Heart Rate Analysis and Telemedicine: New Concepts & Maths

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Abstract: Our paper deals with some new aspects of ambulatory (Holter) ECG monitoring extending its indications and using for risk management purpose. Remote sensing consists of the transmittal of patient information, such as ECG, x-rays, or patient records, from a remote site to a collaborator in a distant site. Our earlier developed internet based ECG system was unique for on/off-line analysis of long-term ECG registrations. After the 5-year experience in a smaller region of Budapest, Hungary involving a municipal hospital and the surrounding outpatient cardiology departments and general practitioners, we decided to integrate into our new ECG equipment, the CardioClient the results. In the first clinical study of the four was a wavelet, non-linear heart rate analysis in sudden cardiac death patients using the Internet and the GPRS mobile communication. After the wavelet transformation by the Haar wavelet and the Daubechies 10-tap wavelet, the phase-space of the wavelet-coefficient standard deviation and the scale parameters showed an excellent separation in the scale-range of 3-6 between the two groups: in that region, the average scaling exponents was 0.14+-0.04 for Group-A, and 1.22+-0.27 for Group-B ($p<0.001$). In the next study, we used the Internet database of long-term ambulatory, mobile, GPRS electrocardiograms for the for risk stratification of patients through the cardiovascular continuum. From our ambulatory mobile GPRS ECG database the following a priori groups were defined after a 24 months follow-up: G1: N=227 patients (without manifest cardiovascular disease, clusterized 'boxes' based on the age, sex, cholesterol level, diabetes, hypertension); G2: N=89 patients (postinfarction group); G3: N=66 (patients with chronic heart failure) with (+) or without (-): all-cause death (acD), myocardial infarction (MI), malignant ventricular arrhythmia (MVA), sudden cardiac death (SCD). The actual vs. predicted values were analyzed with chi-square test. The best significance levels ($p<0.001$) were found with method in G1/MI+, G2/SCD+, G3/acD+, G3/SCD+

groups. In the third study a wavelet analysis of late potentials based on long-term, high-resolution, mobile, GPRS ECG data was performed. These pathological changes were also detected by the Haar and Daubechies_4 wavelets, but in a narrower space (110-128 ms and 180-240) and with lesser significance (p<0.01). Late potentials were found in Group-A (N=21) in 18 cases with Morlet, 16 with Haar, 19 with Daub-4 analysis, and in 15 cases using all the 3 waves; for Group-B the data were 5, 9, 8, 5, respectively. In the fourth clinical study the prognostic value of the nonlinear dynamicity measurement of atrial fibrillation waves detected by GPRS internet long-term ECG monitoring were analyzed. The multivariate discriminant model selects the best parameters stepwise, the entry or removal based on the minimalization of the Wilks' lambda. Three variables remained finally: x1 = CI mean-value at log r=-1.0 (m9-14), x2 = CI mean-value at log r=-0.5 (m12-17), and x3 = CD_cg. The Wilks' lambda was 0.011, chi-square 299.68, significancy: p<0,001.

1 Introduction

Telemedicine can be divided into three areas: aids to **decision-making, remote sensing, and collaborative arrangements for the real-time management of patients at a distance**. As an aid to decision-making, telemedicine includes areas such as remote expert systems that contribute to patient diagnosis or the use of online databases in the actual practice of medicine. Collaborative arrangements consist of using technology to actually allow one practitioner to observe and discuss symptoms with another practitioner whose patients are far away.

2 Technical Aspects

In the older telemedicine wireless system (HeartSpy, Heart Observer), the mobile ECG equipment transfers the continuously stored signals to the WEB server by a GPRS (General Packet Radio System protocol) route. The high resolution (24 bit, 0.5 ms sampling rate) full digital ECG recorder sends the compressed data via wireless network. The size of each ECG packet is 120 byte, the averaged communication bandwidth between 56 and 118kbit/s. The WEB server contains the ECG Knowledge- and Data-base, and broadcasts the ECGs to the medical users. The medical staff could real-time, continuously monitor the patients with PC, or mobile phone [1]. In the CardioClient, the 12-lead ECG is registered and two leads are served for the heart rate analysis. ***Figure 1*** represents the architecture of the internet, wireless ECG system.

Our online monitoring has two meanings. The first is the conventional, i.e. during the registration the cardiologist could observe continuously the ECG. Secondly, some measured non-linear parameters are calculated in every four hours, and a few hours time-delay a message generate. In the case of significant changes of these non-invasive parameters, the pts get a message to attend the cardiologist. The less significant changes of the parameters elongate the monitoring for days (it means the ‘continuous’). During the on-line monitoring, the conventional pathologic ECG signs (arrhythmia, definitive morphological changes) send a warning massage to the patient, the GP and the cardiologist.

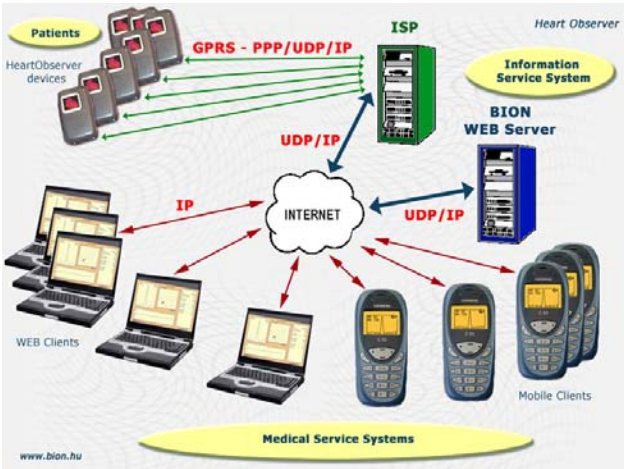

Figure 1
The architecture of the mobile telemedicine system

3 Clinical Concerns

Up to now, the prediction of atrial fibrillation (AF) recurrence and of sudden cardiac death (SCD) is unsolved [2-5]. Sudden cardiac deaths occur >= 75% at home and the patients` chance of arriving the hospital alive is in the range of 3% to 5%. How to do the prevention more effectively and economically - that is the important question. The arrhythmia risk stratification in CHF or other cardiac disease for the improvement of the prognosis and the prevention of SCD is essential. Using our mobile, internet, long-term ECG, the indications of the ambulatory (Holter) ECG could be extended to a larger population. Some works in these areas are presented in this paper, where more sophisticated math analysis was used on the long-term ECG recordings.

3.1 Wavelet, Non-Linear Heart Rate Analysis in Sudden Cardiac Death Patients Using the Internet and the GPRS Mobile Communication

The first aim of our study was to develop an effective ECG surveillance system for the prevention of sudden cardiac death (SCD) and determine the most powerful beat-to-beat heart rate dynamic values as indicators for this monitoring. The second aim was to determine the role of non-linear heart rate variability indexes in a sudden cardiac death (SCD) population [6-8]. The analysis based on the data of 27 chronic heart failure patients with SCD (Group-A) and 27 without (Group-B) it, which was selected from a 168 chronic heart failure patients population monitored for 24 hours two weekly. The inclusion criteria were Holter recordings at least 2 weeks before the SCD (the patients were monitored weekly), absence of acute myocardial infarction in the previous 1 year. SCD was defined as death occurring within 15 minutes of a change in symptoms or during sleep. Clinical features of the two groups: male/female (Group-A: 14/13, Group-B 14/13; age: 62.4±7, 59.7±6; CAD: 22, 21; other cause: 5, 6; NYHA II. class: 18, 17; NYHA III. Class 9, 10; EF: 36.2±6, 36.9±5, respectively).

We used multiresolution wavelet analysis for the 24 hour R-R interbeat time-series. After the wavelet transformation by the *Haar* wavelet and the *Daubechies* 10-tap wavelet, the phase-space of the wavelet-coefficient standard deviation and the scale parameters showed an excellent separation in the scale-range of 3-6 between the two groups: in that region, the average scaling exponents was 0.14±0.04 for Group-A, and 1.22±0.27 for Group-B ($p<0.001$) (***Figure 2***).

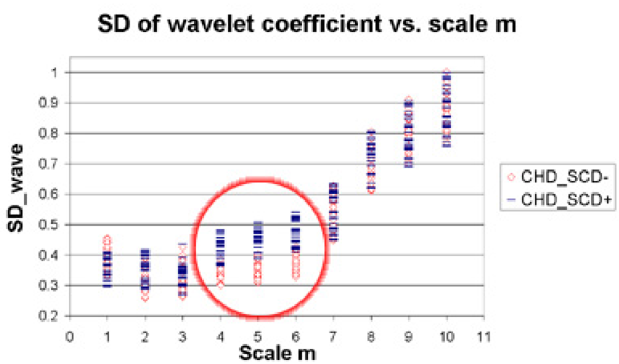

Figure 2

Discrimination value of wavelet coefficient between SCD+ and SCD- patients groups

3.2 Internet Database of Long-Term Ambulatory, Mobile, GPRS Electrocardiograms for the for Risk Stratification of Patients through the Cardiovascular Continuum

In this work we present a telemedicine application using an internet ECG database for risk stratification of patients with various cardiovascular disease state. The data mining [9,10] serves for indexing (finding the most similar time series in the database given a query time series Q, and some similarity/dissimilarity measure D(Q,C). The PAA method was used in this study.

From our ambulatory mobile GPRS ECG database the following a priori groups were defined after a 24 months follow-up: G1: N=227 patients (without manifest cardiovascular disease, clusterized 'boxes' based on the age, sex, cholesterol level, diabetes, hypertension); G2: N=89 patients (postinfarction group); G3: N=66 (patients with chronic heart failure) with (+) or without (-): all-cause death (acD), myocardial infarction (MI), malignant ventricular arrhythmia (MVA), sudden cardiac death (SCD).

The dimensionality reduction via PAA was used, where a time series C of length n can be represented in a w-dimensional space by a vector $\bar{C}=\bar{c}_1,\ldots \bar{c}_w$. The ith element of $\bar{C}$ is calculated:

$$\bar{C}_i = w/n \sum_{j=n/w(i-1)+1}^{(n/w)\,I} C_j$$

The dimension of time series is reduced from n to w, the data is divided into w equal sized frames. The mean value of the data falling within a frame is calculated and a vector of these values becomes the data-reduced representation. The Haar wavelet approximation was used in our study – the principle was the same as in PAA. Each time series was normalized (a mean of zero and a standard deviation of one). A 128 length data segment was used for discretization, the lookup table contains the breakpoints calculated from the Gaussian distribution. The Euclidean distance of two time series Q and C of the same length n is:

$$D(Q,C) = \sqrt{\textstyle\sum_{i=1}^{n} (q_i - c_i)^2}$$

During the 18 months testing period an other 136 patients (the patient groups were identical: G1, G2, and G3) examined and the results (predicted four end-point: acD, MI, MVA, and SCD) formed the a posteriori groups. The actual vs. predicted values were analyzed with chi-square test. The best significance levels ($p<0.001$) were found with method in G1/MI+, G2/SCD+, G3/acD+, G3/SCD+ groups.

3.3 Wavelet Analysis of Late Potentials based on Long-Term, High-Resolution, Mobile, GPRS ECG Data

The time-frequency analysis of left ventricular late potentials is a more sophisticated method than the commercial ones. Some authors used the wavelet method which would be the best solution for the analysis of this kind of data [11-14].

The ECGs was recorded with 32-bit A/D converter and a sampling frequency of 1 kHz, and a modified V1-V3 bipolar leads were used for the registrations. The analysis based on 10,000 (approximately 3 hours) QRS windows starting 100 ms before and 250 ms after the QRS onset. The Haar, the Daubechies_4 and the Morlet (frequency parameter (c) = $2*\pi*5.33$) wavelets were used in the calculations. The Morlet wavelet HR-ECG analysis used a combined wavelet stratification method of Couderc and Selmaoui [10, 11]. In this case, the wavelet transform was applied on 512 ($=2^9$) points, from 128 ms before the beginning of the QRS to 384 ms after QRS onset. Ten different scales were calculated from the modified V1-V3 leads of our GPRS ECG. This single lead was used as the calculated magnitude vector (MV) of standard are differ from the XYZ leads analysis. Using the discrete wavelet transform for the Morlet wavelet, first it computed in the frequency domain and then in the time domain. Using a set of discrete scaling parameters each signal is decomposed into a set of 10 bandpass beat signal logarithmically equally spaced with a centre frequencies from 40 Hz to 250 Hz. The scaling exponent (m) varying linearly between 1.96 and 4.20 by steps of 0.25. The energy was the third dimension of the time-scale plane (means of the wavelet coefficients values at scale s and sample n) which was plotted with a color scale.

The discrete, dyadic wavelet calculations were used for the the Haar, and the Daubechies_4 wavelets. The 4 coefficients of Daub-4 waves: $C_0 = 0.6830127$, $C_1 = 1.1830127$, $C_2 = 0.3169873$, $C_3 = - 0.1830127$. The DWT of Haar and Daub-4 wavelet transform was applied on the same 512 ($=2^9$) points as in the Morlet transform.

The study population consists of two postinfarction groups: Group-A: malignant ventricular arrhythmia or sudden cardiac death (N= 21; age: 60.3±11; male:13), Group-B: without them (N= 96; age:61.7±12; male 52). All patients were followed for 24 months, the GPRS 24 hour mobile ECG was repeated monthly.

For the analysis of the two groups the wavelet energy was changed for the mean square of wavelet coefficients, and the statistical p-value of the ANOVA test between the two groups was used. Abnormal time-frequency components were found between 90 and 130 ms after QRS onset in the 55-106 and in the 155-250 Hz frequency range, the p-values were < 0.001 with the Morlet waves (***Figure 3***).

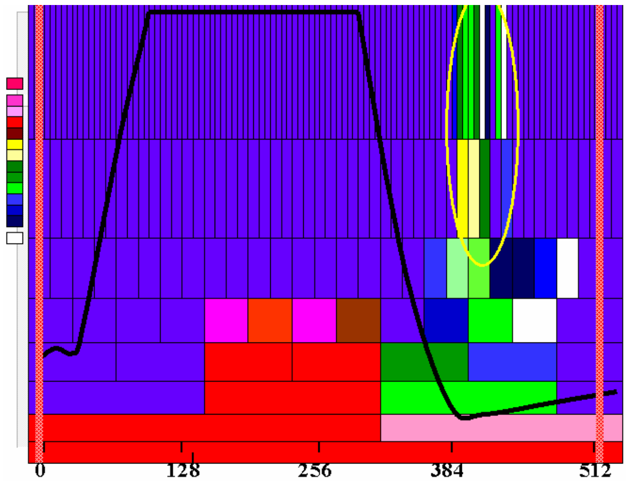

Figure 3
The ellipse shows the Region-of-Interest (ROI) of late potentials in the scalogram. The colors represents the SD values in the time-scale map. Black line: part of the ECG, the time-window: 512 ms.

These pathological changes were also detected by the Haar and Daubechies_4 wavelets, but in a narrower space (110-128 ms and 180-240) and with lesser significance ($p<0.01$).

Late potentials were found in Group-A (N=21) in 18 cases with Morlet, 16 with Haar, 19 with Daub-4 analysis, and in 15 cases using all the 3 waves; for Group-B the data were 5, 9, 8, 5, respectively.

Our work might be the first in the comparative wavelet analysis of long-term mobile, GPRS electrocardiography with high resolution ECG hardware. The results showed that using a very long analyzing segment (10,000 QRS-complex) the signal-to-noise ratio could be beneficially changed for analyzing late potentials of ambulatory wireless ECG data.

3.4 Prognostic Value of the Nonlinear Dynamicity Measurement of Atrial Fibrillation Waves detected by GPRS Internet Long-Term ECG Monitoring

In this study, a five-minute ECG was recorded with our mobile-internet equipment in 68 patients with paroxysmal atrial fibrillation (t<24 hour). Immediately after the arrhythmic episode, a 28-day continuous mobile, internet ECG was recorded for monitoring the atrial fibrillation recurrence. The nonlinear dynamicity of the f-waves was determined with advanced math method. Multivariate discriminant analysis was used analyzing the difference between the two groups (recurrent PAF [Group-2, N=29] or not [Group-1, N=39). The ECG pre-processing consists of the

R-wave detection (smooth – first derivative – largest deflection), the signal averaging in all time windows around the detected R-waves, the determination of template QRS by averaging the deflections in the corresponding time. For the measurement of complexity [15-17], the Grassberger-Procaccia Algorithm (GPA) was used, its main principle is to determine the correlation dimension using the correlation integral.

The CI of a (chaotic) deterministic system is given by

$C_m(r) = Ar^D e^{-mld\Delta tK}$,

A is a constant, D the correlation dimension, K is the correlation entropy, m the embedding dimension, l the embedding delay and Δt the sample interval.

$Cm(N,r)= 1/N_{dis}\ \Sigma_{i=\{i\_ref\}}\ \Sigma_{j=/i/>=W}\ \Theta_{(r-|x(i)-x(j)|)}$

where $N = L-(m-1)l$ is the number of delay vectors resulting from the time series of length L in reconstructed phase space of embedding dimension m. The Heaviside Θ (theta) is 1 for positive arguments and 0 otherwise. The inner sum counts the number of delay vectors within a distance r from a reference vector. The outer sum adds the results over a set $\{i_{ref}\}$ of reference vectors and the normalization factor N_{dis} is the total number of distance involved int he summations. We used 10000 randomly chosen reference vectors, which is equal to one third of the number of samples int he time series (sampled down to 30000 samples) as suggested Theiler.

The steps of the GPA were:

- The Correlation Integral ($C_m(r)$) dimension for different embedding (delayed) dimension (m) is calculated.
- If ($C_m(r)$) shows scaling (=linear part on double logarithmic scale) the Correlation Dimension (D) and Correlation entropy (K) are estimated with coarse-grained D_{cg} and $K_{cg.}$
- If (Cm(r)) shows no scaling a distance r and an embedding dimension m are chosen at which the coarse-grained Dcg and Kcg are estimated. ***Figure 4*** shows the Correlation Integral ($C_m(r)$) dimension for different embedding (delayed) dimension (m); if ($C_m(r)$) shows scaling (=linear part on double logarithmic scale) the Correlation Dimension (D) and Correlation entropy (K) are estimated with coarse-grained D_{cg} and K_{cg}.

The amplitude values of CI, CD, CE at various m were determined with their coarse-grained values. The DSC model selects the best parameters stepwise, the entry or removal based on the minimalization of the Wilks' lambda. Three variables remained finally: x1=CI mean-value at log(r)=-1.0 (m9-14), x2=CI mean-value at log(r)=-0.5 (m12-17), and x3=CD_cg. The Wilks' lambda was 0.011, chi-square 299.68, significancy: $p<0,001$.

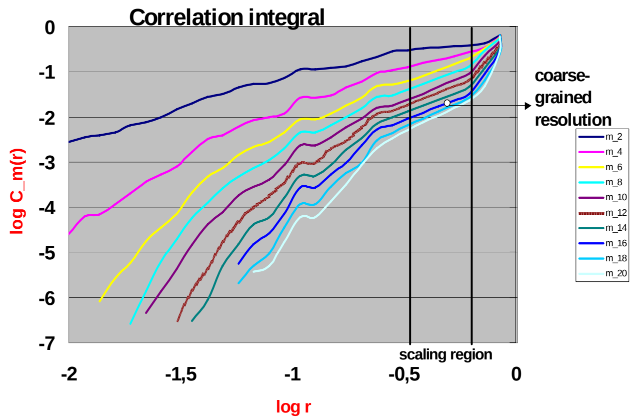

Figure 4

The relation of Correlation Integral ($C_m(r)$) to r value with the scaling region

Acknowledgment

The internet based ECG system combines the advantages of online and offline monitoring. Using various risk scores as predictor values, the telemedicine ECG management would be designed. The worsening indicator parameters indicate immediate change of patient management (re-checking the clinical signs and symptoms, change of therapy, hospital admission). In the case of borderline decision situation (mild change of the indicator values) the ambulatory registration will extend for longer time or repeat more frequently. The accessibility to the standard medical care of the moderate to high risk cardiovascular patients is markedly increased. The frequent and repeated ECG monitoring put the patient to the 'good place in good time' preventing from serious or lethal complications. The opinion of The Task Force Committee on Heart Rate Variability (in 1996!) was: 'At present, the nonlinear methods represent potential tool for HRV assessment. Advances in technology and the interpretation of the results of nonlinear methods are needed before these methods are ready for physiological and clinical studies.' Our studies show that more sophisticated math analysis of heart-rate variability, beat-to-beat analysis in atrial fibrillation would be real tools in cardiology. As repeating our question (Congress of ESC, 2002): 'Internet-based continuous Holter monitoring for the prevention of sudden cardiac death: Is this the Rosetta stone and Who will be Mr. Champollion?'.

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