Herzschr Elektrophys 11:229–234 (2000)

H. Väänänen
P. Korhonen
J. Montonen
M. Mäkijärvi
J. Nenonen
L. Oikarinen
K. Simelius
L. Toivonen
T. Katila

Non-invasive arrhythmia risk evaluation in clinical environment

Received: 30 October 2000
Accepted: 27 November 2000

H. Väänänen MSc (✉) · J. Montonen
J. Nenonen · K. Simelius · K. Simelius
T. Katila
Laboratory of Biomedical Engineering
P.O. Box 2200
Helsinki University of Technology
02150 Helsinki, Finland
E-mail: Heikki-Vaananen@hut.fi

H. Väänänen · P. Korhonen · J. Montonen
M. Mäkijärvi · J. Nenonen · L. Oikarinen
K. Simelius · L. Toivonen · T. Katila
Medical Engineering Centre
BioMag Laboratory
Helsiniki University Central Hospital
00029 Helsiniki, Finland

P. Korhonen · M. Mäkijärvi · L. Oikarinen
L. Toivonen
Division of Cardiology
Department of Medicine
Helsinki University Central Hospital
00029 Helsiniki, Finland

Summary We have applied various methods to extract parameters from high-resolution magnetocardiographic (MCG) and electrocardiographic (ECG) recordings for characterizing the risk of life-threatening arrhythmias. The methods include detection of late fields and late potentials at the end of the QRS, abnormalities in spectral variability and signal fragmentation during the QRS, and variability in the heart rate. In addition, we have developed methods to convert MCG signals measured with any sensor configurations to a common presentation form. The signal processing methods have been implemented on a user-friendly interface which allows fast and easy use in a clinical environment.

Key words Magneto cardiography – arrhythmia risk evaluation – signal-averaged electrocardiography

Introduction

There is a constant clinical interest for non-invasive identification of patients at risk of fatal arrhythmias. Variety of methods have been developed for this purpose. Despite the fact that the negative predictive value of such methods is often high, the positive predictive accuracy has remained only around 30%. As the sensitivity and the usability of the instruments for recording both the high-resolution (HR) magneto- and electrocardiographic (MCG, ECG) signals and multichannel mappings have improved, the need for more sophisticated signal analysis methods has also increased. Automatic algorithms are user-independent and can detect small features in signal morphology. They can also extract specific features from temporally and spatially large data sets.

The main approaches for non-invasive arrhythmia risk stratification can be divided into three categories according to their physiological scope of interest: 1) the activation discontinuities during the ventricular depolarization are studied in late potential and late field analysis meth-

ods, in the so-called 'Berlin fragmentation analysis method', and in spectral turbulence analysis; 2) the heterogeneity during the repolarization of the ventricles is studied in QT dispersion analysis; 3) the function of the autonomic nervous system is studied in heart rate variation analysis. All these parts can be used as arrhythmia risk indicators either separately or by combining the independent components of each method.

In this paper, a short overview of the MCG risk analysis methods is given. The focus is on the methods that we have applied for analyzing 5-min ECG and MCG mappings in the BioMag Laboratory of Helsinki University Central Hospital (1). We have also studied methods to convert MCG signals measured with any sensor configurations to a common presentation form, in the viewpoint of multicenter MCG studied in the future.

Recordings and preprocessing

Measurements

The BioMag Laboratory at Helsinki University Central Hospital is equipped with a state-of-the-art 67-channel HR-MCG recording system, operated in a magnetically shielded room (1). The MCG data are measured via the chest of a supine patient at rest. Simultaneously with MCG, 64 ECG channels can be recorded, including the standard 12-lead ECG and xyz-lead systems.

We have implemented the methods presented in the next chapters into a user-friendly Xwindows interface. As an outcome, the user can produce a two-page report containing the basic results after a patient measurement. The report includes numerical results and figures illustrating each method of the analysis and is suitable for clinical work. The software has already been tested in large patient series for assessing the arrhythmia risk (2, 3).

Averaging

To analyze specific parts of the heart function, the continuous ECG/MCG signal has to be triggered to identify the heart beats. Each QRS complex is triggered by finding the time instant where the slope of the signal exceeds the predefined threshold value. After triggering, the signal averaging is often applied to improve the signal-to-noise ratio. The beat invariant features are enhanced in averaging and, thus, smaller details can be analyzed. Although, the invariance of the ECG or MCG morphology is not strictly fulfilled, the averaging is usually acceptable if there is no physiological reason to expect any dissimilarity.

The similarity of the beats included in the average is further increased by rejecting the abnormal or too-noisy beats. We have used a template beat, selected from a few representative beats by an experienced user, to which the successive beats are then compared for similarity. Next the maximum cross-correlation between the template and a triggered beat is used for precise timing. The rejection is performed by using noise criteria, two different distance measurements, and a so-called "tube" criterium, where an envelope of the signal is formed by moving the signal both in time and amplitude direction (Fig. 1) (4).

MCG signal conversion

Comparison of MCG data recorded with different multichannel magnetometers is difficult because differing sensor types and locations do not allow measurements from the same locations in respect of the body. In addition, the comparison of the signals recorded in one measurement with different types of sensors is problematic. Multichannel MCG signals exhibit significant differences, both in spatial distribution and in time domain. For example, the amplitudes and even durations of the QRS waveforms may vary considerably between planar and axial gradiometers (5). Therefore, in our analysis the seven axial gradiometers and the 30 planar gra-

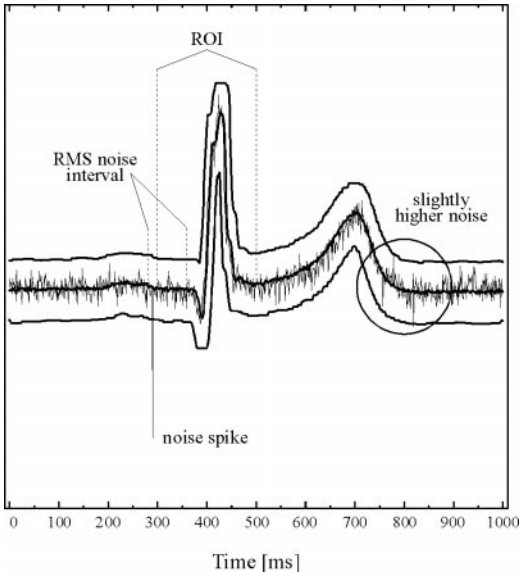

Fig. 1 The rejection of beats in signal averaging can be based on whether they fit inside a predefined range of variation on the selected interval. The tube is formed as an envelope of all the signals that are calculated by shifting the original signal on the region of interest (ROI) vertically and horizontally (4)

diometer pairs are usually converted to 33 first-order axial gradiometers before further analysis. This presentation permits a more straightforward comparison to the MCG studies at other centers and to the conventional ECG signal morphology.

Our signal conversion is based on the minimum-norm estimate (MNE) for intracardiac current density (6). MNE is the current distribution which has the smallest norm and is compatible with the measured data. It is defined as a linear combination of the lead fields, L_k: $J^* = \sum_{k=1}^{N} \omega_k L_k(r)$.

Here N is the number of the sensors, and the lead field of the *kth* sensor, L_k, can be thought of as a transfer function from the myocardial current sources to the sensor. We can compose an inner-product matrix: $\Gamma_{ij} = < L_i L_j >$ the weighting coefficients ω_k are then found from the measured signals b^m by $\omega = \Gamma^{-1} b^m$. Since the lead fields in a large array are almost linearly dependent, regularization techniques are needed in inversion of Γ (6).

The MNE can be computed on a 2D surface or in a 3D volume. In our case, we composed a triangulated surface with 169 node points, following the shape and size of the sensor array. This virtual surface was placed at 12 cm below the sensor array, and the MNEs were computed on the 169 nodes in an infinite and homogeneous conducting space (5).

Extrapolation with MNE is based on evaluating the lead fields of virtual sensors, and composing matrix of products between virtual and measurement sensors. Then, extrapolated signals at each time point are obtained as in (6).

Recently, Burghoff et al. (5) tested two transformation methods to convert MCG data recorded on seven healthy volunteers with two differing SQUID systems. Both procedures yielded good reconstruction of temporal and spatial MCG patterns, providing excellent experimental validation for the MCG signal conversion.

Analysing methods

Long-term recordings have certain benefits over short-term recordings: they permit better analysis of the heart rate variability, QT dynamics or spontaneous arrhythmias. Still, short-term measurements in a controlled environment have superior temporal resolution and signal-to-noise ratio, which makes the analysis of so-called micro signals possible. In the following, we describe methods designed for analyzing the high-resolution short-term measurements.

Late field/potential analysis

The delayed fragmented ventricular depolarization has, in invasive studies, been shown to be related to propensity for ventricular tachycardias. The most often used method for detecting corresponding low amplitude fragmented activation at the end of the QRS follows the guidelines given by Simson (7). First, the signal is high-pass filtered with a cut-off frequency of 25 or 40 Hz. Filtering is usually utilized bi-directionally using an infinite impulse response filter. To produce a "filtered QRS", a vector magnitude is formed from the filtered x-, y- and z-ECG signals, or an envelope of each of the filtered MCG channels is formed using the Hilbert transform (8) (Fig. 2). From the filtered QRS, the onset and the offset of the QRS complex are defined on the basis of noise levels before and after the QRS complex. The QRS duration, the duration of the low amplitude signal (LAS) below 1 pT (or 40 μV in ECG) from the QRS offset, and the root mean square amplitude during the last 40 ms of the QRS complex (RMS40) are calculated and used as risk parameters.

Fragmentation analysis

The propensity for ventricular tachycardias can also be sought by detecting intra-QRS changes. The Berlin fragmentation analysis is based on a binomial filtering (9). The signal is first band-pass filtered on 37 to 90 Hz, and the extrema of the filtered signal are marked (Fig. 2). The fragmentation of each QRS complex is then characterized by the number of the extrema (M) and the product of M and the sum of scaled amplitude differences between the neighboring extrema, called fragmentation index (S).

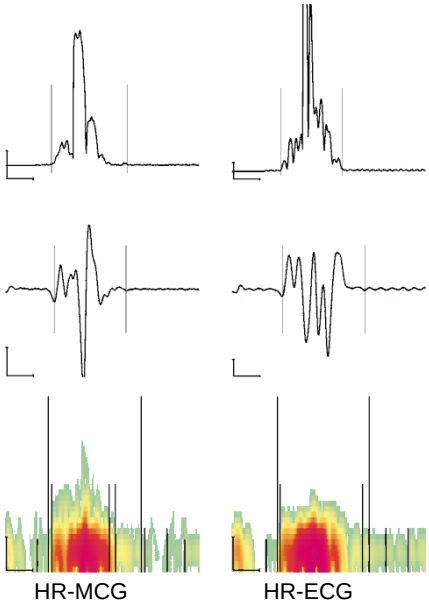

Fig. 2 Examples of filtered MCG and ECG signals measured from a VT patient; Up: envelope (MCG, scale ticks 1 pT/50 ms) and vector magnitude (ECG, scale ticks 20 μV/50 ms) of the high-pass filtered QRS, middle: binomial filtered QRS (scale ticks: 1 pT/50 ms (MCG) and 50 μV/50 ms (ECG)), down: a spectrotemporal analysis of the QRS (scale ticks: 100 Hz/50 ms). Presented results are from the same measurement from the channels that gives the highest risk value in each method

Spectral turbulence analysis

Intra QRS changes can also be analyzed by analyzing the discontinuities in frequency content of the signal which are analyzed. Although the wavelets are often used for frequency analyses, the Fast Fourier transform (FFT) is still the basis of

the most utilized methods. In spectral turbulence analysis (10) the short-term Fourier spectra in each channel are calculated over 4-term Blackman-Harris windowed and differentiated segments of 25 ms in duration (Fig. 2). The spectra are calculated over the QRS at 2 ms steps, and the resulting spectrogram is quantified using correlations between the spectra. The QRS onset and offset are defined as the time instants where the total power spectral density (standard deviation of the signal) exceeds the noise limit in two consecutive spectra. The resulting parameters are the QRS-duration, inter slice correlation mean (ISCM) and standard deviation (ISCSD), low slice correlation ratio (LSCR) and the spectral entropy (SE), i.e., the mean of the discordance between the spectra and the mean of the spectra.

Repolarization analysis

Heterogeneity of the ventricular repolarization is also an indicator of vulnerability for malignant arrhythmias. The heterogeneity has been studied by analyzing the dispersion of the time from the onset of the Q-wave to the apex or the end of the T-wave (QT time) and the duration of the terminal part of the T-wave (T_{apex}–T_{end}).

We have developed an automated algorithm to determine the QT_{apex} and the QT_{end} time (2). The apex of the T-wave is defined as the peak of the parabola fitted to the highest amplitude deviation from the T-P baseline after the QRS. In simple (monophasic) T-waves, the end of the T-wave is defined as the time instant where the steepest tangent after the T-wave apex and the baseline cross. In complex T-waves, also the second derivative is used to detect discontinuities after the apex and the software excludes U-waves using the guidelines presented by Lepeschkin and Surawich (11). The onset of the QRS is defined as in late potentials/field analysis.

The QT dispersion is calculated as the difference between the longest and the shortest QT times. In addition, the local dispersion of the QT times or the standard deviation of the durations can be easily calculated and used as risk parameters.

In addition to the QT times, some other parameters reflecting the repolarization properties have also been used. Relative smoothness score measures the correlations between the potential or field maps during the ST segment (12). Another method for detecting the spatial variations is the QRST integral, where distribution of the time integral from the onset of the QRS to the end of the T-wave is analyzed (13). The morphology of the T-wave is described by the time instants of the maximum slope before and after the T_{apex} and the time interval where the signal is above 90% of amplitude of the T_{apex}. The number of the extrema in T-wave and the ratio between the area under the T-wave signal before and after the T_{apex} have also been used.

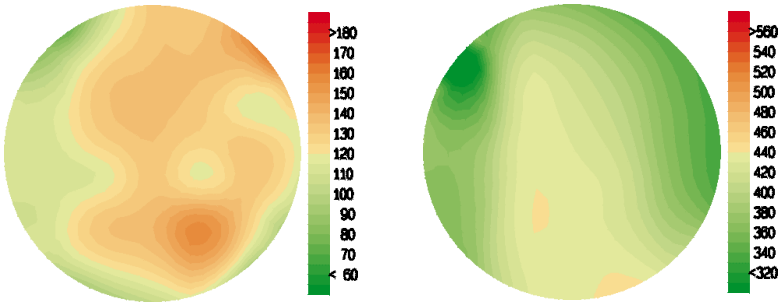

Fig. 3 Isovalue colormaps from a VT patient; left: QRS duration (ms), right: QT end time (ms). The values on the red area exceed the limit value used in risk stratification

Spatial parameter maps

Spatial features in multichannel ECG/MCG mappings can provide valuable information of the arrhythmia vulnerability to complement the analyses of morphological tracings. In the case of multichannel MCG data, we have calculated the distributions of the time-domain parameters, as well as the distributions of QT-apex and QT-end times and displayed them as isovalue colormaps (Fig. 3). The spatial heterogeneity in such presentations can be used as a further criterium to assess the arrhythmia risk. In addition, extrema trajectory plots revealing the spatial route of the maxima and the minima in MCG distributions have been used in arrhythmia risk evaluation (13).

Heart rate variability

The heart rate variability (HRV) gives information about the function of the autonomic nervous system (Fig. 4). The HRV analysis from the short-term recordings assigns some special requirements over the long-term measurements. The time intervals containing abnormal beats cannot simply be rejected. The HRV data have to be corrected from artefacts due to the triggering algorithm and ectopic beats to form an estimate of the sinusrhythm. Possible artefacts are either detected automatically as outlayers in HRV time series or by manual checking. We have interpolated the erroneous time instants by dividing the interval between correct sinus beats into a set of intervals, by algorithm based on a method introduced by Cheung 1981 (14), so that local variability is minimized. In the time domain, the

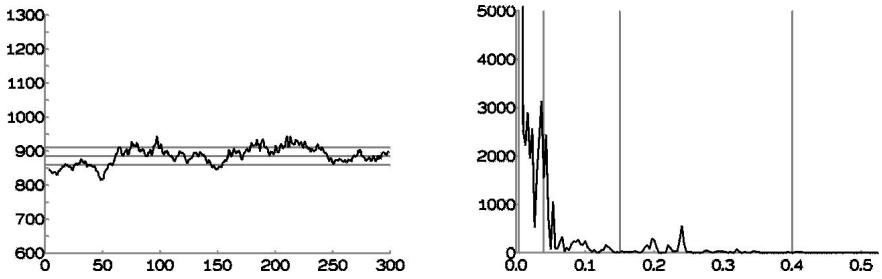

Fig. 4 Left: an instantaneous RR time (ms/s), right; power spectral density (ms^2/Hz/Hz)

mean and the standard deviation of the RR-time are then calculated. For the frequency domain parameters, the data is resampled using the convolution with a rectangular window (15) before utilizing the Fast Fourier transform. Before calculating the spectra the mean of the data are removed, the data are windowed by Hanning window, and the bias due to the windowing is removed. For quantification, the powers of the three segments of the spectra, from 0.003 to 0.04 Hz, from 0.04 to 0.15 Hz, and from 0.15 to 0.4 Hz, are calculated.

Patient studies

Late potentials/fields method have been shown to give good results in several studies (3, 16–19). Korhonen et al. studied 100 patients after myocardial infarction; 38 of them had history of VT (3). In classification, criteria for VT: the duration of the QRS complex ≥115 and duration of the low-amplitude signal (<300 fT) ≥30 ms were defined giving the sensitivity of 92% and the specificity of 61% for risk detection. Mäkijärvi et al. (16) and Moshage et al. (17) had previously reported a sensitivity of 70% and a specificity of 80% in smaller patient series. These results are slightly better than reported in corresponding HR-ECG studies (18, 19).

Oikarinen et al. (2) published a study of QT dispersion comprising ten patients with and eight patients without ventricular tachycardia after myocardial infarction. MCG was recorded in 42 locations and the dispersion between the shortest and longest QT interval was determined both manually and automatically. As a main result of the study, the patients prone to ventricular tachycardia after myocardial infarction exhibited significantly larger dispersion of the QT intervals in comparison with other infarction patients.

Some of the latest attempts to assess the vulnerability to ventricular arrhythmias have utilized magnetocardiographic QRST integral mapping. According to the results of these two preliminary studies, MCG QRST integral mapping seems to be able to differentiate VT/VF patients from normal controls well (20). The method was less successful in separating VT/VF patients from MI patients without documented VT/VF.

Discussion and conclusion

The cardiac risk stratification is an important part of modern health care. The HR-ECG and HR-MCG have shown both similar and complementing roles in non-invasive risk assessment. The approach taken in the HUCH BioMag Laboratory to combine different methods to analyze a 5-min recording has proven technically suitable for patient screening. The analysis is presently being carried out in several patient series, and the first results from retrospective patient studies have been clinically promising. However, the evaluation of the real clinical value of this approach cannot be made until the reference values of all the parameters are specified and the recently started prospective evaluation has been finished.

In general, the testing and validating of the new analysis methods with large normal and patient data sets is absolutely essential. The development of the measurement facilities improves the signal quality and makes it possible to detect even smaller features in the QRST signal morphology and spatial distributions. The analyzing methods are becoming more validated and user-independent to use. Some of the methods traditionally used only for signal averaged signals can also be adapted for non-averaged data to reveal non-stationary features in heart function. However, every new method or feature extracted from the heart signal must go through large tests and validations before it has any clinical value.

Besides the studies referred to above, the signal analysis methods described in this paper can also be applied in several other patient groups. Recent reviews of cardiomagnetic signal analysis and source localization methods give a wider description of the different approaches and patient studies (21, 22).

References

1. Montonen J, Ahonen A, Hämäläinen M, Ilmoniemi R, Laine P, Nenonen J, Paavola M, Simelius K, Simola J, Katila T (2000) Magnetocardiographic functional imaging studies in the BioMag Laboratory, In: Aine C et al. (eds) Biomag96 Proc. of the 10th Internat. Conf. on Biomagnetism. Springer, New York pp 498–501
2. Oikarinen L, Paavola M, Montonen J, Viitasalo M, Mäkijärvi M, Toivanen L, Katila T (1998) Magnetographic QT-interval dispersion in post myocardial infarction patients with sustainend ventricular tachycardia – validation of automated QT measurements. PACE 21: 1934–1942
3. Korhonen P, Montonen J, Mäkijärvi M et al. (2000) Late fields of the magnetocardiographic QRS complex as indicators of propensity to sustained ventricular tachycardia after myocardial infarction. J Cardiovasc Electrophysiol 11:413–420
4. Paavola M, Simelius K, Montonen J, Nenonen J, Katila T (1995) Averaging in cardiographic signal processing. In proceedings of Finnish Signal Processing Symposium
5. Burghoff M, Nenonen J, Trahms L, Katila T (2000) Conversion of magnetocardiographic recordings between two different multichannel SQUID devices. IEEE Trans Biomed Eng 47:869–875
6. Numminen J, Ahlfors S, Ilmoniemi R, Montonen J, Nenonen J (1995). Transformation of multichannel magnetocardiographic signals to standard grid form. IEEE Trans Biomed Eng 42(1):72–78
7. Simson MB (1981) Use of signals in the terminal QRS complex to identify patients with ventricular tachycardia after myocardial infarction. Circulation 64(2):235–242
8. Montonen J, Katila T, Leiniö M, Madekivi S, Mäkijärvi M, Nenonen J, Siltanen P (1988) Time and frequency domain analyses of cardiac micropotentials. In: Atsumi K, Kotani M, Ueno S, Katila T, Williamson S (eds) Biomagnetism ’87. Denki University Press, Tokyo, pp 278–281
9. Link A, Trahms L, Zimmermann R, Oeff M (1994) Complex-binomial bandpass filters for analyzing phase and envelope of high-frequency components in cardiac signals. In: Computers in cardiology 1994. IEEE Computer Society Press, pp 617–629
10. Kelen GJ, Henkin R, Starr A-M, Caref EB, Bloomfield D, El-Sherif N (1991) Spectral turbulence analysis of the signal averaged electrocardiogram and its predictive accuracy for inducible sustained monomorphic ventricular tachycardia. Am J Cardiol 67:965–975
11. Lepeschkin W Surawicz B (1952) The measurement of the QT interval of the electrocardiogram. Circulation 6:378–388
12. Hailer B, van Leeuwen P, Lange S, Wehr M (1999) Spatial distribution of QT dispersion measured by magnetocardiography under stress in coronary artery disease. J Electrocardiol 32:207–216
13. Stroink G, Meeder RJ, Elliott P, Lant J, Gardner MJ (1999) Arrhythmia vulnerability assessment using magnetic field maps and body surface potential maps. PACE 22:1718–1728
14. Cheung MN (1981) Detection of and recovery from errors in cardiac interbeat intervals. Psychophysiology 18(3):341–346
15. Berger RD, Akselrod S, Gordon D, Cohen RJ (1986) An efficient algorithm for spectral analysis of heart rate variability. IEEE Trans Biomed Eng 33(9):900–904
16. Mäkijärvi M, Montonen J, Toivonen L, et al. (1993) Identification of patients with ventricular tachycardia after myocardial infarction by high-resolution magnetocardiography and electrocardiography. J Electrocardiol 26:117–124
17. Achenbach S, Moshage W, Flüg M et al. (2000) Comparison of the QRS duration and RMS40 in signal-averaged recordings of the multichannel MCG to the signal-averaged ECG. In: Aine C et al. (eds) Biomag96: Proc. of the 10th Internat. Conf. on Biomagnetism. Springer, New York, pp 433–436
18. Breithardt G, Borgrefe M (1987) Recent advances at risk of ventricular tachyarrhythmias: Role of ventricular late potentials. Circulation 75:1091–1096
19. Denniss AR, Richards DA, Cody DV et al. (1986) Prognostic significance of ventricular tachycardia and fibrillation induced at programmed stimulation and delayed potentials detected on the signal-averaged electrocardiograms of survivors of acute myocardial infarction. Circulation 74:731–745
20. Hren R, Steinhoff U, Gessner C, Endt P, Goedde P, Agrawal R, Oeff M, Lux RL, Trahms L (2000) Value of magnetocardiographic QRST integral maps in the identification of patients at risk of ventricular arrhythmias. PACE 22:1292–130421
21. Troink G, Moshage W, Achenbach S: Cardiomagnetism. In: Andrä W, Nowak H (eds.) Magnetism in Medicine. Wiley VCH, Berlin, pp 136–189
22. Mäkijärvi M, Montonen J, Nenonen J (2000) Clinical application of magnetocardiographic mapping. In: Shenasha M et al (eds) Cardiac Mapping. Futura, New York, in press