DOI 10.1007/s10527-017-9711-x
Biomedical Engineering, Vol. 51, No. 3, September, 2017, pp. 183-188. Translated from Meditsinskaya Tekhnika, Vol. 51, No. 3, May-Jun., 2017, pp. 23-27.
Original article submitted August 5, 2016.

Current Medical and Technical Concepts in the Analysis of Endocardial Signals in Atrial Fibrillation

A. P. Zaretskiy[1]*, A. P. Kuleshov[1], and G. A. Gromyko[2]

Atrial fibrillation (AF) is the commonest arrhythmia seen in clinical practice, though our understanding of the mechanisms of its generation, propagation, and reinitiation remains incomplete. This is limiting not only from the scientific point of view, but also from the practical, as regulatory documentation for the treatment of this pathology cannot be developed without an accepted theory. There has been a recent increase in interest in a theory based on the observation that spiral waves, or rotors, with specific properties for each atrium, are the source of the trigger for fibrillation and may therefore serve as targets for radio-frequency treatment in low-invasive endocardial procedures. There is also an approach based in seeking areas of the atrium in which complex fractionated atrial endograms (CFAE) can be recorded. We present here the basic concepts of analysis of atrial signals during atrial fibrillation, reflecting both the technical and medical aspects.

Introduction

Currently the main theories of the causes of atrial fibrillation (AF) are presented to doctors to aid decision-taking in clinical cases. Nonetheless, these recommendations are not based on mathematical analysis and interpretation of signals. Thus, for example, the use of spectral analysis to identify different forms of AF in terms of its organization and formation, the contribution of ventricular components to the signal, and other characteristics may improve the effectiveness of therapeutic tactics and post-operative patient management [1].

As in recording of surface electrocardial signals (ECS), recording of endocardial signals (EnCS) during AF requires consideration of the presence of ventricular activity as noise which must be removed from the signal. Thus, correct analysis and interpretation of AF on recording EnCS requires extraction or removal of signal components associated with ventricular activity, i.e., V spikes (apparent on the surface ECG as the QRS complex and the T wave). Unfortunately, a number of factors interfere with this operation [2]. Firstly, the amplitude of the atrial spike in the EnCS is much smaller than the amplitude of the ventricular spike. Secondly, these two features have overlapping spectral distributions, making the use of filters with linear characteristics ineffective. Both simple algorithms based on the signal subtraction principle [3] and adaptive methods based on multidimensional signal processing [4] have been proposed as solutions for these problems in recent years.

From the clinical point of view, assessment of the dominant atrial frequency (DAF) is an important task in the analysis of EnCS in AF. Comparison of ECS with EnCS showed that assessment of ECS frequency in AF can be used as an index of interatrial cycle length [5]. Analysis of recorded EnCS in paroxysms of AF with low DAF suggests spontaneous termination of fibrillation activity, while high DAF is associated with drug resistance [6]. It must also be noted that the probability of successful pharmacological cardioversion is greater when DAF is <6 Hz [7]. Furthermore, for patients with DAF >6.5, the risk of early recurrence of AF is greater [8], so when selecting patients for cardioversion there is also value in analyzing DAF. Considering the question from another point of view suggests that quantitative determination of the reproducibility of paroxysms is also important in the treatment of AF, as this provides clinical information for selecting subsequent therapeutic tactics (cardioversion or radio-frequency ablation) [9-11].

[1] Moscow Institute of Physics and Technology (State University), Dolgoprudny, Moscow Region, Russia; E-mail: a.p.zaretskiy@gmail.com
[2] Academician N. N. Burdenko Main Military Clinical Hospital, Ministry of Defense of the Russian Federation, Moscow, Russia.
* To whom correspondence should be addressed.

Features of the Recording of Endocardial Signals

Like the recording of the surface ECG, the analysis and interpretation of the pathophysiological features of endocardial signals allows effective treatment strategies to be selected. This type of analysis can be used not simply to select the most effective treatment methods for individual cases, but also to develop new tactics based on the use of radio-frequency ablation [12], antiarrhythmic agents [13], and implanted cardioverter-defibrillators [14]. In this context, the blind signal processing (BSP) algorithm (Fig. 1) can be applied to EnCS to distinguish the sinus rhythm from fibrillation [15], to analyze the organization of AF [9] and its synchronization [16], and to assess the effects of radio-frequency ablation on the endocardium and its status after use of antiarrhythmic agents [17].

It should be noted that use of the BSP algorithm leads to incorrect interpretation of the EnCS when an organized atrial rhythm is seen as AF (Fig. 2).

Attention should be drawn to the fact that the flutter rhythm in Fig. 2a has a well organized structure and is discriminated from the ventricular component. This EnCS shows the ventricular component on depolarization, while the other three signals are identified using an algorithm for extracting atrial activity from the mixed signal after ventricular contraction. We note that the BSP algorithm can alter the shape of segments of the atrial signals, which is apparent on further analysis and interpretation. For unorganized AF (Fig. 2b), the BSP algorithm provides better extraction of atrial activity, decreasing the ventricular component because of the irregularity of atrial activity.

These problems with the use of the BSP algorithm led to the development of new algorithms [18]. First, a method of adaptive removal of the ventricular component (ARVC) can be used to address these tasks, this being based on the use of adaptive filtration to process the signal from the reference channel to assess noise which is then subtracted from the investigation channel [19]. In this case, the investigation channel recording the EnCS contains atrial and ventricular components. On the other hand, the reference channel can be lead II in a standard surface ECG. This channel is selected because a greater amplitude of the ventricular component and identical refractory periods are seen on the ECS and EnCS [20]. The last approach is generally used to extract the atrial signal from the EnCS in the BSP algorithm, because the atrial and ventricular activity signals are regarded as independent and uncorrelated processes, though they are mixed when the EnCS is recorded with an endocardial electrode. Thus, correct analysis of the EnCS in paroxysms of atrial fibrillation requires selection of a reference signal on the surface ECG (lead I or II). The dimensionality of the features will thus be 2×2 (2 surface and 2 endocardial leads) which also provides for analysis of dissociation. A fast independent components analysis (ICA) algorithm is preferred in this situation because of the

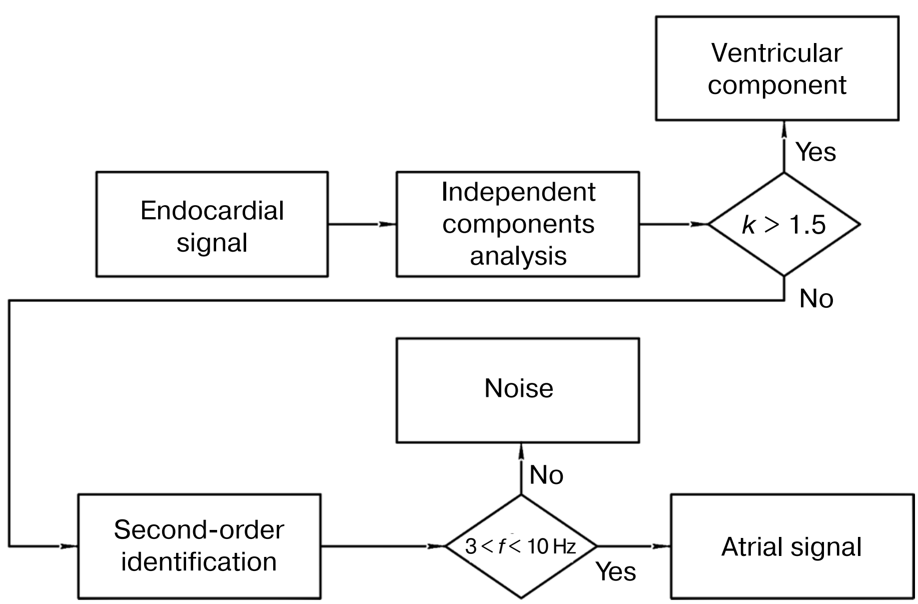

Fig. 1. Block diagram of blind signal processing algorithm.

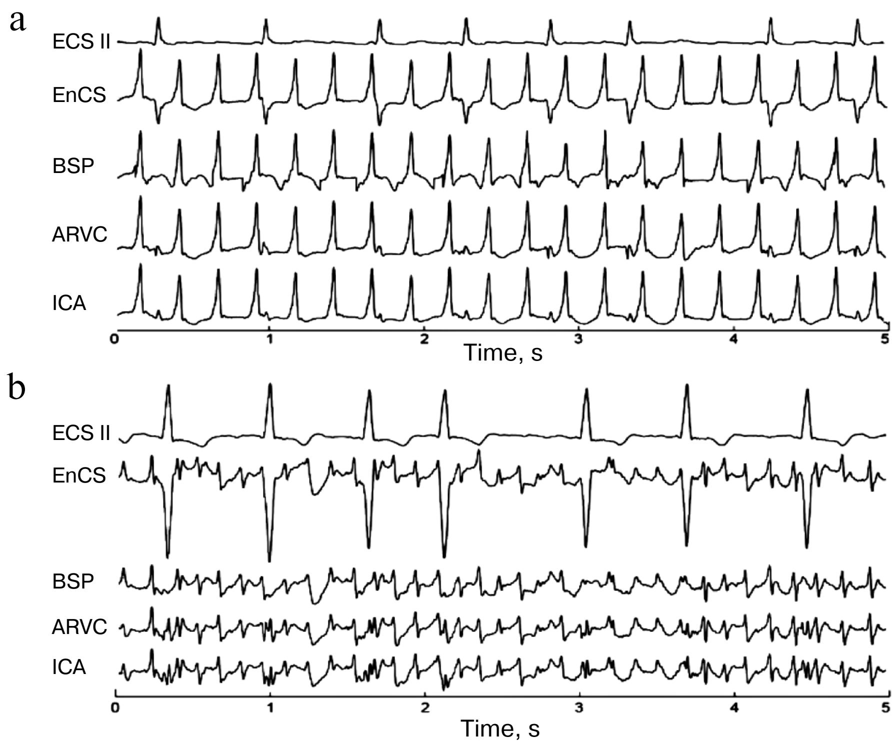

Fig. 2. Visualization of incorrect operation of BSP algorithm: a) organized AF; b) disorganized AF [18].

rapid convergence and correct working characteristics [21]. Comparison of the results of using different algorithms and methods has demonstrated the effectiveness of using ICA (Fig. 2).

Analysis of Spectral Power

Most studies determine spectra by discrete Fourier transformation (DFT) of the autocorrelation function of the signal. In this case, the atrial component of the EnCS is divided into shorter overlapping segments, which are then analyzed using a window transformation, such as the Welch transformation [22, 23]. The final stage in this approach consists of averaging the power spectra of the corresponding segments to obtain the overall spectrum of the whole EnCS.

There are two means of calculating the spectral power density of a discrete signal: 1) assessment of its autocorrelation function followed by application of DFT; 2) application of DFT to EnCS followed by calculation of the square of the value to obtain the periodogram. As shown by the evaluation of similar studies, the second method is used more often because of the efficiency of DFT, which has been demonstrated in many areas [24, 25]. Spectral analysis of signal power has to start with a plot of the results. Thus, Fig. 3, a and b, present examples of EnCS and their spectra processed and visualized using LabView.

We will consider the results presented. Thus, Fig. 3a shows an EnCS recorded on the distal electrodes of an ablation catheter at the mouth of the right superior pulmonary vein. Figure 3b shows the spectrum of the recorded signal, which allows extraction of the dominant frequencies typical of EnCS in this area of the left atrium. Before determining the spectral characteristics of the signal, some cases require window filtration, for example using a Hamming window [25]. It should be noted that on this plot (Fig. 3b), frequency on the abscissa is designated in Hz, while some clinicians find it more convenient to analyze results in beats per minute (bpm). Spectral analysis of the EnCS recorded can also differentiate signals typical of the right and left atria.

Frequency–Time Analysis

As noted previously, spectral analysis of signal power provides for evaluation of signal behavior during the time

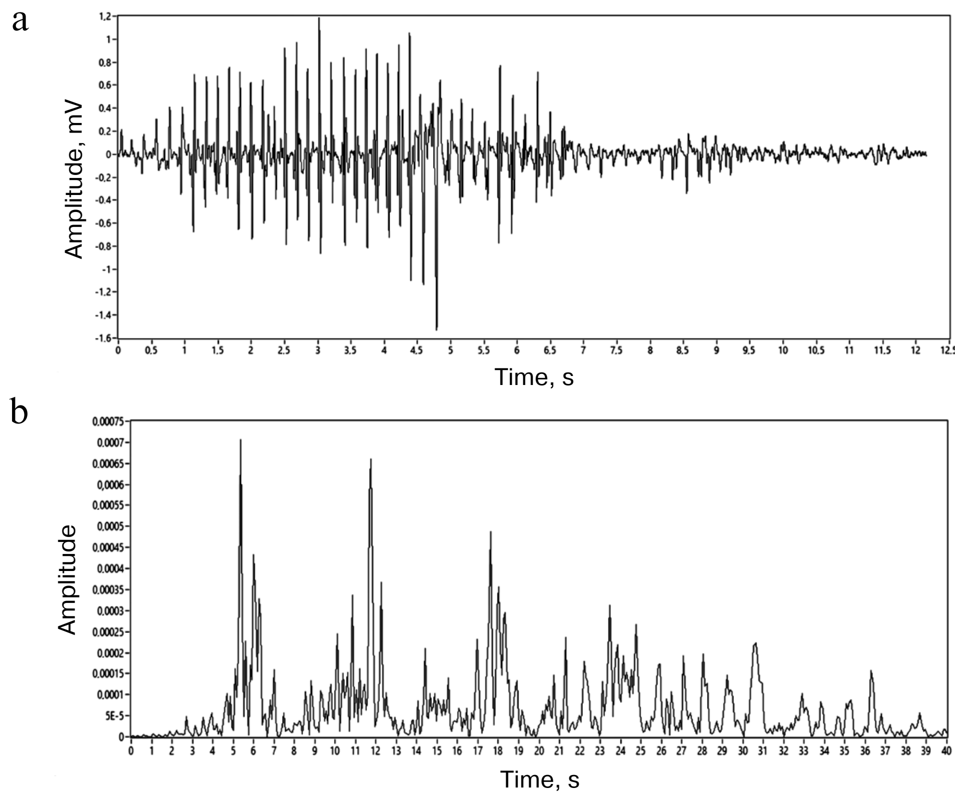

Fig. 3. Example of spectral analysis: a) Bipolar EnCS of distal catheter electrodes; b) spectrum of bipolar EnCS of distal catheter electrodes.

interval being analyzed and for recognition of the dominant frequency of atrial fibrillation (DFAF), which is a special aim from the point of view of clinical electrophysiology. Analysis of the area of interest suggests that waves of fibrillation have time-dependent properties and carry with them the main information required [26]. Results from many studies [27-33] have demonstrated the effects of the sympathetic and parasympathetic systems on the circadian rhythm, along with the frequency characteristics of the signal in these interactions. The most widely used approach to analysis of these signals is use of Fourier transformation for each segment of a EnCS during paroxysms of AF. This method is termed transient Fourier transformation (TFT). Use of this method allows for adaptive selection of a time window for analysis of the signal segment. The result is a two-dimensional function in which time and frequency resolution is selected on the basis of two criteria. As in the case of periodograms, the spectrogram of the signal can be obtained by calculating the square of the amplitude for presentation of the signal in the frequency–time space. Resolution using this method is limited by the length of the time window.

The ambiguous and controversial requirements for time and frequency resolution using the TFT method demonstrate the need to use other methods in practical electrophysiology. The TFT method is based on a linear relationship of the signal, while newer methods [29] use a square relationship, which provides higher resolution. One of these methods, effective for analysis of frequency relationships in paroxysmal AF, is the Wigner–Ville cross-distribution. This method is one of the most widely employed in practice, because it uses a time segment which is relatively long compared with the time window and is able to analyze variation in DFAF [30].

Assessment of Spectral Profile

The spectral analysis methods presented above have limitations associated with the fact that they consider only the central peak of spectral activity, harmonic analysis not being considered. However, it should be noted that assessment of the harmonics of EnCS is of clinical interest [31]. The essence of this method is the distribution of sequential short segments of atrial activity in time. Spectra and parameters describing changes in DFAF are then analyzed, and fibrillation waves are removed from the signal (assessment based on morphology). Thus, the spectrum of each segment is modeled as a whole-signal spectrum displaced in frequency and amplitude. Transformation in the frequency area is by DFT using a logarithmic frequency scale. This specific scale allows two or more spectra to be aligned by shifting them, even if they have different frequencies and associated harmonics [32]. The spectral profile is dynamically updated from preceding spectra, with comparison with each new spectrum using the weighted least squares method. Displacement in frequency is needed to obtain optimum concordance, which then gives a measure of the deviation in the rate of increase in the amplitude of atrial EnCS activity with and without fibrillation. An important feature of this approach is its improved visualization of peaks in the spectral profile. This makes the spectral profile more convenient for analysis of harmonics, whose amplitudes provide better visualization of waves of AF paroxysms.

The drawbacks of this assessment method include the fact that atrial and ventricular activity cannot be clearly separated. This requires implicit use of a Markov chain for greater accuracy on assessing DFAF [33]. Markov chains consist of a finite number of states in a defined set of probabilities for the transition between adjacent states. Analysis of these data leads to the conclusion that an optimum solution can be obtained using the Viterbi algorithm for assessment of DFAF because of the existence of a matrix of transition states and an optimal signal:noise ratio.

Conclusions

Recent advances in signal analysis and processing have now provided effective solutions for processing endocardial signals for analysis of processes occurring during atrial fibrillation. These points give value to studies of EnCS processing with the aim of removing ventricular activity from the signal for subsequent analysis of specifically atrial activity. Development of methods and means in this area has supported approaches to the analysis of fibrillation waves. Thus, the methods, algorithms, and signal processing models addressed in this article were analyzed by the authors for subsequent use in developing methods for low-invasion mapping of microrotors in the left atrium on the basis of mathematical processing and analysis of the distribution of action potentials in the endocardial area for subsequent radio-frequency treatment in patients with the paroxysmal and persistent types of atrial fibrillation.

This study was supported by the Russian Foundation for Basic Research (Grant No. 16-37-60012).

REFERENCES

1. Bollmann, A., Husser, D., Mainardi, L., Lombardi, F., Langley, P., Murray, A., Rieta, J. J., Millet, J., Olsson, S. B., Stridh, M., and Sörnmo, L., "Analysis of surface electrocardiograms in atrial fibrillation: Techniques, research, and clinical applications," Europace, **8**, No. 11, 911-926 (2006).
2. Sörnmo, L., Stridh, M., Husser, D., Bollmann, A., and Olsson, S. B., "Analysis of atrial fibrillation: From electrocardiogram signal processing to clinical management," Philos. Trans. A Math. Phys. Eng. Sci., **367**, No. 1887, 235-253 (2009).
3. Slocum, J., Byrom, E., McCarthy, L., Sahakian, A., and Swiryn, S., "Computer detection of atrioventricular dissociation from surface electrocardiograms during wide QRS complex tachycardias," Circulation, **72**, No. 5, 1028-1036 (1985).
4. Rieta, J. J., Castells, F., Sánchez, C., Zarzoso, V., and Millet, J., "Atrial activity extraction for atrial fibrillation analysis using blind source separation," IEEE Trans. Biomed. Eng., **51**, No. 7, 1176-1186 (2004).
5. Holm, M., Pehrson, S., Ingemansson, M., Sörnmo, L., Johansson, R., Sandhall, L., Sunemark, M., Smideberg, B., Olsson, C., and Olsson, S. B., "Non-invasive assessment of the atrial cycle length during atrial fibrillation in man: Introducing, validating and illustrating a new ECG method," Cardiovasc. Res., **38**, No. 1, 69-81 (1998).
6. Niwano, S., Sasaki, T., Kurokawa, S., Kiryu, M., Fukaya, H., Hatakeyama, Y., Niwano, H., Fujiki, A., and Izumi, T., "Predicting the efficacy of antiarrhythmic agents for interrupting persistent atrial fibrillation according to spectral analysis of the fibrillation waves on the surface ECG," Circulation, **73**, No. 7, 1210-1218 (2009).
7. Bollmann, A., Kanuru, N. K., McTeague, K. K., Walter, P. F., DeLurgio, D. B., and Langberg, J. J., "Frequency analysis of human atrial fibrillation using the surface electrocardiogram and its response to ibutilide," Am. J. Cardiol., **81**, No. 12, 1439-1445 (1998).
8. Langberg, J., Burnette, J. C., and McTeague, K. K., "Spectral analysis of the electrocardiogram predicts recurrence of atrial fibrillation after cardioversion," J. Electrocardiol., **31**, 80-84 (1998).
9. Faes, L., Nollo, G., Antolini, R., Gaita, F., and Ravelli, F., "A method for quantifying atrial fibrillation organization based on wave-morphology similarity," IEEE Trans. Biomed. Eng., **49**, No. 12, 1504-1513 (2002).
10. Alcaraz, R. and Rieta, J. J., "A review on sample entropy applications for the non-invasive analysis of atrial fibrillation electrocardiograms," Biomed. Signal Process Control, **5**, 1-14 (2010).
11. Sih, H. J., "Measures of organization during atrial fibrillation," Annali dell'Istituto Superior di Sanita, **37**, No. 3, 361-369 (2001).
12. Nademanee, K., McKenzie, J., Kosar, E., Schwab, M., Sunsaneewitayakul, B., Vasavakul, T., Khunnawat, C., and Ngarmukos, T., "A new approach for catheter ablation of atrial fibrillation: Mapping of the electrophysiologic substrate," J. Am. Coll. Cardiol., **43**, No. 11, 2054-2056 (2004).
13. Shan, Z., Van Der Voort, P. H., Blaauw, Y., Duytschaever, M., and Allessie, M. A., "Fractionation of electrograms and linking of activation during pharmacologic cardioversion of persistent atrial fibrillation in the goat," J. Cardiovasc. Electrophysiol., **15**, No. 5, 572-580 (2004).

14. Dosdall, D. J. and Ideker, R. E., "Intracardiac atrial defibrillation," Heart Rhythm, **4**, No. 3, 51-56 (2007).
15. Shkurovich, S., Sahakian, A. V., and Swiryn, S., "Detection of atrial activity from high-voltage leads of implantable ventricular defibrillators using a cancellation technique," IEEE Trans. Biomed. Eng., **45**, No. 2, 229-234 (1998).
16. Mase, M., Faes, L., Antolini, R., Scaglione, M., and Ravelli, F., "Quantification of synchronization during atrial fibrillation by Shannon entropy: Validation in patients and computer model of atrial arrhythmias," Physiol. Meas., **26**, No. 6, 911-923 (2005).
17. Houben, R. P. and Allessie, M. A., "Processing of intracardiac electrograms in atrial fibrillation. Diagnosis of electropathological substrate of AF," IEEE Eng. Med. Biol. Mag., **25**, No. 6, 40-51 (2006).
18. Rieta, J. J. and Hornero, F., "Comparative study of methods for ventricular activity cancellation in atrial electrograms of atrial fibrillation," Physiol. Meas., **28**, No. 8, 925-936 (2007).
19. Widrow, B., Glover, J. R., McCool, J. M., et al., "Adaptive noise cancelling: Principles and applications," Proc. IEEE, **63**, No. 12, 1692-1716 (1975).
20. Malmivuo, J. and Plonsey, R. Bioelectromagnetism: Principles and Applications of Bioelectric and Biomagnetic Fields, Oxford University Press (1995), p. 358.
21. Hyvarinen, A., Karhunen, J., and Oja, E., Independent Component Analysis, John Wiley & Sons, Inc. (2001), p. 412.
22. Welch, P. D., "Use of Fast Fourier Transform for estimation of power spectra: A method based on time averaging over short modified periodograms," IEEE Trans. Audio Electroacoust., **15**, No. 2, 70-73 (1967).
23. Hamming, R. W., Digital Filters, Prentice-Hall signal processing series, Prentice-Hall, Englewood Cliffs (1977), p. 283.
24. Manolakis, D. G., Ingle, V. K., and Kogon, S. M., Statistical and Adaptive Signal Processing: Spectral Estimation, Signal Modeling, Adaptive Filtering, and Array Processing, Artech House, Boston (2005), p. 485.
25. Najim, M., Modeling, Estimation and Optimal Filtering in Signal Processing, Digital Signal and Image Processing Series, J. Wiley & Sons, London (2008), p. 372.
26. Stridh, M., Sörnmo, L., Meurling, C. J., and Olsson, S. B., "Characterization of atrial fibrillation using the surface ECG: Time-dependent spectral properties," IEEE Trans. Biomed. Eng., **48**, No. 1, 19-27 (2001).
27. Shkurovich, S., Sahakian, A. V., and Swiryn, S., "Detection of atrial activity from high-voltage leads of implantable ventricular defibrillators using a cancellation technique," IEEE Trans. Biomed. Eng., **45**, No. 2, 229-234 (1998).
28. Kuleshov, A. P., Ilyin, A. V., and Zaretsky, A. P., "Continuous visualization of P–Q intervals in portable devices for monitoring human organism functional state," Sovremen. Tekhnol. Med., **8**, No. 1, 41-47 (2016).
29. Cohen, L., Time-Frequency Analysis, Prentice Hall PTR, Englewood Cliffs, N. J. (1995), p. 451.
30. Boashash, B., "Estimating and interpreting the instantaneous frequency of a signal. Algorithms and applications," Proc. IEEE, **80**, No. 4, 540-568 (1992).
31. Everett, T. H., 4th, Moorman, J. R., Kok, L. C., Akar, J. G., and Haines, D. E., "Assessment of global atrial fibrillation organization to optimize timing of atrial defibrillation," Circulation, **103**, No. 23, 2857-2861 (2001).
32. Stridh, M., Sörnmo, L., Meurling, C. J., and Olsson, S. B., "Sequential characterization of atrial tachyarrhythmias based on ECG time–frequency analysis," IEEE Trans. Biomed. Eng., **51**, No. 1, 100-114 (2004).
33. Sandberg, F., Stridh, M., and Sörnmo, L., "Frequency tracking of atrial fibrillation using hidden Markov models," IEEE Trans. Biomed. Eng., **55**, No. 2, 502-511 (2008).