracardiac signals as mentioned above.

By assistance of this pacemaker an algorithm for automatic amplitude adjustment based on the measurement and analysis of the ventricular evoked response has been developed and implemented.

Clinical Results

According to the requirements discussed above for clinical investigations a pacemaker system consisting of fractally coated pacemaker leads (TIR 60-UP/BP, BIOTRONIK) and the implantable dual chamber pacemaker Physios CTM 01 (BIOTRONIK) is used. Up to now 13 patients (3 women, 10 men) with II. and III. degree AV block and age between 19 and 79 years (mean age 53.8 ± 16.2 years) were included in this study.

As an important prerequisite for clinical use in diagnosis and therapy a good long-term stability of the VER measurement has been verified. During 12 months after implantation the morphology of the VER which is characterized by a negative R-wave and a positive T-wave changes only slightly in long-term measurements up to the one-year follow-up (figure 3).

Investigations referring to the influence of pacing rate and physical load were performed with respect to typically changes in the VER's morphology. As the example (figure 4) and the statistic evaluation of the R-wave amplitude and VER-duration (figure 5) demonstrate, R-wave is increased and duration is shortened significantly with higher pacing rate. The strong reduction in signal duration is caused by an increas-

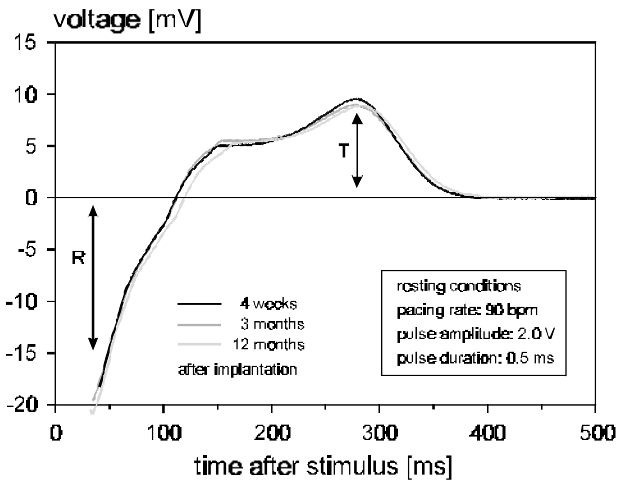

Figure 3. *Long-term stability of the VER.*

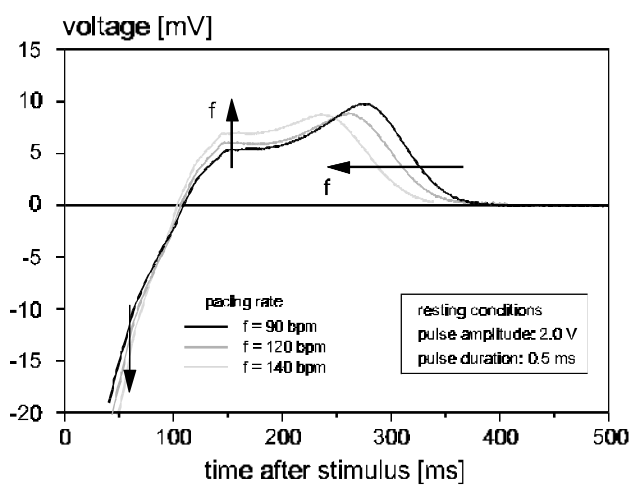

Figure 4. *Influence of pacing rate on the signal morphology of the VER.*

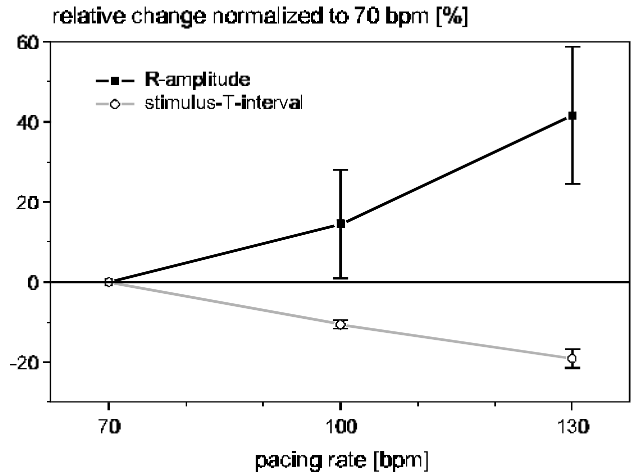

Figure 5. R-wave amplitude and VER duration (stimulus-T-wave-interval) depending on pacing rate. Changes of amplitude and duration are normalized to the values determined at 70 bpm.

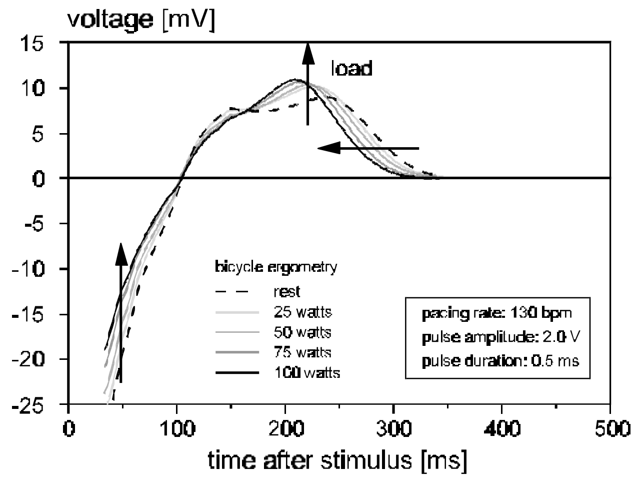

Figure 7. Influence of physical load on the morphology of the VER. Load was increased in steps of 25 watts every 3 minutes.

ing K^+-flow out of the myocardium cells during repolarization and by a shortening of the action potentials due to that [6].

Under pharmacological influence of Orciprenaline (0.5 µg/kg/min) simulating the adrenergic receptors measurements of the VER show a decrease in R-wave amplitude and a shortening and increase in amplitude of the T-wave (figure 6) caused by cellular effects: Due to stimulation of the adrenergic receptors the Ca^{2+}-flow into the myocardium cells is increased resulting in a higher plateau voltage and an accelerated repolarization of the action potential [6].

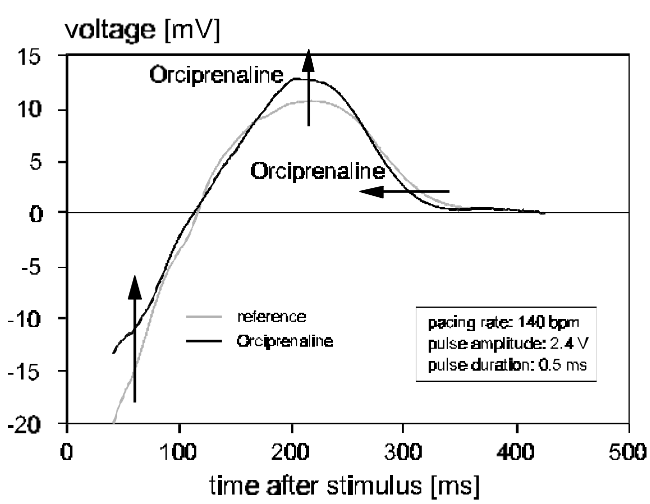

Figure 6. Influence of pharmacological adrenergic stimulation caused by Orciprenaline.

Investigations under physical load were made on bicycle ergometry where load was increased in steps of 25 watts every three minutes. To separate the influences of load and pacing rate exercises were carried out under constant pacing rate of 130 bpm. These measurements show the same characteristic changes of the VER as under pharmacological adrenergic stimulation by Orciprenaline. The results are shown in figure 7 for an example and in figure 8 for the mean values of T-amplitude, VER-duration and R-amplitude. Increasing load causes an increasing and

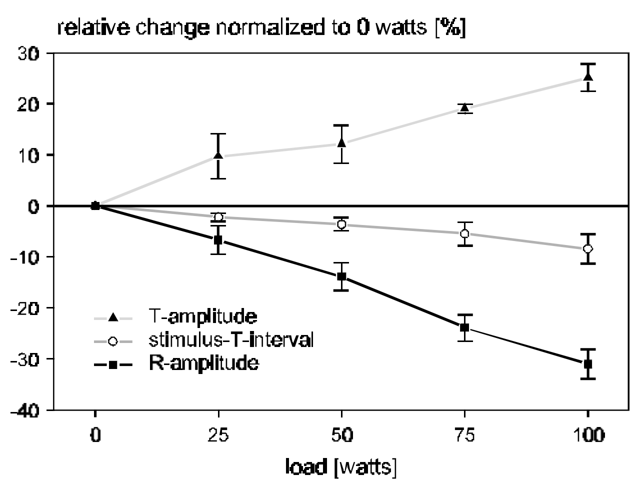

Figure 8. R- and T-wave amplitude and VER duration (stimulus-T-wave-interval) depending on physical load. Changes of amplitude and duration are normalized to the values determined at rest.

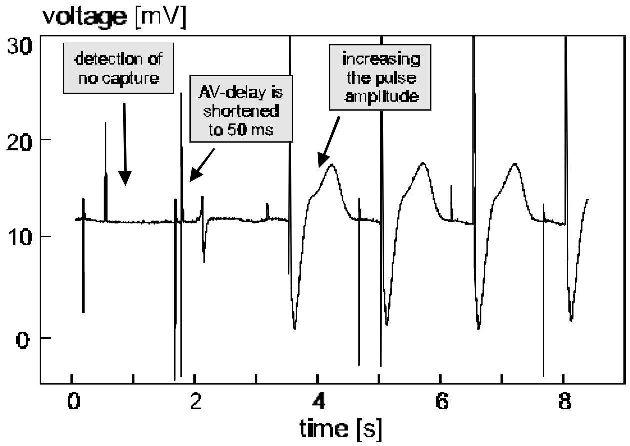

Figure 9. *Automatic capture recognition by detecting the VER.*

shortening T-wave and a decreasing R-wave amplitude. Therefore, the measurement of the VER reflects effects on the cellular level as discussed before for medication.

As the VER occurs only following an effective pace, the VER is a highly suitable signal for automatic capture recognition by pacemakers. Figure 9 shows the response of the developed algorithm in DDD-mode: Following the first ventricular pacing pulse loss of capture is detected. Afterwards the algorithm reduces the AV-delay to avoid disturbances due to fusion beats, because these signals have no definite waveform. The second ventricular pulse is not effective, too, and an intrinsic activity of the heart follows by chance. After that, the AV-delay is adjusted to its original value and the output voltage of the pacemaker is increased to obtain an effective stimulation. The VER following the next pacing pulse proves the effective stimulation.

The algorithm for automatic amplitude adjustment was checked using a programmable pacemaker system during pacemaker implantations (16 Patients: 8 male, 8 female, 63 ± 21 years). This system reliably detected effective and not effective stimulation in single and dual chamber mode. Fusion beats provoked by adjustment of the pacing rate close to the intrinsic rate did not disturb the algorithm.

Conclusions

The developed pacemaker system Physios CTM 01 allows the measurement and transmission of intracardiac signals with high resolution. The special filter characteristics provide an undisturbed measurement of VER and MAP. Therefore, this pacemaker system is the basis for a profound analysis of the information content of intracardiac signals. The Logos pacemaker allows the investigation of the feasibility and reliability of the new pacemaker functions. Therefore, it accelerates the development of new pacemaker functions to a high degree.

Intracardiac signals like MAP and VER provide access to the cardiac state on an electrical cellular level. Therefore, they are well suited to monitor efficacy of the electrotherapy by implantable pacemakers. This ranges from vital functions like the control of capture, via the establishment of physiological pacing by optimizing AV-delay or adjustment of pacing rate to hemodynamic needs, to extended diagnostic support, e.g. for non-invasive transplant monitoring [5], ischemia early detection or dual chamber pacing in case of cardiomyopathies. These characteristic properties define the automatic monitoring pacemaker which has to be based on the evaluation of cardiac signals. Clinical applications are discussed in further articles of this issue.

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