Equivalent Dispersion Dependence – a New Diagnostic Algorithm Concept for Pacemakers

I. KHASSANOV, O. ANOSOV, B. HENSEL
Department of Biomedical Engineering, Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany

S. PETERSEN
Biotronik GmbH & Co. KG, Erlangen, Germany

Summary

We recently proposed a promising approach to forecasting AF on the basis of multisite intracardiac electrograms (IEGM). We used the formalism of wave theory and wavelet decomposition of IEGM signals measured in two spatially separated points of the atria, introducing equivalent concepts of group and phase velocities, attenuation coefficient, and refraction index to describe myocardial excitation. This novel method was applied to experimental clinical data to show that the introduced equivalent dispersion dependence (EDD) for the myocardial excitation wave under physiological conditions is similar to the EDD that is obtained for resonant wave-medium interaction. Furthermore, the EDD resonant quality parameters decreasing early before the onset of atrial fibrillation (AF) can serve as predictors of fibrillation. To test the proposed concept as a basis for a pacemaker diagnostic algorithm, we applied the developed method to the data gained through a conventional dual-chamber pacemaker implanted for biatrial pacing in a patient suffering from AF paroxysms. We measured the IEGMs from two distant electrodes in the atria, i.e., the right atrium and the coronary sinus leads, to analyze the EDD resonance quality parameter. The analysis results showed that the dispersion has a resonant character in the normal state of the myocardium, while the resonance parameters are smeared due to a rather unstable state of the patient heart prone to frequent AF paroxysms. Thus, the developed approach provides the basis for a diagnostic algorithm that can be implemented in implantable devices using current pacemaker technology.

Key Words

Atrial fibrillation, myocardial excitation wave, equivalent dispersion dependence, pacemaker intracardiac electrogram (IEGM)

Introduction

Recent progress in pacemaker therapy is marked by the development of multi-chamber devices, increased capacity and quality of signal analysis, and the "synergetic" impact of modern technologies such as mobile telecommunications.

The multi-chamber devices aimed at ensuring cardiac resynchronization therapy and treating paroxysmal atrial fibrillation (AF) provide more detailed information on the timing of cardiac events as well as on the course of myocardial excitation. This can be achieved through waveform analysis of multisite intracardiac electrograms (IEGMs) measured on pacemaker leads. In this regard, the ever increasing sampling and digital capacity of the pacemakers support the implementation of new mathematical approaches and diagnostic algorithms. Moreover, achievements in telecommunication technologies such as Home Monitoring (Biotronik, Germany) bridge the gap between the patient pacemaker or ICD and a service centre with an incomparably large processing capacity.

Thus, the development of new methods for analyzing intracardiac signals – being a significant task in itself – is also one of the challenges of advancing pacemaker technology. We recently proposed a promising approach to forecasting AF on the basis of multisite IEGMs [1,2]. We used the formalism of wave-packet propagation in passive media to characterize the spread of electrical excitation in excitable media, namely the atrial myocardium. We introduced equivalent concepts of group and phase velocities, attenuation coefficient, and refraction index to describe the myocardial excitation wave and applied the wavelet approach to construct an analogue of the classical dispersion dependence for active media. Using wavelet decomposition, we developed a method for reconstructing the myocardial dispersion dependence on the basis of electrical intracardiac signals that are measured in two spatially separated points of the atria. This novel method was applied to two different sets of experimental data and to data obtained from numerical simulation of the atrial myocardium. We have shown that the introduced equivalent dispersion dependence (EDD) under physiological conditions is similar to the one that is obtained for resonant wave-medium interaction.

Analysis of experimental clinical data sets has clearly shown that the number of cardiac cycles with a resonant form of the equivalent dispersion dependence predominates in the normal state of the myocardium while it decreases early before the onset of atrial fibrillation. We have set up the hypothesis that an increasing number of non-resonant cardiac cycles is a precursor of atrial fibrillation and thus can serve to predict fibrillation already at an early stage before its onset. The proposed concept can be the basis of a diagnostic algorithm applied to investigate the properties of the atrial as well as the ventricular myocardium. Now we apply the developed method to the data obtained with a conventional pacemaker in order to demonstrate perspectives of the method to be implemented in implantable devices.

Equivalent Dispersion Dependence for the Myocardium

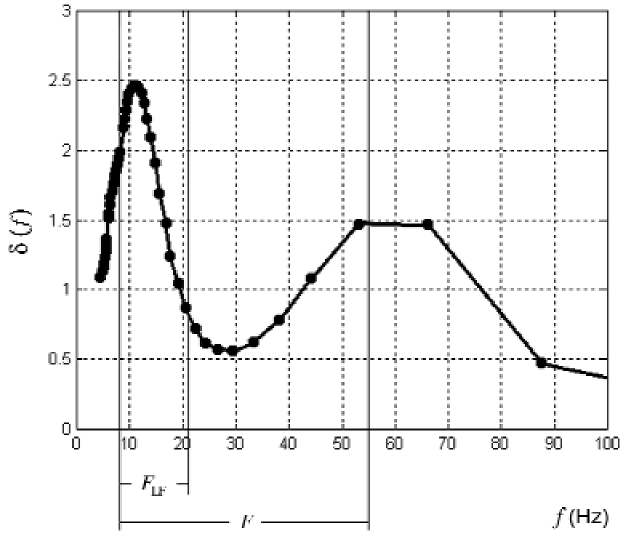
Electrical excitation propagates in the myocardium in a so-called autowave process that is commonly observed in a large number of systems in nature called active media [3]. This is a chain process of electrical excitation of cells known as cellular action potential that is maintained as a propagating solitary wave receiving energy from the metabolism processes taking place in myocytes. The excitation wave is thus not simply coupled to the medium in which it propagates, but is generated by the medium itself.

The shape of an excitation wave strongly depends on the local microscopic properties of the medium, and its analysis allows us to draw conclusions about the state of the myocardium and its pathological alterations. This local view of the myocardium is widened by simultaneous analysis of the signals from more than one electrode at different extended locations.

Macroscopic dispersion characteristics of a medium can be described by dispersion dependence, i.e., the frequency-dependent complex refraction index $\eta(f)=n(f)+i\delta(f)$. Here $n(f)$ is the real part of the refraction index of the medium. The imaginary part $\delta(f)$ characterizes the transmission of energy between the wave and the medium. To reconstruct the EDD of the myocardium, we applied wavelet analysis to IEGM signals measured simultaneously at two different points in atria (for details see [2]). In short, we apply the introduced dispersion formalism not directly to the signals measured at those different points, but to their wavelet [4] components of the same level. By calculating η for wavelet components of different levels, we finally obtain the complex refraction index and its dependence on the wavelet level. Changing from the wavelet level to the characteristic frequency f we get an estimate of the frequency-dependent refraction index for excitation wave propagation in the myocardium, i.e., $\eta(f)=n(f)+i\delta(f)$.

We tested the efficiency of the method in two experimental clinical studies [2]. We analyzed fragments (duration: 12 s to 16 s) of IEGMs that were measured simultaneously with two bipolar leads introduced into the right atrium and the coronary sinus of patients with a high risk of AF. One of the studies was done in mitral valve prosthesis patients prone to developing AF during the first days after the operation. Monophasic action potentials (MAPs) were monitored in a group of patients immediately after the valve replacement over periods of up to two weeks [5]. The MAPs were recorded at a sampling rate of 500 Hz using two special MAP leads positioned epicardially on the atria.

It has been shown that for each patient the dispersion characteristics of the transmission coefficient $\delta(f)$ varies with time. For some beats it has a very pronounced resonant character, while for others no reso-



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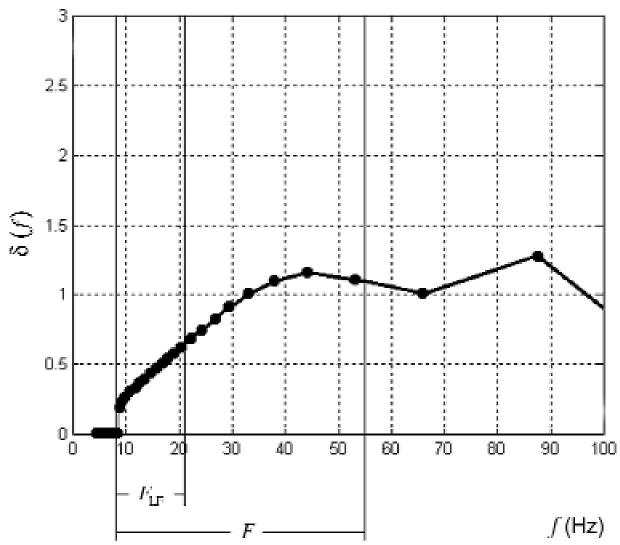

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Figure 1. Frequency dependence of the transmission coefficient δ (f) for the wavelet components of the atrial monophasic action potential (MAP) signals measured in the same patient, but in two different cardiac cycles. The resonance quality factor (see text) has considerably different values for the two beats: R = 44.9% (panel a) and R = 18.7% (panel b). Here F is the band used for the analysis and F_{LF} is the low-frequency band.

nance features are evident. Figure 1 depicts two examples of the transmission coefficient $\delta(f)$ calculated for different cycles in the same patient. As can be seen in Figure 1, a distinct resonance peak with a maximum at 12 Hz is present for one cardiac beat, while the resonance features are almost smeared out for the other.

The analysis of the MAPs in patients with AF paroxysms has shown that in the normal state (i.e., early before the onset of AF) the number of cycles with resonance features is much higher than the number of non-resonant ones. Shortly before the onset of AF, the number of non-resonant cycles increases and even becomes dominant. In order to quantify the state of the myocardium, we introduced a parameter for the resonance coupling properties of the myocardium, i.e., a parameter *R* characterizing the quality of the resonance in the transmission coefficient $\delta(f)$, and followed its variation with time until AF developed. The parameter is calculated from the total area *S* under the $\delta(f)$ curve over the whole analyzed frequency range *F* and the partial area S_{LF} in the low frequency range F_{LF}:

$$R = 100\frac{S_{LF}}{S}$$ (see Figure 1).

The parameter value is small without resonance in the range F_{LF}, but increases with a more and more pronounced resonance. An analysis range *F* of 8 – 55 Hz was chosen. The low-frequency range F_{LF} was defined between 8 – 21 Hz. Using these frequency ranges one obtains R = 44.9% with a pronounced resonance (Figure 1a) and R = 18.7% without any resonance features (Figure 1b). The course of the resonance parameter *R* monitored over two sequential AF episodes in the patient showed variations marked by a significant decrease of the resonance parameter *R* already early before their onset. A smaller resonance parameter *R* indicates a less strong coupling of the excitation wave to the atrial myocardium.

Parameters of Equivalent Dispersion Dependence in a Pacemaker Patient

The next development step is to prove the possibility of implementing the method in devices such as pacemakers and implantable cardioverter-defibrillators (ICDs). With this objective in mind, we applied the method to analyze the IEGM sequences recorded by a standard Logos (Biotronik) pacemaker implanted along with standard leads in a patient (a right atrial lead was implanted into the lateral position and the left atrial lead was placed into the coronary sinus). The device was indicated to deliver biatrial pacemaker therapy to a patient suffering from daily AF paroxysms of 2 – 6 hours duration. The heart frequency trend interrogated prior to EDD monitoring are shown in Figure 2.

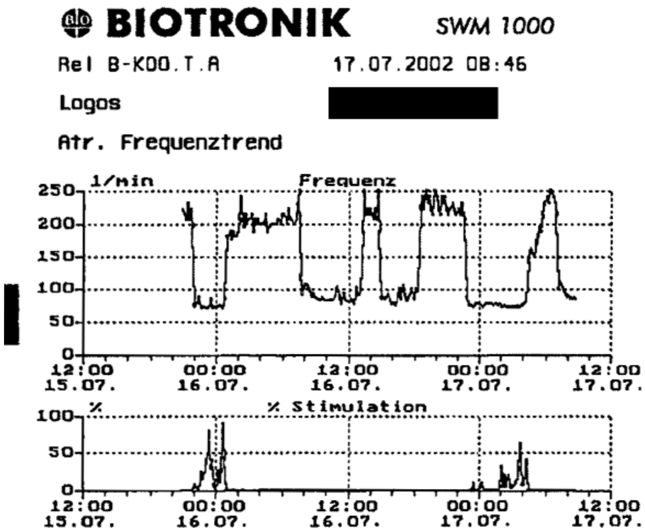

Figure 2. The frequency trend data interrogated prior to IEGM monitoring for the equivalent dispersion dependence analysis. The atrial fibrillation episodes in the patient are marked by periods of sustained high frequency.

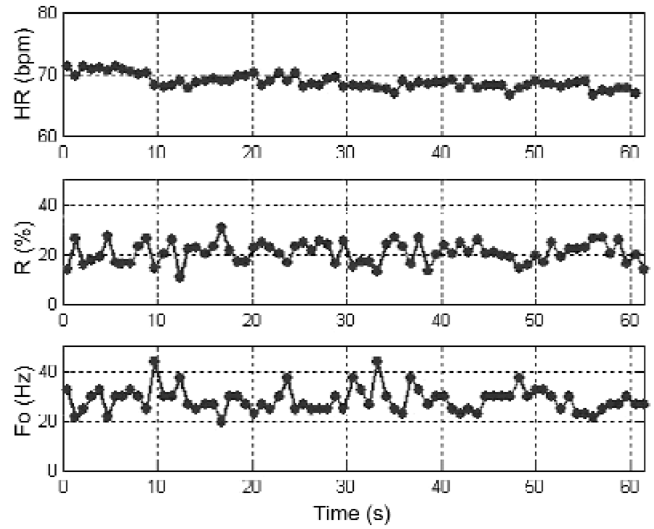

Figure 3. Upper panel: Fragment of the patient's heart rate (HR) trend. Lower panel: The trend of the resonance quality criterium R and trend of the resonance frequency F_0 of the transmission coefficient $\delta(f)$, respectively.

Figure 3 depicts the heart rate trend and the results of the EDD analysis of the appropriate IEGM sequences interrogated from the pacemaker. While the heart rate trend demonstrates sinus rhythm in normal physiological range, the resonance quality parameter fluctuates below the values characteristic for good excitation-myocardium resonant conditions. Accordingly, frequency F_0 of the maximum of the transmission coefficient $\delta(f)$ for a large fraction of heart beats is shifted to the frequency range exceeding 20 Hz. These features characterize a highly unstable state of the heart prone to AF paroxysms.

Discussion and Conclusion

We have developed a novel method of determining atrial myocardial properties by analyzing the dispersion that occurs for the wave propagation of the electrical excitation. For this purpose, we measured the electrical signals from two distant electrodes in the atria. The signals were decomposed using wavelets in order to obtain the frequency-dependent equivalent complex refraction index, the equivalent dispersion dependence (EDD). In this way the properties of the atrial myocardium can be analyzed in the range of frequencies between 5 Hz and 100 Hz.

Furthermore, we applied the EDD method to analyze the pacemaker IEGM data of a patient with AF paroxysms. The analysis results showed that the dispersion has a resonant character in the normal state of the myocardium, while the resonance parameters are smeared due to a rather unstable state of the heart prone to frequent AF paroxysms.

Thus, by monitoring the resonant parameters of pacemaker IEGMs one can obtain a gauge for forecasting impending AF paroxysms. The developed approach provides a promising tool for monitoring the state of the myocardium and predicting arrhythmias. With the present state of pacemaker technology, the EDD method is a plausible approach for gaining information on the state of the myocardium in regard to resonant propagation of the excitation wave. The developed method can be the basis for a diagnostic algorithm to be implemented in implantable devices.

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Contact
Ildar Khassanov, PhD
Cardiovascular Research
Department of Biomedical Engineering
Friedrich-Alexander-University
Erlangen-Nuremberg
Turnstrasse 5
D-91054 Erlangen
Germany
Fax: +49 9131 2 71 96
E-mail: ikhassanov@biomed.uni-erlangen.de