Trajectories of Spectral Clusters of HRV Related to Myocardial Ischemic Episodes

J. Souza Neto[1], João Luiz A. de Carvalho[2], Francisco Assis de O. Nascimento[3], Adson F. da Rocha[4], Luiz F. Junqueira Jr.[5]

[1,2,3,4]Grupo de Processamento Digital de Sinais (GPDS), Departamento de Engenharia Elétrica (ENE), Universidade de Brasília (UnB), Brasília-DF, Brasil, 70910-900
Phone: +55 61 273 5977, Fax: +55 61 307 2328
[5]Laboratório Cardiovascular , Faculdade de Medicina (FMD), Universidade de Brasília (UnB), Brasília-DF, Brasil, 70910-900
Phone: +55-61-307-2274, Fax: +55-61-273-3907
szneto@uol.com.br, jlacarv@terra.com.br, assis@unb.br, adson@ene.unb.br, lfjjnq@embratel.net.br

Resumo - Este artigo analisa as trajetórias de grupos espectrais das bandas de muito baixa, baixa e alta freqüência espectral da variabilidade da freqüência cardíaca (HRV) antes, durante e após episódios isquêmicos miocárdicos transitórios e prolongados. Estas trajetórias foram observadas em mapas de curvas de nível derivados de análise tempo-escala usando a Transformada *Wavelet* Contínua com a função de base DOG (Derivative of Gaussian). Foram analisados segmentos de 5 minutos de ECG normais e com episódios isquêmicos ST+ e ST-, registrados na derivação V_4, obtidos da *European ST-T Database*. Padrões claramente distintos de trajetórias foram observados antes, durante e após os episódios, bem como padrões consistentes e peculiares de trajetórias para cada tipo de episódio.

Palavras-chave: Escalogramas, *Wavelets*, CWT, Tempo-escala, Tempo-freqüência, HRV, Isquemia miocárdica.

Abstract - This paper shows the trajectories of VLF, LF and HF spectral clusters of HRV signals before, during and after transient and maintained myocardial ischemic episodes. These trajectories were observed on contour maps derived from a time-scale analysis using Continuous Wavelet Transform (CWT) with the DOG (Derivative of Gaussian) basis function. Five minutes of normal ECG segments and with ischemic ST+ and ST- episodes registered in V_4 lead, taken from the *European ST-T Database*, have been analyzed. Clearly distinct patterns of trajectories were observed before, during and after the ST+ and ST- types of episodes, and between these and the normal ones, consistent and differing patterns of trajectories for each type of episode have been noticed.

Key-words: Scalograms, Wavelets, CWT, Time-scale, Time-frequency, HRV, Ischemia.

Introduction

Ischemic heart disease constitutes one of the most common fatal diseases in the western hemisphere. Myocardial ischemia is caused by insufficient blood flow to the contractile cells and may lead to infarction with its severe sequellae of heart failure, arrhythmias, and death. During the last years, ambulatory monitoring of the electrocardiographic (ECG) signal has become an important noninvasive test for detecting cardiovascular diseases. Ischemic ECG changes can precede the onset of anginal pain and, hence, may be a sign of "silent myocardial ischemia". Therefore, it is essential to develop methods that detect early changes in the ECG, possibly indicating the onset of an acute ischemic syndrome.

The spectral analysis of Heart Rate Variability (HRV) allows to distinguish and to quantitatively evaluate the different activities of the autonomic nervous system. Some alteration of the HRV rhythms has been associated with pathological condition, in particular, increasing power in the LF (Low Frequency) component has been associated with ischemic attack and other pathologies (Bifulco et al, 2000).

Nonstationarity, an important aspect of biological variability, can be associated with patterns of different drifts in the mean value of a given signal, or with changes in its variance that may be gradual or abrupt. Time series of beat-to-beat heart intervals, obtained from digitized electrocardiograms, are known to be non-stationary and exhibit extremely complex behavior (Ivanov et al, 1996).

Two kinds of methods have been used to get around the nonstationarity problem. The first method suggests that HRV data should be systematically tested for nonstationarities and that

only stationary segments should be analyzed. Representativeness of these segments, in some cases, in comparison with the original HRV signal, is, however, questionable. The other method tries to remove the slow non-stationary trends from the HRV signal before analysis. The detrending is usually based on first or higher order polynomial models, or on smoothness priors approach (Tarvainen et al, 2002). Nevertheless, because of the low-pass filtering, some VLF (Very Low Frequency) information is corrupted with this approach.

The wavelet transform technique is appropriate for studying non-stationary signals. It represents the time-domain signals over different scales, enabling an identification of both large-scale (low-frequency) and small-scale (high-frequency) fragments. It has been shown that the continuous wavelet transform (CWT) helps avoiding problems related to window length and shape, typically encountered with short-time Fourier Transform (STFT) and Auto-Regressive (AR) spectrum estimation (Lotric et al, 2000).

Time-scale and time-frequency analysis tools like the smoothed-pseudo Wigner-Ville distribution (Lee et al, 2001), the discrete Gabor spectrogram (Zhang et al., 2000), the Choi-Williams distribution (Dehkordi et al, 1999), and the cone-shaped distribution (Adelmann, 1999), have already been employed for the analysis of the HRV signal. Nevertheless, not much attention has been paid to the dynamics of the spectral distribution of HRV during ischemic episodes.

Myocardial Ischemia

Ischemia is considered to be a major cause of cardiac dysfunction, and a basis for the occurrence of myocardial infarction and dangerous arrhythmias. The main characteristic of ischemia at the cellular level is the depolarization of the cellular membrane potential. This causes a difference of potential between the normal and ischemic tissue, which causes the flow of an “injury current”. This “injury current” is manifested in the ECG by an ST depression or elevation, depending on the anatomical region affected and the dipole created with respect to the recording electrodes.

The ST-T complex of the ECG represents the time period from the end of the ventricular depolarization to the end of the corresponding repolarization in the electrical cardiac cycle. More often it is a smooth, continuous waveform beginning with the J-point (i.e., junction between the end of the QRS complex and the beginning of the ST segment), slowly rising to the peak of the T-wave and followed by a rapid descent to the isolelectric baseline or the onset of the U wave. Ischemic changes of the ECG frequently affect the entire repolarization wave shape (whole ST-T complex) and thus are inadequately described by isolated features, such as ST slope, ST-J amplitude, and positive and negative amplitudes of the T-wave, even if these are obtained as an average of several signal samples (Papadimitriou et al, 2001).

The first stage of ischemia is characterised by a T-wave amplitude increase without a simultaneous ST segment change. As the ischemia extends transmurally through the myocardium, the intracellular action potential shortens and the injured cells become hyperpolarised. This hyperpolarisation, in turn, produces an “injury current” that is reflected on the ECG as an upper or down horizontal ST segment deviation. At the final stage, the ischemia is so extense that the terminal portion of the active depolarisation waveform, represented on the ECG by the QRS complex, is altered. This stage is usually associated with myocardial necrosis (Bezerianos et al, 2000).

The European ST-T Database

The ECG signals of the European ST-T database (ESDB) are a set of long-term Holter recordings (Taddei et al, 1992). This database consists of 90 continuous two-channel records, taken from ambulatory ECG recordings of 79 patients. Each record was sampled at 250 Hz and each one is two hours in duration. The leads used included modified leads V_1, V_2, V_3, V_4 and V_5 and modified limb leads I and III (MLI and MLIII).

Each record in the European ST-T database contains at least one ischemic ST or T episode. Cardiology specialists have annotated these episodes in the original database. The localization of the ST and T episodes has been accomplished according to a pre-defined set of rules (Taddei et al, 1992).

In accordance with the electromagnetic current dipole theory, the reduction of the distance between the recording electrodes and the cardiac signal source will enhance the detection of the subtle alterations in the repolarization patterns. Therefore, a signal from the precordial (chest), lead V_4, has been analyzed in order to benefit from its better signal quality.

The 16 records used in this study (16 patients) are listed in Table 1 and their coronariopathy was coded as: 1- Normal coronary arteries, 2 - Anterior myocardial infarction (MI), 3 - One-vessel disease (LAD), 4 - One-vessel disease (RCA), 5 – Inferior MI, 6 – Three-vessels disease, 7 – One-vessel disease (LCX), 8 – Infero-lateral MI, 9 – Arterial hypertension, 10 - MI.

Table 1 – Clinical data of selected ESDB records.

Record	Angina	Coronariopathy	Episodes
E0105	Mixed	5-6	5
E0107	Mixed	7	3
E0111	Mixed	3	2
E0113	Mixed	6	8
E0119	Rest	1	3
E0121	Rest	1	2
E0123	rest	2	4
E0125	rest	2-3	5
E0127	rest	3	4
E0139	Mixed	4	2
E0147	Mixed	6	5
E0155	Rest	3	1
E0159	Mixed	5-6	2
E0161	Mixed	4	4
E0163	Effort	6-9-10	2
E0607	Rest	6-8-9	4

Scalograms

The wavelet spectrogram, or scalogram, is the squared modulus of the CWT. It is a distribution of the energy of the signal in the time-scale plane, expressed in power per frequency unit (for the HRV signal, ms^2/Hz), like the spectrogram. Both, spectrogram and scalogram can be thought of as smoothed versions of the Wigner-Ville distribution, providing reduced cross-term effects (Rioul et al, 1991).

The continuous wavelet transform of a discrete sequence x_n is defined as the convolution of x_n with a scaled and translated version of the wavelet basis function $\psi_0(\eta)$:

$$W_n(s) = \sum_{n'=0}^{N-1} x_{n'} \psi^* \left[\frac{(n'-n)\delta t}{s} \right], \qquad (1)$$

where the (*) denotes the complex conjugate. By varying the wavelet scale *s* and translating along the localized time index *n*, one can construct a picture showing both the amplitude of any features versus the scale and how this amplitude varies with time (Torrance et al, 1997).

The wavelet basis function for the Derivative of a Gaussian (DOG) function is:

$$\psi_0(\eta) = \frac{(-1)^{m+1}}{\sqrt{\Gamma\left(m+\frac{1}{2}\right)}} \frac{d^m}{d\eta^m}\left(e^{(-\eta/2)}\right), \qquad (2)$$

where *m* is the derivative of the Gaussian. If *m* equals 2, we have the Marr or Mexican hat wavelet. A real wavelet function like the DOG wavelet returns only a single component and is better suited to isolate peaks or discontinuities. Tests have also been performed with Morlet and Paul basis functions and the results were not satisfactory in terms of definition of the spectral clusters.

The representation of the DOG basis function in the time and in the frequency domains is shown in figure 1.

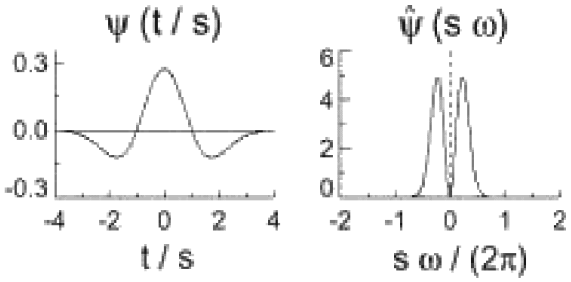

Figure 1 - Wavelet DOG with m = 2; left, time domain; right, frequency domain.

A non-orthogonal analysis (such as the one used in this study) is highly redundant at large scales, where the wavelet spectrum at adjacent times is highly correlated. The non-orthogonal transform is useful for time series analysis, where smooth, continuous variations in wavelet amplitude are expected. The most noticeable difference is the fine scale structure using the DOG. This is because the DOG is real valued and captures both the positive and negative oscillations of the time series as separate peaks in wavelet power.

Whereas in the Fourier analysis the frequency resolution Δf is constant, in wavelet analysis the ratio $\Delta f/f$ is constant. Thus, instead of a linear frequency resolution, a logarithmic resolution is obtained, so that the relative frequency resolution remains the same over the entire frequency interval under observation. In this case, the absolute frequency resolution is obviously much better for lower than for higher frequencies. The importance of logarithmic frequency resolution may simply be illustrated by looking at the ratios among the frequencies of characteristic peaks – beginning with the peak around 0.013 Hz, each next peak is at about twice the frequency. If a logarithmic frequency axis is used, the peaks are approximately equidistant. The logarithmic frequency resolution of the wavelet analysis makes it possible for this method

to capture simultaneously very different rhythms within a single signal.

To make the maps clearer for analysis, we chose to use the inverse of the Fourier period, instead of the wavelet scale, as the dimension of the *y* axis. For the DOG, the Fourier period is approximately four times larger than the scale (Torrance et al, 1997).

Frequency Bands of HRV Signals

In the time domain, the HRV signal is neither periodic nor completely random. In the frequency domain, the signal consists mainly of three spectral peaks, i.e., a high-frequency (HF) peak around 0.25 Hz, a low-frequency (LF) peak around 0.1 Hz, and a very low frequency (VLF) peak, which is also called the 1/f component because its spectral magnitude increases with the decrease of frequency. The 1/f component is fractal in nature, the power spectrum of which obeys an inverse fractional power law (Yang et al., 1997).

The very low frequency band is related to vasomotor activity as modulated by the renin-angiotensin control system among others; the LF band with blood pressure and baroreflex control; and the HF band with respiration. The HF band is related to parasympathetic modulation, while the LF band to parasympathetic and sympathetic combined modulation.

Methodology

A MATLAB (The MathWorks, Inc.)-based software developed at the Brasilia University Electrical Engineering Department and Cardiovascular Laboratory - ECGLAB (Carvalho et al, 2001), was used to detect QRS complexes series in the ECG. To ensure correct identification of every QRS complex, the signals were also manually edited.

These unevenly sampled signals were processed using cubic splines interpolation and sampled at 4 Hz. Sequences of 5-minutes of the RR signal were considered.

In this study we decided to consider the changes of the sympatho-vagal balance during three different 5-minute intervals related to ischemic episodes: one just before the onset of the ischemia, as detected by the beginning of ST displacement; another during the ischemic attack, with the peak or valley of the episode recognized as the instant in which the ST displacement reaches its maximum or minimum absolute value; and the third one just after the end of the attack.

Results

The evolution over time of the power concentrated in the VLF, LF and HF frequency bands have been analyzed and yielded the results described as follows.

The figures shown refer to results of record e0119. These results are representative of the group of 16 records. In figure 2, the trajectories of the main spectral clusters of the VLF, LF and HF frequency bands in a normal (non-ischemic) segment of HRV are shown. It can be seen that the trajectories are almost linear and horizontal.

In figure 3, the trajectories of the main spectral clusters at the onset of an ischemic episode of ST depression are shown. Before the onset of the attack the spectral array shows an increasing of the energy of the LF and VLF components and, at the same time, a positive frequency shift of these spectral clusters. The result may be interpreted as a sympathetic activation with a mild simultaneous withdrawal of vagal tone. In correspondence with the onset of the attack, the power of the spectra is mainly concentrated in the VLF component.

Just after the onset of the attack, within the frequency range between 0.03 Hz and 0.22 Hz, four distinct peaks can be observed. There are now two frequency components in the LF band. These results confirm the findings of Lotric in (Lotric et al, 2000).

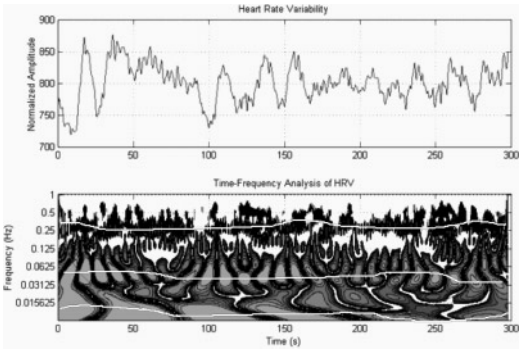

Figure 2 – HRV of normal segment of ECG; top, time domain; bottom, time-scale domain with lines marking the trajectories of VLF, LF and HF spectral clusters.

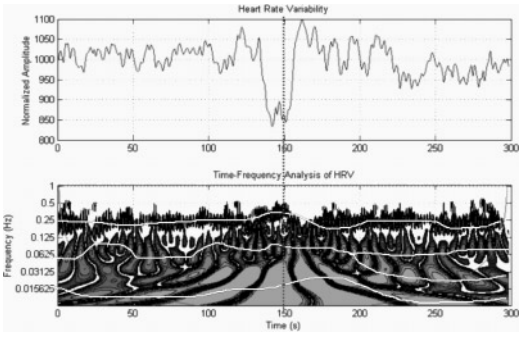

Figure 3 – HRV of the onset of an ST depression episode; top, time domain; bottom, time-scale domain with lines marking the trajectories of VLF, LF and HF spectral clusters. The vertical line marks the beginning of the ischemic episode.

In figure 4, the trajectories of the main spectral clusters of the VLF, LF and HF frequency bands at the amplitude valley of an ischemic episode of ST depression are presented. Before the valley of the attack the spectral array shows an increasing of the energy of the LF and the VLF components and, after the valley, the appearance of the fourth spectral cluster in the LF band.

Figure 5 shows the trajectories of the main spectral clusters at the end of an ischemic episode of ST depression. Before the end of the attack four spectral clusters can be clearly seen. After the end of the episode, the two LF components merge into one single component.

Within each PSD estimate, the intensity of the very low-frequency (VLF) component is clearly stronger than the intensity of low-frequency (LF) or high-frequency (HF) component. Using the CWT, we had a more detailed look into the VLF interval.

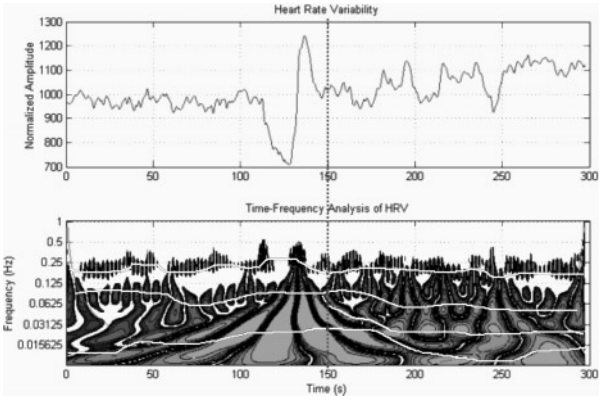

Figure 4 – HRV of the valley of an ST depression episode; top, time domain; bottom, time-scale domain with lines marking the trajectories of VLF, LF and HF spectral clusters. The vertical line marks the time instant of the amplitude valley of the episode.

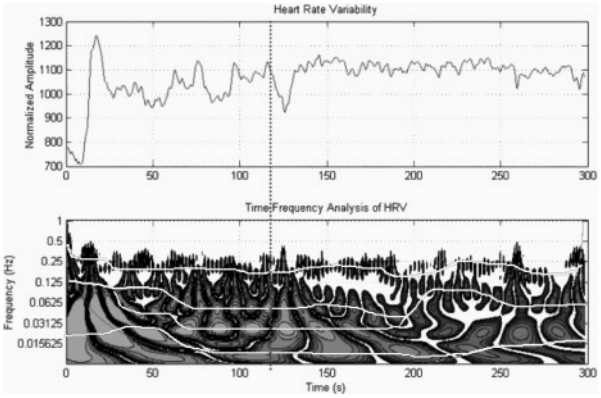

Figure 5 – HRV of the end of an ST depression episode; top, time domain; bottom, time-scale domain with lines marking the trajectories of VLF, LF and HF spectral clusters. The vertical line marks the end of the episode.

The time-variant spectral parameters suggest an early surge of the LF component in the HRV power spectrum. It precedes by approximately one minute the tachycardia and the ST displacement, generally indicative of the onset of an ischemic episode. This finding suggests an arousal or enhancement of sympathetic activity immediately before the acute ischemic attack (Bianchi et al, 1993).

The observed RR series stresses how the heart rhythm changes as the ischemic attack evolves: both the RR duration values and RR variance are reduced inside the event, and slow oscillations are evident during the period immediately preceding the beginning of an ischemic episode. The end of the ischemic episode coincides with the reappearance of a single predominant LF component. Furthermore, towards the end of the ischemic attack a very small HF component seems to reappear even if in an erratic way, denoting recuperation of parasympathetic modulation.

However, in interpreting the results of this study, it must be underlined that HRV analysis is a noninvasive tool to measure the fluctuations of cardiac autonomic modulator outflow and not the mean level of cardiac autonomic activity. Moreover, the LF and HF components of HRV cannot be considered to be exclusive markers of sympathetic and vagal activities in all the conditions. Therefore, the results of studies using power spectral analysis to evaluate cardiac autonomic control must be cautiously interpreted.

Discussion and Conclusions

The limited number of patients (only 16) and the lack of fundamental clinical data mean that the presented results should be treated with caution. Nevertheless, and in function of these results, it would seem probable to think that a wider study with more guarantees would give more definitive results with regard to the behavior of the different HRV indexes in relation to ischemia and at the same time enable us to test the influence of diverse clinical conditioners.

In any case, the results described herein, are of indisputable value in their own right, confirming the relationship between HRV, heart autonomic control and ischemia. As a general evaluation of the results obtained, it can be deduced that the study of HRV in the frequency domain is a technique of clear clinical interest in the monitoring of myocardial ischemia, particularly if we take into account its noninvasive character. Its evaluation in real time supplies diagnostic information of interest, especially for changes in ST, which are registered with no clinical history of angina, and do not show unequivocal signs of ischemic origin. Lastly, the appearance of relevant patterns in the moment prior to the electrical manifestations of ischemia, reinforces

the usefulness of this analysis technique as an early diagnostic tool.

References

Adelmann, H.G. (1999), “Heart Rate Variability Analysis in Clinical Pharmacology by Joint Time-Frequency Methods”, *Computers in Cardiology*, v. 26, p. 643-645.

Bezerianos, A., Vladutu, L., Papadimitriou, S. (2000), “Hierarchical State Space Partitioning with a Network Self-organising Map for the Recognition of ST-T segment changes”, *Medical and Biological Engineering and Computing*, v. 38, p. 406-415.

Bianchi, A.M., Mainardi, L., Petrucci, E., Signorini, M.G., Mainardi, M., Cerutti, S. (1993), “Time-Variant Power Spectrum Analysis for the Detection of Transient Episodes in HRV Signal”, *IEEE Transactions on Biomedical Engineering*, v. 40, n. 2, p. 136-144.

Bifulco, P., Cesarelli, M., Bracale, M. (2000), “HRV Adaptive Spectral Estimation for Transient Detection”, *Proceedings of the 22 Annual EMBS international Conference*, p. 3165-3167, Jul.

Carvalho, J.L., Rocha, A.F., Junqueira, L.F. (2001), "Desenvolvimento de Sistemas de Aquisição, Processamento e Análise de Sinais Eletrocardiográficos", *7º Congresso de Iniciação Científica da Universidade de Brasília,* Anais, p. 488. UnB/CNPq, Ago.

Dehkordi, M., Erfanian, A., Foroutan, A. (1999), “Time-frequency Analysis of the Heart-Rate Variability during Physical and Physical-Pharmacological Tests”, *Proceedings of the First Joint BMES/EMBS Conference – Serving Humanity, Advancing Technology*, p. 261, Oct.

Ivanov, P.C., Rosenblum, M.G., Peng, C.K., Mietus, J., Havlin, S., Eugene Stanley, H., Goldberger, A.R. (1996), “Scaling Behaviour of Heartbeat Intervals obtained by Wavelet-based Time-series Analysis”, *Nature*, v. 383, p. 323-327, Sept.

Lee, J.W., Kim, K.S., Song, C.G., Kim, J.S., Lee, M.H. (2001), “Time-frequency Analysis of HRV for patient with vasovagal syncope”, *Electronics Letters*, v. 37, n. 20, p. 1214-1215.

Lotric, M.B., Stefanovska, A., Stajer, D., Rovan, V.U. (2000), “Spectral Components of Heart Rate Variability determined by Wavelet Analysis”, *Physiology Measurements*, v. 21, p. 441-457.

Papadimitriou, S., Mavroudi, S., Vladutu, L., Bezerianos, A. (2001), “Ischemic Detection with a Self-Organizing Map Supplemented by Supervised Learning”, *IEEE Transactions on Neural Networks*, v. 12, n. 3, p. 503-515.

Rioul, O., Vetterli, M. (1991), “Wavelets and Signal Processing”, *IEEE SP Magazine,* October, 1991, p. 14-38.

Taddei, A., Distante, 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 Cardiography”, *European Heart Journal,* v. 13, p. 1164-1172.

Tarvainen, M.P., Ranta-aho, P.O., Karjalainen, P.A. (2002), “ An Advanced Detrending Method With Application to HRV Analysis” *IEEE Transactions on Biomedical Engineering,* v. 49, n. 2, p. 172-175.

Torrance, C., Compo, G.P. (1998), “A Practical Guide to Wavelet Analysis”, *Bulletin of the American Meteorological Society,* v. 79, n. 1, p. 61-78.

Yang, F., Liao, W. (1997), “Modeling and Decomposition of HRV Signals with Wavelet Transforms”, *IEEE Engineering in Medicine and Biology,* p. 17-22, Jul/Aug.

Zhang, J.W., Liu, J.R., Zheng, C.X., Tao, W.Z., Thakor, N. V., Xie, A. (2000), “Noninvasive Early Detection of Focal Cerebral Ischemia”, *IEEE Engineering in Medicine and Biology*, p. 74-81, Nov./Dec.