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Magnetocardiography capabilities in myocardium injuries diagnosis

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ABSTRACT

Objective: The electrophysiological properties of the myocardium are extremely heterogeneous. Verification of new magnetocardiography (MCG) signs appears an important aspect for severity assessment of ischemic myocardium damage, ischemic heart disease (IHD) course prognosis, determining of indications for preventive "aggressive" therapy and estimation of its efficacy in patients with IHD. The objective of this research was the investigation of magnetocardiography (MCG) capabilities in diagnosis of ischemic and inflammatory myocardial injuries using new MCG markers of the spatiotemporal organization of myocardium excitation. Methods and results: There were 128 patients examined in three groups. Group 1 contained 34 healthy volunteers. Group 2 contained 62 patients with IHD diagnosis. Group 3 included 32 comparatively young patients with acute myocarditis diagnosis. MCG-mapping of patients was performed at rest on the 7-channel MCG-scanners "Cardiomagscan" V 3.1 (Company KMG, Ukraine) in non-shielded MCG laboratory. 11 MCG markers were determined for selected time intervals of the cardiac cycle. Obtained data provided evidences about significant differences in values of proposed MCG markers for various groups. In patients with AMI, rate of parameters change is higher than without AMI (Sub-groups 2.1 and 2.2 differ by 8 MCG markers). Patients of 2nd and 3rd groups are different from healthy patients by 8 of 11 markers. Analysis of the obtained data has demonstrated good capabilities of MCG in differential diagnostics. Application of discriminatory analysis allowed us to get classification functions, which could be used (with 82% accuracy) to qualify the just examined patient to the investigated categories. Conclusion: Based on the new methodological approach during the studies, the most informative MCG-criteria of space-temporal organization of myocardium excitation in patients with IHD has been proposed. The method is able to distinguish healthy subjects and myocarditis patients and patients with IHD without previous MI with high sensitivity and specificity.

Keywords: Transmural Electric Heterogeneity; Magnetocardiography; Myocardial Ischemia; Myocarditis; Differential Diagnostics

1. INTRODUCTION

Nowadays routine clinic-functional diagnostic methods of ischemic heart disease (IHD) are mostly based on clinical signs of disease and ECG *ST* segment shift in rest and during functional tests. It is well known that changes of *ST* segment and T wave could be aroused not only from IHD, but also from many other diseases. Diagnostic difficulties are frequently caused by abnormal clinical implication of IHD, including painless myocardial ischemia. Coronary angiography (CAG) still remains the basic method for IHD diagnosis. CAG is usually used for patients with IHD symptoms and with positive or controversial results of screening tests (stress ECG, stress echocardiography) in order to confirm availability and expansion of vascular injuries, for estimation of revascularization feasibility and adequacy, coronary atherosclerosis progression or regression. At the same time, in being dependent of the population distinctions of the examined series, 19% to 57% of the examined patients may not have significant coronary artery stenosis [1].

Search and verification of new electrophysiological

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signs appears important aspects for severity assessment of ischemic myocardium damage, IHD course prognosis, determining of indications for preventive "aggressive" therapy and estimation of its efficacy in patients with IHD. Magnetocardiography (MCG) is a noninvasive measurement technology for magnetic signals generated by the heart's electrical activity sources [2]. As compared to ECG, advantages of MCG are determined by its extreme sensitivity to tangential components of myocardial currents and lover (as opposed to ECG) dependency of monitored magnetic field parameters against the influence of multilayer anisotropic conductive medium, surrounding the current source. Furthermore, MCG is sensitive to vortex flows (circular currents, injury currents), which couldn't be registered with ECG at all. Thereby, MCG is able to detect activation disorders caused by myocardial ischemia more accurately and at an earlier stage than ECG [5]. During investigations of limitations of the IHD diagnosis at rest, it was determined that MCG exceeds ECG with diagnosis accuracy 60% - 90% for different examined populations [6-10]. Analysis of the current density distribution maps allowed to distinguish IHD-patients with and without haemodynamically significant stenosis with 62.8% sensitivity and 61.3% specificity [7]. K. Toltstrup in his investigation of 75 patients with acute retrosternal pain notes that while stress EchoCG possesses sensitivity 91.3% and specificity 75%, MCG in rest possesses sensitivity 87.1% and specificity 85.7% [9]. As a result of investigation of the patients' group with stable exertional angina before carrying out the coronary arteriography, Chen, *et al.* [10] have demonstrated the specificity of MCG scanning up to 97% and sensitivity—80% to 85%. During retrosternal pain in patients with complete block of the left bundle-branch, it is important to perform early diagnosis of acute coronary syndrome. Park, *et al.* [11] have identified high sensitivity and specificity of MCG as compared to Troponin I investigation.

Non-coronary myocardial diseases, particularly myocarditis, are often accompanied by expressed pain syndrome, but clinically available practical methods of differential diagnostics are insufficiently informative.

Objective of this research was to investigate MCG capabilities in diagnosis of ischemic and inflammatory myocardial injuries using new MCG markers of the spatiotemporal organization of myocardium excitation.

2. MATERIALS AND METHODS

2.1. Basic Characteristics of Examined Patients

There were 128 patients examined in three groups.

Group 1 contained 34 healthy volunteers aged from 27 to 40 years (mean age 36 ± 6.4 years), passed through the comprehensive laboratory and instrumental research, including ECG at rest and post-exercise ECG, Echo-CG.

Group 2 contained 62 patients with the diagnosis of IHD. The following criteria were used to exclude patients from examination: complete block of the left bundle-branch on the ECG, Stage IIB-III of chronic heart failure, severe diabetes, Stage III of hypertensive disease, renal and hepatic failure, obstructive respiratory diseases, locomotorium diseases preventing exercise testing. Patients of the Group 2 were divided into 2 Sub-groups (2.1 and 2.2). Sub-group 2.1 was composed on the base of random retrospective study of data obtained in examination of 183 patients during 2001-2002 years in the Kath. Krankenhaus, Department of Medicine, Philippusstift (Essen, Germany). MCG examinations were performed using MCG system MCG-7 (SQUIG AG, Germany) with participation of authors of this paper as MCG-7 system developers. 30 patients with low-grade indications of IHD resulted from the clinical and instrumental research were selected from the common examined group. Selected patients had slightly changed ECG, neither myocardial infarction (MI) anamnesis, nor signs of myocardial hypertrophy according to Echo-CG results; thereat, according to the angiographic study data, stenosis of one, two or three vessels or of trunk of the left coronary artery with diameter less than 50% were detected in all of these patients. Mean age of examined patients was 55 ± 10 years.

Sub-group 2.2. In order to estimate informative value of new MCG markers at rest in patients with acute MI (AMI) dependent on myocardial ischemia signs availability, detected during exercise test, we have analyzed examination results of 32 patients with Q-wave AMI (30 man and 1 women) 31 - 70 years old (mean age 54.2 ± 1.8 years), which underwent medical treatment in the intensive care unit of the NSC "M. D. Strajesko Institute of Cardiology", NAS of Ukraine. AMI diagnosis was determined on the base of standard criteria [12]. On the 10th - 12th day of AMI, patients were subjected to exercise examination (treadmill test under modified Bruce protocol using treadmill "Cardioperfect", USA), and to MCG. During exercise test myocardial ischemia signs were detected in 21 patients (Sub-group 2.2A); in 11 patients (Sub-group 2.2B), test findings were negative. Sub-groups were comparable both by clinical-anamnesis data and by medical treatment.

Group 3 included 32 comparatively young patients (17 to 29 years, mean age 23 ± 2.4 years), which underwent medical treatment in the non-coronary heart diseases and clinical rheumatology unit of NSC "M. D. Strajesko Institute of Cardiology", NAS of Ukraine, and in the rheumatology unit of General Military-Medical Clinical Center DM of Ukraine with acute myocarditis. "Myocarditis" was diagnosed on the base of disease relation with recently previous virus infection or presence of the chronic infection nidus in the body, results of clinical instrumental and laboratory researches and with account

of diagnostic criteria, recommended by New York Heart Association. Young ages of patients make it possible to decrease significantly the IHD probability.

2.2. Magnetocardiography

MCG-mapping of patients was performed at rest on the 7-channel MCG-scanners "Cardiomagscan" V 3.1 (Company KMG, Ukraine) in non-shielded MCG laboratory premise of the NSC "M. D. Strajesko Institute of Cardiology", NAS of Ukraine and in MCG laboratory of the General Military-Medical Clinical Center DM of Ukraine.

Magnetic field of the heart was registered in 36 points of the 8 cm pitch rectangular grid 3 × 3 with simultaneous recording of the second standard ECG lead. On the base of 36 synchronous averaged MCG-curves momentary, equi-induction maps of magnetic field distribution were plotted using 2D interpolation algorithms. In contrary to the previous MCG investigations using "inverse solution" algorithm, equi-induction maps of magnetic field distribution were transformed into current density vectors (CDV) distribution maps, followed-up by application of original indicants.

Each CDV distribution map was used for calculation of single-step magnitudes of the maximal and global current density, and then curves were plotted representing variations of these values during the overall cardiac cycle or its separate segments. Duration of the maximum CDV was used as the maximum density value (Max). Arithmetic sum of duration values of all CDV for given single-step map was used as the global current density magnitude (Sum). Every following point of the curves (separate single-step map) was plotted with 4 ms interval for ventricular depolarization and 10 ms for ventricular repolarization. Then cardio-cycle intervals durations were sequentionally calculated using current density variation curves. Time points when variation curves of maximum or global current density values reached zero line were considered as start and end of the time interval. More detailed description of this magnetic mapping technology and basic data interpretation concept is reviewed in [13].

In order to estimate temporal organization of ventricular depolarization, we have chosen the following MCG markers:

1) time interval duration from the start of the QRS complex to the R-wave peak—t_1;

2) magnitude of the maximum (Max_R) and global (Sum_R) current densities at the R-wave peak;

3) depolarization interval duration—QRS;

4) angle difference between directions of the maximum CDV at the R and T peaks—Delta RT

In order to estimate disturbance ratio of the temporal organization of ventricular repolarization, we have chosen the following time intervals:

1) interval of the regional electric heterogeneity (beginning——of ST- Ta), which characterize the regional electric heterogene- ity of myocardium in the "ischemia window"; this interval was divided onto two sub-intervals D_1 and D_2, where deviation (displacement) of the maximum current density vector was estimated compared to its original value. In addition, at the moment of 80 ms from the J-point we have registered direction angle of the maximum current density vector and estimated its deviation from the normal direction limits (Delta 80);

2) myocardium transmural electric heterogeneity interval (Ta-e) was also splitted onto two equal sub-intervals D_3 and D_4, where deviation of the maximum current density vector was also estimated.

11 MCG markers {designations in tables} were determined for selected time intervals of the cardiac cycle: {**N1**}—QRS—duration of the QRS complex (ms); {**N2**}—Delta 80—maximum current density vector deviation from the normal direction at 80 ms moment from the J-point; {**N3**}—D_1; {**N4**}—D_2; {**N5**}—D_3; {**N6**}—D_4 (D_1, D_2, D_3, D_4—maximum current density vector deviation at 4 ST-T sub-intervals (starting at 60 ms from the J-point)); {**N7**}—$T_{a\text{-}e}$—time interval duration from the peak to the end of T-wave; {**N8**}—Delta RT—difference between direction angles of the maximum current density vector at R and T peaks; {**N9**}—Sum_R/Sum_T—ratio of the global current density at the R-peak to the global current density at the T-peak; {**N10**}—Max_R/Max_T—ratio of the global maximum current density at the R-peak to the maximum current density at the T-peak; {**N11**}—(QRS—t_1)/t_1—symmetry factor of the QRS complex.

Obtained results were processed with variation and non-parametric statistics methods using applied statistics software packages "Microsoft Excel" and "Statistica" for Windows by calculation of arithmetic mean (M) and standard error of mean (m) values for each variation series. Deviations validity was determined using Student's t-criterion. Deviations were assumed valid for $P < 0.05$. Discriminatory analysis has been performed in order to determine possibility of results prognostication by MCG-data. The "model" was applied allowing prediction concerning the set particular patient would belong to. For this purpose we used step-by-step discriminatory analysis with inclusion of the variable with maximum contribution into differences between data sets at each analysis step.

2.3. Results

Results of the primary data procession are listed in **Tables 1(a)** and **(b)** and **2(a)** and **(b)**.

Obtained data evidence about significant differences in values of proposed MCG markers for various groups. Thus, patients of Groups 2 and 3 differ from healthy pa-

Table 1. Values of MCG markers in groups and sub-groups (M ± m).

(a)

Groups	MCG-markers					
	QRS (ms)	**Delta 80**	**D_1**	**D_2**	**D_3**	**D_4**
1	77.8 ± 1.73	3.1 ± 0.64	3.2 ± 0.54	2.7 ± 0.34	2.6 ± 0.36	4.5 ± 0.4
2	80.2 ± 1.69	52.2 ± 7.56	7.9 ± 0.75	8 ± 0.84	5.6 ± 0.68	10.4 ± 1.3
2.1	73.2 ± 1.77	61.6 ± 11.4	7.2 ± 1.06	5.5 ± 0.96	3.9 ± 0.71	8.2 ± 1.3
2.2.A	87.8 ± 3.2	51.9 ± 14.3	10.4 ± 1.44	12.8 ± 1.55	8.1 ± 1.4	15.9 ± 2.8
2.2.B	84.7 ± 2.79	27.3 ± 8.87	5.0 ± 0.69	5.5 ± 1.06	5.5 ± 1.51	5.9 ± 1.1
3	83.6 ± 2.43	36.8 ± 8.92	7.8 ± 1.52	7.9 ± 1.72	6.5 ± 1.53	14.4 ± 2.5

(b)

	MCG-markers				
	Ta-e	**Delta RT**	**Sum_R/Sum_T**	**Max_R/Max_T**	**$(QRS-t_1)/t_1$**
1	110.3 ± 1.66	21.2 ± 1.95	4.8 ± 0.3	3.6 ± 0.25	1.4 ± 0.06
2	96.6 ± 2.11	65.7 ± 7.17	5.1 ± 0.4	4 ± 0.26	1.4 ± 0.05
2.1	93 ± 2.31	31.2 ± 4.21	6.4 ± 0.7	4.3 ± 0.42	1.3 ± 0.05
2.2.A	105.2 ± 4.06	125.8 ± 11.7	3.4 ± 0.4	3.7 ± 0.41	1.6 ± 0.11
2.2.B	90 ± 5.05	45.4 ± 6.6	4.5 ± 0.6	3.7 ± 0.5	1.5 ± 0.12
3	102.7 ± 5.24	40.4 ± 3.91	8.6 ± 0.8	5.2 ± 0.48	1.6 ± 0.1

Table 2. Student's test results for deviations validity of MCG markers in different groups.

(a)

Comparison Groups	**MCG-markers (part 1)**					
	QRS (ms)	**Delta 80**	**D_1**	**D_2**	**D_3**	**D_4**
1 - 2	0.320	<0.001	<0.001	<0.001	<0.001	<0.001
1 - 3	0.055	0.001	0.007	0.006	0.018	0.001
2 - 3	0.251	0.194	0.971	0.988	0.592	0.165
2.1 - 2.2	<0.001	0.598	0.077	<0.001	0.011	0.024
2.1 - 2.2.A	<0.001	0.598	0.077	<0.001	0.011	0.024
2.2.A - 2.2.B	0.474	0.154	0.002	<0.001	0.224	0.004
2.1 - 2.2.B	0.002	0.023	0.089	0.993	0.334	0.204
2.1 - 3	0.146	0.001	0.236	<0.05	0.672	0.233

(b)

Comparison Groups	**MCG-markers (part 2)**				
	T_a-T_e	**Delta RT**	**Sum_R/Sum_T**	**Max_R/Max_T**	**$(QRS-t_1)/t_1$**
1 - 2	<0.001	<0.001	0.678	0.003	0.977
1 - 3	0.010	<0.001	<0.001	0.003	0.089
2 - 3	0.286	0.003	<0.001	0.027	0.080
2.1 - 2.2	0.013	<0.001	0.001	0.259	0.016
2.1 - 2.2A	0.013	<0.001	0.001	0.259	0.016
2.2A - 2.2B	0.028	<0.001	0.143	0.917	0.435
2.1 - 2.2.B	0.597	0.083	0.056	0.366	0.147
2.1 - 3	0.067	0.078	0.048	0.875	0.048

tients by 8 of 11 markers; herewith patients with myocarditis were additionally different by the value of Sum_R/Sum_T. Groups 2 and 3 were different from each other by the values of 3 parameters.

It's interesting to compare MCG markers for different courses of IHD (in sub-groups of the Group 2). In patients with AMI, rate of parameters changes is higher than without AMI (Sub-groups 2.1 and 2.2 differ by 8 MCG markers). Among patients with AMI data analysis have demonstrated much higher rate of MCG changes under the positive stress-test (Sub-group 2.2A as compared to 2.2B), moreover these sub-groups were different from each another by 5 MCG markers values. Therefore, when compared to the Sub-group 2.1 (without MI in anamnesis), Sub-group 2.2A differed by 8 parameters, while Sub-group 2.2B—only by 2 parameters.

Analysis of obtained data has demonstrated good capabilities of MCG in differential diagnostics.

Application of discriminatory analysis allowed us to get classification functions, that could be used (with certain accuracy) to qualify just examined patient to the investigated categories. **Table 3** demonstrates the input of each variable to the patients qualifying model to one or another group.

Value of Wilks' Lambda 0.35, p-level p = 0.0001 at F-criterion 11.5 evidence about rather good discrimination. Using classification functions, obtained as a result of discriminative analysis, we can qualify patient to one of three investigated categories with 82% accuracy. There are three discriminant functions (a discriminant function is a linear combination of the discriminating variables) obtained with standardized coefficients for the three most informative variables, selected by the program—**Table 4**.

Resulted discriminant functions have the following form:

$$\begin{aligned}\text{Group1} = &-0.02\times\text{N2}+1.33\times\text{N9}+10.83\times\text{N11}\\ &-0.04\times\text{N8}+0.31\times\text{N7}-0.07\times\text{N6}\\ &+0.23\times\text{N4}-0.02\times\text{N3}-28.14\end{aligned}$$

$$\begin{aligned}\text{Group2} = &\ 0.01\times\text{N2}+1.35\times\text{N9}+10.62\times\text{N11}\\ &-0.04\times\text{N8}+0.31\times\text{N7}-0.01\times\text{N6}\\ &+0.23\times\text{N4}-0.02\times\text{N3}-25.29\end{aligned}$$

$$\begin{aligned}\text{Group3} = &-0.01\times\text{N2}+1.91\times\text{N9}+13.52\times\text{N11}\\ &-0.04\times\text{N8}+0.28\times\text{N7}-0.05\times\text{N6}\\ &+0.40\times\text{N4}-0.11\times\text{N3}-36.16\end{aligned}$$

Every new observation is calculated vs. these three functions. New patient would be qualified to the class with maximum qualification value (*i.e.*, with high probability he has correspondent disease).

Scattering graph of canonical values allows to visualize variability of results and to observe the data cloud for each selected group. Scattering graph of canonical values (**Figure 1**) represents the patient groups splitting.

Table 3. Summary table for discriminatory analysis of data for three main groups (Groups 1, 2, 3).

	Wilks' Lambda	F-remove (2.129)	p-level
N2—**Delta 80**	0.39	7.40	0.001
N9—**Sum_R/Sum_T**	0.49	25.83	0.000
N11—**$(QRS- t_1)/t_1$**	0.39	8.24	0.000
N8—**Delta RT**	0.40	9.50	0.000
N7—**T_{a-e}**	0.39	6.59	0.002
N6—**D_4**	0.38	6.09	0.003
N4—**D_2**	0.38	5.71	0.004
N3—**D_1**	0.36	2.29	0.105

Table 4. Standardized (normalized) coefficients of the discriminant function.

	Group 1	Group 2	Group 3
	p = 0.32374	p = 0.44604	p = 0.23022
N2—**Delta 80**	−0.02	0.01	−0.01
N9—**Sum_R/Sum_T**	1.33	1.35	1.91
N11—**$(QRS- t_1)/t_1$**	10.83	10.62	13.52
N8—**Delta RT**	−0.04	−0.01	−0.04
N7—**T_{a-e}**	0.31	0.26	0.28
N6—**D_4**	−0.07	−0.01	0.05
N4—**D_2**	0.23	0.31	0.40
N3—**D_1**	−0.02	0.04	0.11
Constant	−28.14	−25.29	−36.16

It's very important to develop new differential criteria between IHD patients with slight ECG changes and without MI in anamnesis and with myocarditis with indistinct clinical implications.

Using discriminatory analysis we have obtained discriminant functions with standardized coefficients for the most informative MCG markers of the Sub-group 2.1 and Group 3 (**Tables 5**, **6**).

Value of Wilks' Lambda 0.57, p-level p = 0.0001 at F-criterion 5.77 evidence about rather good discrimination.

Using classification functions, obtained as a result of discriminative analysis, we can qualify patient to one of two investigated categories with 82% accuracy.

As a result of discriminative analysis, obtained discriminant functions have following form:

$$\begin{aligned}\text{Sub-group2.1} = &\ 0.59\times\text{N2}+0.90\times\text{N9}+1.13\times\text{N11}\\ &-0.004\times\text{N8}+0.16\times\text{N7}-0.03\times\text{N6}\\ &+0.17\times\text{N4}-26.58\times\text{N3}-36.16\end{aligned}$$

Table 5. Summary table for discriminatory analysis of data for the Sub-group 2.1 and Group 3.

	Wilks' Lambda	F-remove (2.129)	p-level
N1—**QRS**	0.60	2.18	0.146
N9—**Sum_R/Sum_T**	0.72	14.02	0.000
N11—**$(QRS- t_1)/t_1$**	0.62	4.11	0.048
N2—**Delta 80**	0.64	5.98	0.018
N4—**D_2**	0.61	3.85	0.045
N6—**D_4**	0.59	1.46	0.233
N3—**D_1**	0.59	1.44	0.236

Table 6. Coefficients of the discriminant function for the Sub-group 2.1 and the Group 3.

	Sub-group 2.1	Group 3
	p = 0.48387	p = 0.51613
N1—**QRS**	0.59	0.64
N9—**Sum_R/Sum_T**	0.90	1.22
N11—**$(QRS- t_1)/t_1$**	1.13	3.23
N2—**Delta 80**	0.00	−0.02
N4—**D_2**	0.16	0.25
N6—**D_4**	−0.03	0.01
N3—**D_1**	0.17	0.24
Constant	−26.58	−36.84

$$\begin{aligned}\text{Group3} = {} & 0.64\times\text{N2} + 1.22\times\text{N9} + 3.23\times\text{N11} \\ & - 0.004\times\text{N8} + 0.25\times\text{N7} - 0.01\times\text{N6} \\ & + 0.24\times\text{N4} - 36.84\times\text{N3} - 36.16\end{aligned}$$

3. DISCUSSION

Compared to the surface ECG, MCG has more selective capabilities for registration of electric activity on the certain depth of myocardium [19], *i.e*. provides possibility to estimate electromagnetic activity predominantly of those heart's areas (and muscular layers) with maximum ions flow density. That is why MCG markers, related to the "ischemia window", are more informative in detection of slightly ischemic myocardium even at rest, while ECG changes appears only during ischemia enhancement under exercise testing [20]. Actually, in our investigation, the most effective MCG markers where ones calculated on JT interval, namely Delta 80, D_1 and D_2, which characterize abnormal angular displacement of CDV at the beginning of the "ischemia window" and position changes of ST-segment, which is in agreement with results of foreign authors [21].

It's known that duration of action potential (AP) could

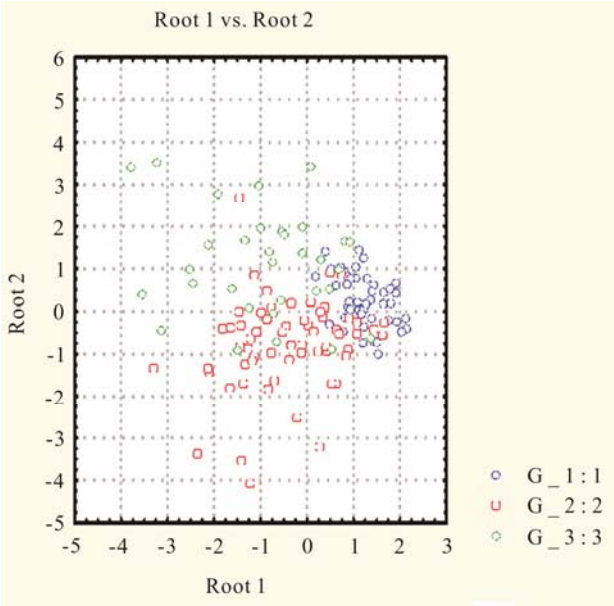

Figure 1. Scattering graph of canonical values for three patient groups.

be increased due to repolarization delay, which became apparent in prolongation of its 3rd phase. In order to describe such changes of AP, L. Hondeghem, *et al.* have proposed to use "triangulation" expression [22] having in mind a phenomenon of AP's form approaching to the triangle shape. It has been proposed to determine traingulation degree as AP time interval duration at 90% and 30% repolarization level. According to the data of numerous researches, triangulation enhancement, independently of its mechanism and causes, evidences about myocardium injury and probability increasing arrhythmia progress [25-27]. On the ECG, different triangulation degree appears as T-wave flattening and/or widening. It could be supposed, that triangulation degree enhancement and T_{a-e} interval elongation reflect the nature of same effects. In several papers, C. Antzelevich, *et al.* claim that T_{a-e}—is only ECG marker, which could be used to judge about degree of arrhythmogenic readiness of myocardium, as a consequence of it's injury [23, 24]. In this paper, we have used new approach to the estimation of the triangulation repolarization degree (T_{a-e} duration) on the base of changes analysis of the global current density curve, which for our opinion increases significantly accuracy and reproducibility of results. Such approach to the analysis of transmural electric heterogeneity was used by authors for the first time for examination of patients with ventricular rhythm disturbances [28].

It's very interesting that T_{a-e} duration changes analysis demonstrates that in some cases triangulation degree could be decreased (duration shortening of Tapex-Tend interval). For example, as compared to the healthy pa-

tients, this marker is lower in the Sub-group 2.1 and Group 3. At the same time, this marker is higher in 2.2A as compared to 2.2B. It could be supposed, that T_{apex}-T_{end} time interval shortening mechanism is caused by predomination of the functional changes of ions flow density over the structural changes. Under conditions of combined, hypoxia occurs molecular oxygen deficiency in the myocardial tissues, and intensity of oxidation processes falls behind the glycolysis intensity. Molecular oxygen, being the final acceptor of protons, is required for the ATP synthesis. As a result of the entire complex of metabolic disorders, ATP synthesis is disrupted and deficiencies of energetic and plastic resources of cells appear and lead to the myocardium functions disorder. Na-K-dependent ATP-ase inhibition leads to disorder of the Na-K pump function, which results in non-homogenous shortening of the third phase of AP, and hence to increasing of the transmural electric heterogeneity. This should be resulted in duration changes of the T_{a-e} interval, which was shorter in patients with slightly ischemic myocardium (Sub-group 2.1—93.0 ± 2.31 vs. 110.3 ± 1.66; $p < 0.05$), as compared to the volunteers of the control group. However, presence of the structural changes and ischemia cause ion mechanisms activation, promoting prolongation of the repolarization at the cost of AP 3rd phase (Sub-group 2.2A and Sub-group 2.2B—105.2 ± 4.06 vs. −90 ± 5.05; $p < 0.05$). This result is very interesting in the sense of comparison of MCG data of AMI patients depending upon ischemia symptoms availability according to the stress-test results with clinical ECG control. Yet at the rest conditions, there was high changes degree revealed of the 5 MCG markers under positive stress-test (Sub-group 2.2A as compared to the Sub-group 2.2B). Thus markers D_1 (10.4 ± 1.44 vs. 5.0 ± 0.69; $p < 0.05$), D_2 (12.8 ± 1.55 vs. 5.5 ± 1.06; $p < 0.05$), D_4 (15.9 ± 2.89 vs. 5.9 ± 1.18; $p < 0.05$), T_{a-e} (105.2 ± 4.06 vs. 90.0 ± 5.05; $p < 0.05$) and Delta RT (125.8 ± 11.7 vs. 45.4 ± 6.6; $p < 0.05$) reliably demonstrate differences between the two sub-groups. Thereby, this paper offers good challenge towards MCG application as additional, safe and cost effective stratification method of AMI patients for disease course prognosis, medical treatment differentiation and its effectiveness control. Employment of the reperfusion and antithrombotic therapy results in mosaic pattern of the formed necrotic zone, interleaved with superior myocardium zones (being at most in ischemic or "stunned" condition). In such patients, reticular microscopic myocardial fibrosis is present [14]. And even magnetic-resonance technique is not able to detect such tiny myocardial injuries *in vivo* [15-17]. At the same time, MCG could be sensitive even to slight changes of repolarization homogeneity, caused by such fibrosis [18]. We don't exclude possibility of new terms appearance for notification of analyzed MCG markers, because investigated phenomena could have different content as compared to standard ECG.

The analysis of MCG markers myocardium excitation abnormalities in myocarditis patients makes it possible to separate differential features as compared to IHD with indistinct clinical and ECG-changes. It could be supposed, that the basic reason of the markers variability in two patient groups—are caused by the differences in intensity and localization of the hypoxia processes, inherent to ischemia and inflammatory process in myocardium.

This conclusion is supported by the fact that the values of MCG markers Delta 80, appeared during the time interval, correspondent to the "ischemia window", were different for Sub-group 2.1 and Group 3 (61.6 ± 11.4 vs. 36.8 ± 8.92; $p < 0.001$). Explanation of increased value of D_2 marker in patients with myocarditis as compared to the IHD patients (7.9 ± 1.72 vs. 5.5 ± 0.96; $p < 0.05$) could be based on our principal conception for MCG data interpretation [19], which claims that CDV direction corresponds to the direction of tissues, where the ions flow was activated. In this case, it could be stated, that increase in CDV deviation on D_2 interval demonstrates the regional abnormal heterogeneity of the ions flow in differently directed myocardium layers. It should be noted reliable increase of the markers Sum_R/Sum_T values (8.6 ± 0.8 vs. 6.4 ± 0.71; $p < 0.001$) in patients with myocarditis, which reflect mutual changes between current densities at the peaks of R and T waves as dissociation between transmembrane ion flows during activation and recovery.

Limitations. There are several limitations in this study. First, the results must however be viewed with caution as the groups of patients are rather small and differ in a number of characteristics. The number of control subjects examined in this study was also relatively small. Recently, as the primary sources are spread over a larger region, reconstructed current density distributions may be used to identify changes in cardiac electric activity although the non-uniqueness of the inverse problem requires that results must be viewed with caution. Finally, conformation of the obtained result of discriminative analysis would be desirable in a larger series.

4. CONCLUSIONS

1) Magnetocardiography using new markers is a new instrument for differential diagnostics of the myocardium electrical injuries of ischemic and inflammatory genesis. The method is able to distinguish between healthy subjects and patients with myocarditis and patients with IHD without previous MI with high sensitivity and specificity.

2) MCG in patients with acute myocardial infarction could be useful to detect ischemic myocardium and

hence, to determine revasculization feasibility.

REFERENCES

[1] Kemp, H.G., Kronmal, R.A., Vietstra, R.E. and Frye, R.L. (1986) Seven year survival of patients with normal coronary arteriograms: A CASS registry study. *Journal of the American College of Cardiology*, **7**, 479-483. doi:10.1016/S0735-1097(86)80456-9

[2] Malmivuo, J. and Plonsey, R. (1995) Bioelectromagnetism: Principles and applications of bioelectric and biomagnetic fields. New York: Oxford University Press. doi:10.1093/acprof:oso/9780195058239.001.0001

[3] Stroink, G., Moshage, W. and Achenbach, S. (1998) Cardiomagnetism. In: Andr. W. and Nowak, H., Eds., *Magnetism in Medicine*, Wiley-VCH, Berlin, 136-189.

[4] Tavarozzi, I., Comani, S., Del Gratta, C., Di Luzio, S., Romani, G.L., Gallina, S., *et al.* (2002) Magneto-cardiography: Current status and perspectives. Part II: Clinical applications. *Italian Heart Journal*, **3**, 151-165.

[5] Fenici, R., Brisinda, D. and Meloni, A.M. (2005) Clinical application of magnetocardiography. *Expert Review of Molecular Diagnostics*, **5**, 291-313. doi:10.1586/14737159.5.3.291

[6] Van Leeuwen, P., Hailer, B., Lange, S. and Grцnemeyer, D. (2003) Spatial distribution of repolarization times in patients with coronary artery disease. *Pacing and Clinical Electrophysiology*, **26**, 1706-1714. doi:10.1046/j.1460-9592.2003.t01-1-00256.x

[7] Hailer, B., Chaikovsky, I., Auth-Eisernitz, S., Schafer, H. and Van Leeuwen, P. (2005) The value of magnetocardiography in patients with and without relevant stenoses of the coronary arteries using an unshielded system. *Pacing and Clinical Electrophysiology*, **28**, 8-11. doi:10.1111/j.1540-8159.2005.09318.x

[8] Park, J.W., Hill, P.M., Chung, N., Hugenholtz, P.G. and Jung, F. (2005) Magnetocardiography predicts coronary artery disease in patients with acute chest pain. *Annals of Noninvasive Electrocardiology*, **10**, 312-323. doi:10.1111/j.1542-474X.2005.00634.x

[9] Tolstrup, K., Madsen, B.E., Ruiz, J.A., Greenwood, S.D, Camacho, J., Siegel, R.J., *et al*. (2006) Non-invasive resting magnetocardiographic imaging for the rapid detection of ischemia in subjects presenting with chest pain. *Cardiology*, **106**, 270-276. doi:10.1159/000093490

[10] Chen, Y. (2005) Resting magnetocardiographic imaging can accurately detect obstructive coronary artery disease in patient with chronic ischaemia. *Journal of the American College of Cardiology*, **45**, 27-69.

[11] Park, J.W. *et al.* (2005) Magnetocardiography predicts coronary artery disease in bundle brunch block patients with acute chest pain. *Journal of Electrocardiology*, **40**, S53.

[12] Van de Werf, F., Ardissino, D., Betriu, A. *et al.* (2003) Management of acute myocardial infarction in patients presenting with ST-segment elevation: The task force on the management of acute myocardial infarction of the european society of cardiology. *European Heart Journal*, **24**, 28-66. doi:10.1016/S0195-668X(02)00618-8

[13] Sosnytskyy, V.M., Vojtovich, I.D., Bojchak, M.P., Myasnikov, G.V., Chaikovsky, I.A. and Sosnitskaya, T.V. (2011) Magnetic mapping of the heart-new information technology of noninvasive electrophysiology. *Reports of the National Academy of Sciences of Ukraine*, **1**, 166-171.

[14] Ertl, G. and Frantz, S. (2005) Healing after myocardial infarction. *Cardiovascular Research*, **66**, 22-32, doi:10.1016/j.cardiores.2005.01.011

[15] Casolo G., Minneci S., Manta R., *et al.* (2006) Identification of the ischemic etiology of heart failure by cardiovascular magnetic resonance imaging: Diagnostic accuracy of late gadolinium enhancement. *American Heart Journal*, **151**, 101-108. doi:10.1016/j.ahj.2005.03.068

[16] Ibrahim, T., Bulow, H.P., Hackl, T., *et al.* (2006) Diagnostic value of contrast-enhanced magnetic resonance imaging and single-photon emission computed tomogramphy for detection of myocardial necrosis early after acute myocardial infarction. *Journal of the American College of Cardiology*, **49**, 208-216.

[17] Kaandorp, T.A., Lamb, H.J., Viergever, E.P., *et al.* (2007) Scar tissue on contrast-enhanced MRI predicts left ventricular remodelling after acute infarction. *Heart*, **93**, 375-376. doi:10.1136/hrt.2006.097675

[18] Goerning, M., Liehr, M., Tute, C., Schlosser, M., Haueisen, J., Figulla, H. and Leder, U. (2009) Magnetocardiography based spatiotemporal correlation analysis is superior to conventional ECG analysis for identifying myocardial injury. *Annals of Biomedical Engineering*, **37**, 107-111. doi:10.1007/s10439-008-9598-5

[19] Sosnitskiy, V.N., Stadnyuk, L.A. and Sosnitskaya, T.V. (2004) Magnetocardiography: New insights onto old ideas. *Heart and Vessels*, **4**, 73-78.

[20] Ikefuji, H., Nomura, M., Nakaya, Y. *et al.* (2007) Visualization of cardiac dipole using a current density map: Detection of cardiac current undetectable by electrocardiography using magnetocardiography. *Journal of Investigative Medicine*, **54**, 116-123. doi:10.2152/jmi.54.116

[21] Jarusevicius, G., Navickas, R., Vainoras, A. *et al.*(2004) JT interval changes in acute myocardial infarction following coronary angioplasty, *Medicina* (*Kaunas*), **40**, 90-93.

[22] Hondeghem, L.M., Carlsson, L., Duker, G. (2001) Instability and triangulation of the action potential predict serious proarrhythmia, but action potential duration prolongation is antiarrhythmic. *Circulation*, **103**, 2004-2013. doi:10.1161/01.CIR.103.15.2004

[23] Antzelevitch, C. (2005) Modulation of transmural repolarization. *Annals of the New York Academy of Sciences*, **1047**, 314-323

[24] Emori, T. and Antzelevitch, C. (2001) Cellular basis for complex T wave and arrhythmic activity following combined I (kr) and I (ks) block. *Journal of Cardiovascular Electrophysiology*, **12**, 1369-1378. doi:10.1046/j.1540-8167.2001.01369.x

[25] Lu, H.R., Vlaminckx, E., Van Ammel, K., De Clerck, F. (2002) Drug—induced long QT in isolated rabbit Purkinje fibers: Importance of action potential duration, tri-

angulation and early after depolarization. *European Journal of Pharmacology*, **452**, 183-152. doi:10.1016/S0014-2999(02)02246-X

[26] Milberg, P., Hilker, E., Ramtin, S., *et al.* (2007) Proarrhythmia as a class effect of quinolones: Increased dispersion of repolarization and triangulation of action potential predict torsades de points. *Journal of Cardiovascular Electrophysiology*, **18**, 647-654. doi:10.1111/j.1540-8167.2007.00793.x

[27] Kuzmin, V.S. and Rozenshtraukh, L.V. (2010) Ionic mechanisms as action of the III class antiarrhythmic drugs. *Cardiology*, **7**, 49-61.

[28] Sosnytskyy, V.M., Stadnyuk, L.A. and Sosnytska, T.V. (2010) Detection of the Ca^{2+} overload in patients presenting with delayed aftedepolarization using cardiac magnetic field mapping at rest. *European Heart Journal*, **31**(Abstract Supplement), 264.

