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3-1-5: Quinidine-induced QT prolongation in guinea pig is automatically analyzed by micro-magnetocardiography system: Comparison with ECG

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Background: Drug-induced QT prolongation is a critical problem for drug development process. The guideline of International Conference on Harmonization requires to evaluate pre-clinical potential hazards of drug-induced QT prolongation. We have developed a micro-magnetocardiography (MCG) system for small animals comprised of ultrafine magnetometer array consisting of a 3×3 matrix of superconducting quantum interference device (SQUID) on a single silicon chip of 10mm square. We compared QT interval in MCG with that in ECG. Methods: Ten male Hartley guinea pigs (250g) were anesthetized with pentobarbital. Platinum needle electrodes were attached to animals. Excessive quinidine (60mg/kg) was administered intraperitoneally. MCG and ECG were recorded simultaneously at baseline, 3, 5, 7, 10, 15 min after injection. QT interval was automatically analyzed (PowerLab, ADInstruments Pty Ltd) and QTc was calculated by Bazett formula. Results: QTc was significantly prolonged from 286±10 to 299±11 msec in ECG (QTc-ECG) (p<0.001). QTc was prolonged from 283±16msec to 295±11 msec in MCG (QTc-MCG) (p<0.002). QTc-MCG correlated well with QTc-ECG at baseline (r2=0.915, p<0.0001), at 3 min after administration (r2=0.816, p=0.0003), at 5 min (r2=0.772, p=0.0008), at 7 min (r2=0.616, p=0.0072), at 10 min (r2=0.595, p=0.0090) and at 15min after (r2=0.707, p=0.0023). The Bland-Altman plot implied a good intermodality concordance placing 9 or 10 out of 10 guinea pigs between the limits of agreement at each time point of measurement. Conclusions: Micro-MCG successfully measured drug-induced QT prolongation with good correlation with ECG in guinea pig. Non-contact characteristics of MCG may enable high throughput screening test of drug-induced QT prolongation.

3-1-6: Towards a biomagnetic measurement of the human vagus nerve

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The vagus nerve innervates many organs parasympathetically. It is known that heart rate is reduced during vagal stimulation. A decrease in vagal activity can indicate increased mortality risk after acute myocardial infarction. Currently, cardiac vagal activity is measured indirectly through heart rate variability (HRV). A direct measurement of vagal activity seems possible, knowing that evoked fields of peripheral nerves have amplitudes of about 100fT. We hypothesize that the assessment of short-term HRV might lead to the identification of intervals containing vagal nerve signals. First, the magnetocardiogram (MCG) of two healthy volunteers was measured by the 63-SQUID system of PTB under mild vagal stimulation like hold breath, Valsalva maneuver and controlled breathing. Then, we repeated the experiments with the sensor placed over the neck while the subjects were lying on the left side. The MCG signals from the neck were sufficient for HRV analysis. The standard HRV parameter pNN60 showed a clear distinction between resting and recovery phases from the activity phase thus indicating vagal changes. Absolute pNN60 values for hold breath and Valsalva maneuver were: 41.18/5.78/34.53 and 45.31/11.34/47.83 (resting/activity/recovery). In controlled breathing, pNN60 values for exhalation were always higher than inhalation values. From the neck signals, we detected also 10-15Hz components with a distinguished spatial pattern and additional high-frequency components (f > 30Hz) during Valsalva maneuver. While a link of these signals to vagal activity cannot be excluded, we speculate their origin to be brain rhythms and muscle activation due to the stimulation activity. Spectral comparison of muscle reference signals and more elaborate study protocols will help to identify the origin of these components.

3-1-7: Towards an optical multichannel cardio-magnetometer for clinical use

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Over the past years, the Fribourg Atomic Physics Group (FRAP) has developed a laser-pumped room-temperature optical magnetometer capable of detecting cardiomagnetic fields[1]. In a gradiometric array using one active sensor to measure the heart field, about two hours were needed for a full cardiomagnetic map. To shorten the measurement time and increase the sensitivity, FRAP initiated a project to develop an multipole sensor array. While on that road, a compact and scalable Cs magnetometer sensor was designed, based on a 28 mm diameterantirelaxation coated Cs cell.
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(themselves mass produced, including quality control). Digital control electronics based on FPGAs were developed, and holographic laser beam multiplexing was implemented. The first year of the project has yielded a second-order gradiometer providing six sensors dedicated to capturing the cardiomagnetic signals. The digital electronics allows the new sensor modules to be easily arranged as either signal- or reference-channels. Initial results using the multichannel system to record heart signals indicate that it will soon be possible to image the cardiac magnetic field in only a few minutes using a larger sensor array covering the whole chest. To show that optical magnetometer technology is suitable for clinical use, a new research group was founded at the University Hospital in Jena. Both the FRAP and Jena groups, in collaboration with the company BMD Sys, will tackle the challenges of completing an optical multichannel magnetometer suitable for clinical use. We present current results and provide an outlook for the clinical system, discussing advantages and disadvantages of the optical magnetometer technology. The authors acknowledge the financial support of the VELUX Foundation and BMBF.[1] G. Bison, R. Wynands, and A. Weis, Optics Express, 11, 904, (2003)

3-1-8: Spatial-filter source imaging for an MCG sensor array with a small coverage

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In MCG, the magnetic field is measured on the subject’s body surface using sensors aligned on a flat surface. The coverage of such a sensor array is generally limited to an area that barely covers a human heart[1]. Therefore, due to the movements during cardiac cycles, instantaneous field maps often become mono-polar, and the results of source localization obtained from such a mono-polar map are generally error-prone.

This paper proposes two kinds of modifications for spatial filters used for source imaging form an MCG map with a limited coverage. The one method is a preprocessing in which the field gradients in the x and y directions are calculated. The graphical representation of these field gradients is referred to as the current-arrow map[1]. In this method, the spatial filter imaging is applied to the current arrow map, instead of being directly applied to the magnetic field data. The other method is to calculate the gram matrix[2] with a region greater than that corresponding to the sensor coverage. This method is applicable to non-adaptive spatial filters in which the gram matrix is used. We demonstrate the effectiveness of these proposed methods using computer simulations and experiments with MCG data taken from a healthy volunteer.

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3-1-9: Intravascular Pressure Curves: Magneto Mechanical Recordings

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Introduction Hypertension is a disorder characterized by blood pressure chronically high. It is monitored, treated and controlled by medicines and/or changes in the lifestyle. It is one of the most important causes of morbidity and mortality by its direct effects on the appearance of heart and vascular diseases. Therefore, is extremely important for patients to determine precisely his values of blood pressure. Objective Graphs of the intravascular blood pressures from left primitive carotid artery and left jugular vein are presented, by using a magneto-mechanical technique with pulse-pressure gauge, a device designed to register the magnetic flux variability of a magnetic marker (MM).

Procedure It is presented the implementation of a device used for registration of the magnetic induction generated by the periodical movements of the MM, which is placed on the skin (non-invasive) over a blood vessel, at the cervical level in the path of the left carotid. This device is composed by a magnetoresistive (MR) sensor KMZ10, which is placed at a fixed distance of 2 cm of the MM.

Discussion This is a technique for measuring the pulse besides monitoring the mechanical activity in a blood vessel segment, by using the mechanical activity of both arteries and veins under expansion of their walls by influx of the bloodstream and the properties of the permalloy in the MR sensors. This monitoring gives us intravascular pressure curves similar to that obtained by a direct measurement of the pressure, but in a non-invasive way.
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3-1-10: Magnetic cardiac signal extraction from measurements of patients with Implantable Cardioverter Defibrillators

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Estimation of sudden cardiac death (SCD) incidence in the United States ranges from 300,000 to 350,000 annually. Event rates for Europe are similar to those in the United States. The proportion of all natural death due to SCD is 13% when a definition of one hour from onset of symptoms is used. Increasing the power in risk stratification for SCD is an important topic in cardiology, especially to improve the indications for Implantable Cardioverter Defibrillators (ICDs). Prospective studies are ongoing for validating the use of QRS-fragmentation [1] as predictor of arrhythmic events. Unfortunately, this kind of studies needs time. A faster way is to do retrospective studies on patients with already implanted ICDs. Until now, it has not been possible to perform measurements of QRS-fragmentation in patients with ICDs. In fact, the presence of this device in the thorax (normally it is located near the left shoulder) of the patient leads to very strong interferences in biomagnetic measurements due to the ferromagnetic case of the batteries. These interferences are an order of magnitude larger than the biomagnetic signal of the heart. For this reason, ICDs or pacemakers are among the exclusion criteria for studies concerning magnetic field imaging (MFI). Here, a post-processing method is presented, based on Blind Source Separation, to extract cardiac signals from biomagnetic signals that are disturbed by an ICD.[1] Increased Intra-QRS Fragmentation in Magnetocardiography as a Predictor of Arrhythmic Events and Mortality in Patients with Cardiac Dysfunction after Myocardial Infarction. (2006) Korhonen P., Husa T, Tierala I, Väännänen H.; Mäkijärvi M; Katila T; Toivonen, L. In J. Cardiovasc. Elect., vol 17(4), pp. 396-401.

3-1-11: Waveform analysis of rest and exercise-induced MCG based on a 3-D vector measurement

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Objective
An aim of this study is to analyze 3-D MCG of resting time (R-MCG) and exercise-induced MCG (ex-MCG) for normal subjects based on a 3-D vector MCG measurement system.

Methods
3-D measurements [1] of both MCGs for eleven male normal subjects (ages: 22-24) were performed using a wooden ergometer in a magnetically shielded room. The R-MCG measurement of resting time was performed during 4 minutes before exercise. After reaching the target heart rate, ex-MCG measurement was carried out for ten minutes. The ex-MCGs filtered with 0.5 to 300 Hz were sampled by 1kHz. Time-frequency analysis (wavelet transforms) and the PCA were applied to each MCG data. And angular distribution using temporal differentiation of averaged data was investigated to QRS and ST segment of each MCG data.

Results and Discussion
From the results of averaged heart rate with all subjects during measurement of ex-MCGs, it was found that the heart rate from starting ex-MCG measurement to 4 minute was sharply decreased and it showed steady state after 4 minute. Dominant frequency of the ST segment in R-MCG was ranged 5.5 to 6.5 Hz in all components. The peak frequency of the ex- MCG was shifted to around 10.5 Hz in Bx and Bz components. The angular distribution of temporal differentiation during the QRS showed no dominant change between R-MCG and ex-MCG. However, the angular distribution during the ST segment of ex-MCG showed higher value (Bx: 17.3 °, Bz: 14.3 °) than that of R-MCG (Bx: 7.8 °, Bz: 8.6 °) in Bx and Bz components. These results show that a 3-D vector MCG measurement is useful for fine discussing the change of the ST segment in ex-MCG.

Reference

3-1-12: Magnetocardiography with high Tc GMR-based mixed sensors

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Mixed sensors are very good candidates for measuring biomagnetic signals. These very sensitive magnetometers are