



An efficient method of addressing ectopic beats: new insight into data preprocessing of heart rate variability analysis*

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Abstract: Heart rate variability (HRV) analysis is affected by ectopic beats. An efficient method was proposed to deal with the ectopic beats. The method was based on trend correlation of the heart timing signal. Predictor of R-R interval (RRI) value at ectopic beat time was constructed by the weight calculation and the slope estimation of preceding normal RRI. The type of ectopic beat was detected and replaced by the predictor of RRI. The performance of the simulated signal after ectopic correction was tested by the standard value using power spectrum density (PSD) estimation, whereas the results of clinical data with ectopic beats were compared with the adjacent ectopic-free data. The result showed the frequency indexes after ectopy corrected had less error than other methods with the test of simulated signal and clinical data. It indicated our method could improve the PSD estimation in HRV analysis. The method had advantages of high accuracy and real time properties to recover the sinus node modulation.

Key words: Frequency domain, Ectopic beat, Heart rate variability (HRV), Power spectrum density
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1 Introduction

Heart rate variability (HRV) analysis is widely used to evaluate the fluctuations of heart beat signals in many fields (Camm *et al.*, 1996; Bettoni and Zimmermann, 2002; Maestri *et al.*, 2010). Frequency domain analysis of HRV is efficient to reflect the automatic nerves system (ANS) modulation containing sympathetic and parasympathetic nerve activities by the indexes of low frequency (LF, 0.04–0.15 Hz) and high frequency (HF, 0.15–0.40 Hz) (Myers *et al.*, 1986; Li *et al.*, 2009). The indexes of frequency analysis are obtained from power spectrum

density (PSD) to estimate ANS activity modulated by the sinus node (SN).

The HRV signal is expected to include normal R-R interval (RRI) modulated by SN, but will be disturbed by ectopic beats that are not originating from SN. The ectopy beats are mainly caused by premature beats, tachycardia, and other arrhythmias and even by QRS wave misdetections (Sapoznikov *et al.*, 1992). They distort HRV signal with spurious frequency components and random spectra in the LF and HF bandwidths. The ectopic beats could be detected from the irregular RRI that results in a sharp transient of time domain indexes at the ectopic beat.

Some techniques are introduced to correct the ectopic confusion by deleting the beat or replacing the beat by a middle value. When the ectopic beat is deleted, the RRI is twice the mean normal heart period (HP); replacing the beat with a middle value is

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proper in the case of a ventricular beat. Another correction is performed by spline interpolation on the erroneous beats to aid in the avoidance of substantial disturbance of PSD estimation (Acar *et al.*, 2000). Unfortunately, when the atrial premature contraction (APC) occurs, the SN rhythm is reset and the coupled RRI and compensational RRI are shorter than two normal RRIs. The interpolation on the period of APC may not reflect the SN rhythm properly. These methods are based on the beat differences as HP or heart rate (HR). The heart timing (HT) method is oriented to the beat location band limited by SN modulation. The HT method (Mateo and Laguna, 2003; Solem *et al.*, 2006) is proposed to correct the ectopic beats. The ectopic RRI on the ectopic beat was removed and then replaced by a proper one in order to restore the SN modulation. The solution was presented to minimize the effect of these types of anomalies in the series of beats and the corresponding PSD-derived clinical indexes. These methods showed a better ability to reset the activity of the SN by PSD test. While providing excellent results, HT-based correction was also associated with heavy computation in prior work.

Our work adopted a trend-predict correction (TPC) method to detect the ectopic beats in RRI sequence. On the presence of ectopic beats, the TPC method based on HT signal was proposed to handle the ectopic beats. The TPC method was tested by a simulated HRV signal compared with other methods. The TPC method was presented to resolve the PSD of actual electrocardiograph (ECG) signal containing ectopic beats from European ST-T database.

2 Materials and methods

2.1 Ectopic correction algorithm

An algorithm was designed to detect the ectopic beats (Mateo and Laguna, 2003), and the deviation value in time t_k was:

$$|r_k| = 2 \left| \frac{t_{k-1} - 2t_k + t_{k+1}}{(t_{k-1} - t_k)(t_{k-1} - t_{k+1})(t_k - t_{k+1})} \right| < U, \quad (1)$$

where t_k is the time of the k th beat following the initial event, t_{k-1} and t_{k+1} are the front and back time, re-

spectively, and U is the suitable threshold which is calculated as function of the standard deviation (SD) to detect the ectopic beat. With this method, the time of ectopic beat occurring could be detected.

The correction method is based on the correlation of preceding sinus beats on the presence of ectopic beat, and is called the TPC method.

If the normal RRI exists before the time t_k when ectopic beat occurs, the predictive RRI (RRI_{pred}) in t_k is constructed as:

$$RRI_{pred} = RRI_{trend} + RRI_{turb}, \quad (2)$$

where RRI_{trend} is reflected by trending component, and RRI_{turb} is the turbulence value between adjacent RRIs. RRI_{trend} is calculated based on weighted value of preceding RRI sequence.

$$RRI_{trend} = \sum_{t=t_k-n}^{t_k-1} w(t) \times y(t), \quad (3)$$

where $y(t)$ is RRI value at time t , n is the number of prior RRI, and $w(t)$ is the weight at time t , which is higher near t_k .

Then RRI_{turb} is calculated by $I[t_k]$ and $E[t_k]$:

$$RRI_{turb} = I[t_k] \times E[t_k]. \quad (4)$$

$I[t_k]$ is judged by the signs of k_1 and k_2 . A tiny value will be added to k_1 and k_2 to avoid zero.

$$I[t_k] = k_1 \times k_2 \times (k_1 + k_2) / |k_1 \times k_2 \times (k_1 + k_2)|. \quad (5)$$

k_1 and k_2 are calculated to present the slopes at t_{k-1} and t_{k-2} :

$$k_1 = (y(t_{k-1}) - y(t_{k-2})) / (y(t_{k-1}) + y(t_{k-2})), \quad (6)$$

$$k_2 = (y(t_{k-2}) - y(t_{k-3})) / (y(t_{k-2}) + y(t_{k-3})). \quad (7)$$

$E[t_k]$ is determined by k_1 , k_2 , RRI_{trend} , and SD_{RRI} :

$$E[t_k] = RRI_{trend} \times \sqrt{|k_1 \times k_2|} / (a + b / SD_{RRI}), \quad (8)$$

where SD_{RRI} is the SD of preceding RRI, and a and b are predictive coefficients.

If the ectopic beats occur at time t_k , the characteristics of ectopic RRI before and after t_k are judged

by RRI_{pred} . The types of ectopic beats such as APC and premature ventricular contraction (PVC) are determined from their characteristics of RRI. For example, the threshold of coupled RRI of APC is lower than $0.85 \times RRI_{pred}$. The sums of coupled RRI and compensatory RRI of APC are lower than $2 \times RRI_{pred}$. When the APC is detected, the coupled RRI is replaced mainly by RRI_{pred} , and the compensatory RRI at t_{k+1} is replaced by next predictive RRI.

2.2 Simulated HRV signal

The simulated signal is:

$$y(t) = 4\cos(2\pi t \times 0.02) + \cos(2\pi t \times 0.095) + \cos(2\pi t \times 0.275) + C, \quad (9)$$

where $y(t)$ is the simulated RRI of HRV signal, t is the time of each RRI, and C is the constant value. $y(t)$ consists of several items that represent different frequency variables. The three cosine components express three frequency components with a central frequency at 0.020, 0.095, and 0.275 Hz, corresponding to indexes of very low frequency (VLF), LF, and HF in frequency domain. It is a simple simulated HRV signal including frequency components with enhancing VLF power (direct current (DC) component).

$y(t)$ reflects the regular heart beat period from SN modulation except that ectopic beats happen. It is hypothesized that one ectopic beat occurred at the time t_k . The RRI at the ectopic time is disturbed by more than 20% alteration of normal RRI.

On the case of PVC, the coupled RRI $y(t_k)_{PVC}$ and the compensatory RRI $y(t_{k+1})_{PVC}$ are simulated:

$$\begin{cases} y(t_k)_{PVC} = 0.5 \times (y(t_k) + y(t_{k+1})) - 0.2 \times C, \\ y(t_{k+1})_{PVC} = 0.5 \times (y(t_k) + y(t_{k+1})) + 0.2 \times C. \end{cases} \quad (10)$$

The two RRIs of APC below are obtained, when $y(t_{k+1})_{APC}$ is not fully compensated:

$$\begin{cases} y(t_k)_{APC} = 0.5 \times (y(t_k) + y(t_{k+1})) - 0.2 \times C, \\ y(t_{k+1})_{APC} = 0.5 \times (y(t_k) + y(t_{k+1})) + 0.1 \times C. \end{cases} \quad (11)$$

The simulated HRV signals containing ectopic beats are achieved as Eqs. (10) and (11). The signals

are corrected by the TPC method in Section 2.1 using the preceding normal RRI before the ectopic beat(s), where the positions of ectopic beats are detected with Eq. (1). The spline interpolation correction (SIC) method and middle value replacing (MVR) method are as contrast. In SIC, the ectopic RRI is removed, and the new RRI is got on the period of ectopic beats by cubic spline interpolation with resample frequency at 4 Hz. In MVR method the ectopic RRI is replaced by the middle value of the two abnormal RRIs. The signals after TPC and MVR are also resampled at 4 Hz.

2.3 Clinical data correction

The evaluation protocol of correction method for clinical data is based on the hypothesis that the frequency indexes at the nearby segments A, B, and C in limited time are similar or are stably changing after SN modulation (Fig. 1). Thus, the differences of frequency indexes between segments A and B, B and C were smaller. It will be possible to evaluate the behavior of ectopic correction method when comparing ectopic-beats-free behavior in segments A and C with the ectopic beats-treated behavior in B (Mateo and Laguna, 2003). The differences of PSD estimation between segments are shown as mean \pm SD, where mean reflects the accuracy of correction result, and SD reflects the precision. The smaller the mean and SD, the higher the accuracy and precision that will be achieved.

A sum of 132 pieces of ECG episodes were gained from the first 48 of 90 data in the European ST-T database (ESDB) previously studied by Taddei *et al.* (1992). These data contained 132 ectopic episodes from annotation files as follows: 91 episodes containing one ectopic beat, 23 containing two, 18 containing three or more. Each ECG episode was divided into three overlapping, 4-min segments: A, B, and C (Fig. 1). Segments A and C had no ectopic beats, whereas B contained the ectopic beat(s). Segment B was between segments A and C, having the overlapping episodes with A and C. The ectopic beats during segment B were handled with TPC method or other methods.

Significant difference between two methods or between two segments was evaluated by paired-sample t -test ($P < 0.05$).

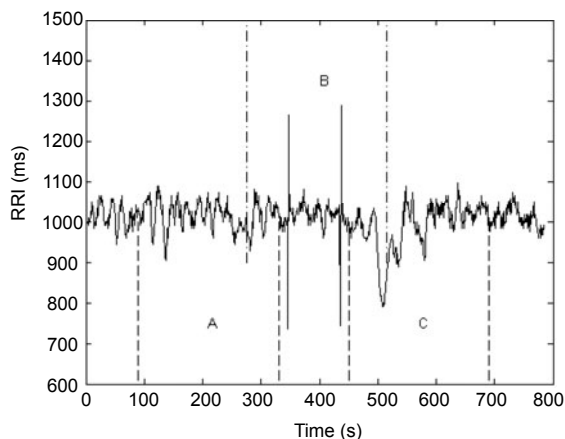


Fig. 1 HRV signals of test window, segments A, B, and C. A and C have no ectopic beats, segment B has at least one. A, B and C are set to four minutes. Segments A and B, C and B have overlapping episodes

2.4 Advanced detrending method

The real HRV signal composed of RRI sequence is usually nonstationary due to hormone modulation and noises (Tarvainen *et al.*, 2002), which are reflected by the VLF and ultra low frequency (ULF). VLF and ULF, called as DC components or trending components by us, have uncertain influence on the PSD estimation (Myers *et al.*, 1992; van Schelven *et al.*, 2000). As the sample length of HRV signal is short (such as four minutes duration), the differential ratio of frequency analysis is unable to distinguish the DC component and other frequency bandwidths, and then the frequency confusion occurs. If the DC component is not removed, it will enhance the LF and HF components. Some works have presented detrending techniques to eliminate the component (Mitov, 1998; Tarvainen *et al.*, 2002; Colak, 2009).

The detrending preprocessing is carried out together with ectopic correction to avoid the influence of DC after spline interpolation.

The RRI sequences are presented by variable Z :

$$Z = RRI_1, RRI_2, RRI_3, \dots, RRI_n, \quad (12)$$

where n is the number of RRI.

Z is divided to Z_{stat} and Z_{trend} ($Z = Z_{\text{stat}} + Z_{\text{trend}}$), where Z_{stat} contains the components of LF and HF. Z_{trend} reflecting the trending component (DC) should be removed.

With the advanced detrending method, Z_{stat} is calculated as:

$$Z_{\text{stat}} = Z - Z_{\text{trend}} = (\mathbf{I} - (\mathbf{I} + \lambda^2 \mathbf{D}_2^T \mathbf{D}_2)^{-1}) \times Z. \quad (13)$$

Here, parameter \mathbf{I} is the observation matrix, \mathbf{D}_2 is the discrete approximation of the second derivative operator. λ is regularization parameter which could be adjusted. When λ is set as 20 and 300, the cut-off frequency is 0.041 and 0.011 times the sampling frequency, respectively. Z_{stat} is a new HRV signal sequence, which contains only the useful frequency components. The method will show its performance with the simulated signal Eq. (9) and be applied to the actual HRV signal.

3 Results

3.1 Ectopic beat simulation

The simulated HRV signals from Eqs. (9)–(11) are introduced to test the ectopic correction methods. In Table 1, the initial value is the initial result of PSD estimation of the simulated HRV signal containing

Table 1 PSD estimations of simulated HRV signals with ectopic correction methods

Simulated HRV signal	UF	LF	HF	LVH
Initial value	1.00	0.50	0.50	1.00
Detrending value	0.963±0.000	0.458±0.000	0.505±0.000	0.908±0.000
One APC existing	1.820±0.200	0.549±0.048	1.271±0.186	0.440±0.069
One PVC existing	2.378±0.321	0.570±0.054	1.808±0.300	0.323±0.053
APC+PVC by TPC	0.964±0.015	0.459±0.011	0.505±0.010	0.910±0.026
APC+PVC by MVR	1.078±0.053	0.507±0.038	0.571±0.033	0.890±0.080
APC+PVC by SIC	0.959±0.013	0.463±0.012	0.496±0.002	0.933±0.023

Data are expressed as mean±SD. PSD is estimated using Welch's periodogram. UF=LF+HF, LVH=LF/HF. The simulated HRV signal is from Eq. (9), with $t=1$ to 300 s, $C=100$. Simulated APC or PVC is at some time (t_k , $k=51-250$) in the signal. On the case of APC+PVC, the distance between APC and PVC is changing from -200 to 200 with steps of 2 beats

only normal RRI. The detrending value is the PSD estimation of the simulated normal signal with the processing of detrending and resample at 4 Hz. The other estimations of the signals containing ectopic beats are made by the process of detrending. The detrending value is regarded as the standard value for correction methods.

Table 1 shows the results of PSD indexes with the influence of PVC or APC simulated 200 times, where the four indexes (UF, LF, HF, and LVH) are disturbed largely in one APC existing or one PVC existing. It indicates that HF enhances more largely than LF when ectopic beats occur. It shows the results when the signals containing both APC and PVC are corrected by the TPC, MVR and SIC methods. The result of TPC method is better than those of the methods of MVR and SIC. It had an advantage to recover the original indexes of HRV PSD.

3.2 Clinical data results

Table 2 shows the differences between the clinical indexes at LF and HF bands by TPC and SIC methods during segments A, B, and C as defined in Section 2.3. ΔLF_A is the difference of LF during segment A between TPC and SIC methods. It is shown during all segments that the SIC method obtains more power by means of LF and HF than TPC when all the means of the differences are negative. The two methods had more differences on correcting segment B presented by ΔLF_B and ΔHF_B , whereas their differences are negligible during segments A and C.

Table 2 Differences between the clinical indexes at LF and HF bands by means of TPC and SIC methods during segments A, B, and C

Diff	Mean±SD	P	Diff	Mean±SD	P
ΔLF_A	-11±65	0.057	ΔHF_A	-8±101	0.359
ΔLF_B	-93±502*	0.034*	ΔHF_B	-71±574	0.157
ΔLF_C	-15±82*	0.033*	ΔHF_C	-7±53	0.131

*Significant difference ($P < 0.05$)

Table 3 shows the differences between each two segments with TPC and SIC methods. For example ΔLF_{AB} is the difference between segments A and B with TPC or SIC method. It can be observed that when the segment B is involved, the mean and SD by SIC are larger than those by TPC, whereas the SD is higher involving segment B than that between the normal segments A and C with SIC method.

4 Discussion

The detrending method is introduced by Tarvainen *et al.* (2002). It was adopted in this research as a necessary preprocessing technique. Because the DC component exists in the normal RRI sequence, its influence is only seen in simulated HRV signals. Kim *et al.* (2009) found the Welch method and autoregressive (AR) model were not appropriate for calculating the LF and HF tested by the real HRV signals resampled at 4 Hz. However, after the processing of detrending, it showed that Welch and AR were able to estimate PSD with less error (Table 1).

Some researchers (Dimmer *et al.*, 1998; Lombardi *et al.*, 2004) had different findings in the LF index, while some (Zimmermann and Kalusche, 2001; Bettoni and Zimmermann, 2002; Amar *et al.*, 2003; Ovreiu *et al.*, 2008) thought that the HF was dominant in paroxysmal atrial fibrillation (PAF) onset or HF was the independent predictor to PAF recurrence (Yamada *et al.*, 2009). Others had their own opinions on LF or HF (Huang *et al.*, 1998; Miyakoshi *et al.*, 2009). These may be due to the different preprocessing of DC and ectopic beats that enhance LF and HF separately.

Some works (Mateo and Laguna, 2003; Solem *et al.*, 2006) used new methods for ectopy correction based on HT signals referred to as the DFT of the interpolated HT signal (FHTIS) method (Table 4), comparing spline interpolation of the 14th order with the incorrect RRI removed (DFT of the interpolated

Table 3 Differences between different segments with SIC and TPC methods

Method	ΔLF_{AB}	ΔLF_{BC}	ΔLF_{AC}	ΔHF_{AB}	ΔHF_{BC}	ΔHF_{AC}
SIC	-111±560*	85±557	-26±394	-101±584*	52±601	-50±279
TPC	-28±245	7±296	-21±378	-38±147*	-13±197	-51±266*

*Significant difference ($P < 0.05$)

Table 4 Differences between segments by FHTIS, FHRIS, SIC, and TPC methods using European ST-T database

Method	ΔLF_{AB}	ΔLF_{BC}	ΔLF_{AC}	ΔHF_{AB}	ΔHF_{BC}	ΔHF_{AC}
FHTIS ¹	-71±575*	103±415*	32±670	-58±213*	38±177*	-20±186
FHTIS ²	-71±575	103±415	32±670	-58±213	38±177	-20±186
FHRIS ^{1,2}	-1256±11767	1288±11657	31±658	-331±2323	314±2292	-17±140
SIC	-111±560*	85±557	-26±394	-101±584*	52±601	-50±279
TPC	-28±245	7±296	-21±378	-38±147*	-13±197	-51±266*

* Significant difference ($P < 0.05$). ¹ Mateo and Laguna, 2003; ² Solem *et al.*, 2006

HR signals (FHRIS)). The 132 pieces of ECG episodes from ESDB were obtained to test their method. The work of FHTIS by Solem *et al.* (2006) continued the work by Mateo and Laguna (2003) to decrease the computation amount for real-time analysis. It was mentioned that the LF index estimation had different precision in their methods when they obtained satisfactory results. It shows FHRIS had poor performance for ectopy correction, whereas SIC was using the cubic spline interpolation.

The HRV signal from ESDB had some acceleration and deceleration of HR. Therefore, the mean and SD are larger in ESDB data than those of simulated signals with TPC method. It showed that the differences of LF and HF between segments A and B and between B and C were lower than the differences between A and C with TPC. The TPC could minimize the error in correcting segment B. In addition, the ectopic beats were detected before each correction method. The ectopic detecting method such as Eq. (1) is not a point in our work.

Detrending decreased the LF by approximately 9% and increased HF by approximately 1% as shown in Table 1. The correction result of the TPC contained a lesser error ratio when considering the effect of detrending. The SIC method had superior performance when dealing with the simulated HRV signal with ectopic beats. SIC had small differences from TPC during the segments A and C of clinical data and may be due to the fact that some RRIs were corrected by TPC. Otherwise, the RRI after SIC may be not suitable to calculate the time domain indexes of HRV.

The preceding normal RRI with the numbers of 8 to 16 is applied to calculate the predictive RRI in TPC, and sometimes the RRI sequence behind the ectopic beat could be used. The total time of the procedure to deal with 300-point episode of simulated HRV signal is no more than 1 s where it requires 114 s to deal with

200 simulated signal numbers. According to the simulation and clinical test, the TPC had a real-time advantage to recover the SN modulation. The indexes of HRV analysis are widely used; however, the HRV estimation could be more accurate with efficient preprocessing methods.

5 Conclusions

The new ectopic correction method was proposed to deal with ectopic beats in the HRV frequency analysis. This method has an advantage to recover the SN rhythm through the PSD estimation by simulated data and clinical data when compared with other methods. The correction method is useful to the real-time HRV analysis. Lastly, this preprocessing method requires further investigation.

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References

- Acar, B., Savelieva, I., Hemingway, H., Malik, M., 2000. Automatic ectopic beat elimination in short-term heart rate variability measurement. *Comput. Methods Programs Biomed.*, **63**(2):123-131. [doi:10.1016/S0169-2607(00)00081-X]
- Amar, D., Zhang, H., Miodownik, S., Kadish, A.H., 2003. Competing autonomic mechanisms precede the onset of postoperative atrial fibrillation. *J. Am. Coll. Cardiol.*, **42**(7):1262-1268. [doi:10.1016/S0735-1097(03)00955-0]
- Bettoni, M., Zimmermann, M., 2002. Autonomic tone variations before the onset of paroxysmal atrial fibrillation. *Circulation*, **105**(23):2753-2759. [doi:10.1161/01.CIR.0000018443.44005.D8]

- Camm, A.J., Malik, M., Bigger, J.T., Breithardt, G., Cerutti, S., Cohen, R.J., Coumel, P., Fallen, E.L., Kennedy, H.L., Kleiger, R.E., et al., 1996. Heart rate variability: standards of measurement, physiological interpretation, and clinical use. *Circulation*, **93**(5):1043-1065. [doi:10.1161/01.CIR.93.5.1043]
- Colak, O.H., 2009. Preprocessing effects in time-frequency distributions and spectral analysis of heart rate variability. *Digital Signal Process.*, **19**(4):731-739. [doi:10.1016/j.dsp.2008.09.004]
- Dimmer, C., Tavernier, R., Gjorgov, N., van Nooten, G., Clement, D.L., Jordaens, L., 1998. Variations of autonomic tone preceding onset of atrial fibrillation after coronary artery bypass grafting. *Am. J. Cardiol.*, **82**(1):22-25. [doi:10.1016/S0002-9149(98)00231-8]
- Huang, J.L., Wen, Z.C., Lee, W.L., Chang, M.S., Chen, S.A., 1998. Changes of autonomic tone before the onset of paroxysmal atrial fibrillation. *Int. J. Cardiol.*, **66**(3):275-283. [doi:10.1016/S0167-5273(98)00241-1]
- Kim, K.K., Kim, J.S., Lim, Y.G., Park, K.S., 2009. The effect of missing RR-interval data on heart rate variability analysis in the frequency domain. *Physiol. Meas.*, **30**(10):1039-1050. [doi:10.1088/0967-3334/30/10/005]
- Li, H., Ma, X.Q., Ye, F., Zhang, J., Zhou, X., Wang, Z.H., Li, Y.M., Zhang, G.Y., 2009. Expressions of cardiac sympathetic norepinephrine transporter and β_1 -adrenergic receptor decreased in aged rats. *J. Zhejiang Univ.-Sci. B*, **10**(3):203-210. [doi:10.1631/jzus.B0820213]
- Lombardi, F., Tarricone, D., Tundo, F., Colombo, F., Belletti, S., Fiorentini, C., 2004. Autonomic nervous system and paroxysmal atrial fibrillation: study based on the analysis of RR interval changes before, during and after paroxysmal atrial fibrillation. *Eur. Heart J.*, **25**(14):1242-1248. [doi:10.1016/j.ehj.2004.05.016]
- Maestri, R., Raczak, G., Danilowicz-Szymanowicz, L., Torunski, A., Sukiennik, A., Kubica, J., La Rovere, M.T., Pinna, G.D., 2010. Reliability of heart rate variability measurements in patients with a history of myocardial infarction. *Clin. Sci.*, **118**(3):195-201. [doi:10.1042/CS20090183]
- Mateo, J., Laguna, P., 2003. Analysis of heart rate variability in the presence of ectopic beats using the heart timing signal. *IEEE Trans. Biomed. Eng.*, **50**(3):334-343. [doi:10.1109/TBME.2003.808831]
- Mitov, I.P., 1998. A method for assessment and processing of biomedical signals containing trend and periodic components. *Med. Eng. Phys.*, **20**(9):660-668. [doi:10.1016/S1350-4533(98)00077-0]
- Miyakoshi, M., Ikeda, T., Miwa, Y., Sakaki, K., Ishiguro, H., Abe, A., Tsukada, T., Mera, H., Yusu, S., Yoshino, H., 2009. Quantitative assessment of cibenzoline administration for vagally mediated paroxysmal atrial fibrillation using frequency-domain heart rate variability analysis. *J. Cardiol.*, **54**(1):86-92. [doi:10.1016/j.jcc.2009.04.009]
- Myers, G.A., Martin, G.J., Magin, N.M., Barnett, P.S., Schaad, J.W., Weiss, J.S., Lesch, M., Sigher, D.H., 1986. Power spectral analysis of heart rate variability in sudden cardiac death: comparison to other methods. *IEEE Trans. Biomed. Eng.*, **33**(12):1149-1156. [doi:10.1109/TBME.1986.325694]
- Myers, G., Workman, M., Birkett, C., Ferguson, D., Kienzle, M., 1992. Problems in measuring heart rate variability of patients with congestive heart failure. *J. Electrocardiol.*, **25**:214-219. [doi:10.1016/0022-0736(92)90105-9]
- Ovrieu, M., Nair, B.G., Xu, M., Bakri, M.H., Li, L., Wazni, O., Fahmy, T., Petre, J., Starr, N.J., Sessler, D.I., et al., 2008. Electrocardiographic activity before onset of postoperative atrial fibrillation in cardiac surgery patients. *Pacing Clin. Electrophysiol.*, **31**(11):1371-1382. [doi:10.1111/j.1540-8159.2008.01198.x]
- Sapoznikov, D., Luria, M.H., Mahler, Y., Gostman, M.S., 1992. Computer-processing of artifact and arrhythmias in heart-rate-variability analysis. *Comput. Methods Programs Biomed.*, **39**(1-2):75-84. [doi:10.1016/0169-2607(92)90060-K]
- Solem, K., Laguna, P., Sornmo, L., 2006. An efficient method for handling ectopic beats using the heart timing signal. *IEEE Trans. Biomed. Eng.*, **53**(1):13-20. [doi:10.1109/TBME.2005.859780]
- Taddei, A., Distanto, G., Emdin, M., Pisani, P., Moody, G.B., Zeelenberg, C., Marchesi, C., 1992. The European ST-T database: standard for evaluating systems for the analysis of ST-T changes in ambulatory electrocardiography. *Eur. Heart J.*, **13**(9):1164-1172.
- Tarvainen, M.P., Ranta-aho, P.O., Karjalainen, P.A., 2002. An advanced detrending method with application to HRV analysis. *IEEE Trans. Biomed. Eng.*, **49**(2):172-175. [doi:10.1109/10.979357]
- van Schelven, L.J., Oey, P.L., Klein, I.H.I., Barnas, M.G.W., Blankestijn, P.J., Wieneke, G.H., 2000. Observer variations in short period spectral analysis of heart rate variability. *J. Auton. Nerv. Syst.*, **79**(2-3):144-148. [doi:10.1016/S0165-1838(99)00106-X]
- Yamada, T., Yoshida, N., Murakami, Y., Okada, T., Yoshida, Y., Muto, M., Inden, Y., Murohara, T., 2009. Vagal modification can be a valid predictor of late recurrence of paroxysmal atrial fibrillation independent of the pulmonary vein isolation technique. *Circ. J.*, **73**(9):1606-1611. [doi:10.1253/circj.CJ-09-0158]
- Zimmermann, M., Kalusche, D., 2001. Fluctuation in autonomic tone is a major determinant of sustained atrial arrhythmias in patients with focal ectopy originating from the pulmonary veins. *J. Cardiovasc. Electrophysiol.*, **12**(3):285-291. [doi:10.1046/j.1540-8167.2001.00285.x]