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Development of Biomedical Apparatuses Based on Supersensitive SQUID-Magnetometer and Its Application to In-Vivo Study of Lab Animals

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***Abstract*— Some improvements of biomagnetic apparatus and measuring procedures have been made such as 2-channel SQUID-magnetometer with changeable base, optimization of antenna, and minimization of power-line disturbances. Potential of developed approaches have been demonstrated for increasing noise-immunity of devices at unshielded environment. Magnetocardiographic examinations have been performed for lab rabbits including experiments with magnetic nanoparticles injected into the animal bodies.**

***Index Terms*—SQUID, biomagnetism, magnetocardiography, animal study.**

I. INTRODUCTION

Today it is actual development of novel perspective methods of functional diagnostics of as whole human organism so as separate organs and specific systems of the human body. So, distribution of the magnetic field above the body surface allows by way of inverse problem solution (IPS) to reconstruct distribution of current sources into the human or animal body, which carries diagnostic information.

Taking into account, that the magnetic fields practically are not distorted by biological tissues, and measurement procedure is non-contact and passive, it is possible to assert that measurement with the use of SQUID-magnetometers is able to give new, most complete information which it is impossible to obtain by traditional facilities.

Such devices work with the super-weak fields and situation especially becomes complicated inside of unshielded apartment. In order to increase measuring accuracy a few means are utilized including calibrating, complex algorithms for noise filtration and compensation, determination of areas having minimal disturbances, optimization of design of pick-up antenna.

The simplest method to improve quality of signal is to determine distribution of disturbances in the place of the biomagnetic measurements and find out the area of minimal disturbances. Such method gives possibility to decrease the disturbances' level at input signal up to one order of magnitude, and sometimes, two ones. Also, at unshielded location it is important to select kind of antenna, which is the most insensitive to the power-line interferences [1-2].

II. PROBLEM SOLVED

It is known that the most difficult task is suppression of noises within the frequency range of useful signal. A main mean here is a spatial selection of the magnetic fields from remote sources based on using superconductive gradiometers, which register the spatial derivative of the magnetic field and consist of several coils connected in a special way.

Another method for improving quality of super-weak signals on a background a strong disturbances, which exceed a useful signal on a few orders of magnitude, is using of multi-channel SQUID-magnetometer systems having both signal and reference channels [3-4].

Among such ones are devices for measuring of magneto-cardiograms and magnetic susceptibility (susceptometer). First kind registers field from active currents into the human heart, but 2nd kind registers response from an object, inserted into the magnetizing field. Above devices with help of the magnetic field map (MFM) can determine the distribution of cardiac currents or distribution of magnetic materials into the human body, e.g. distribution of the drugs or other markers linked with magnetic carriers [5-6].

III. STUDYING MAGNETIC DISTURBANCES AT UNSHIELDED LAB ENVIRONMENT

It was made scaling model with 10th size increasing of each kind of input antennas, such as magnetometer (M), axial gradiometer of the 1st (AG-1) and 2nd (AG-2) order, and planar antenna of the 1st and 2nd orders, i.e. PG-1 and PG-2 [3, 4]. Amplitude of magnetic fields, the 1st and 2nd field gradients have been measured, which originates by different component of external urban magnetic disturbances at the unshielded apartment. Next, signal-to-noise ratios (SNR) for different kinds of antennas have been compared under the action of test source modeling near disturbances.

A. Dependence from Distance to the Room Floor

Measurement procedure includes registration of voltage at the antenna output induced by power-line electromagnetic disturbances at three heights from a floor: 60 cm, 110 cm and 160 cm. Minimal height was select taking into account the sizes of the typical hospital bed and the human body at lying position, maximal height was done from the height of room ceil, middle position – as mean-average value from the maximal and minimum ones.

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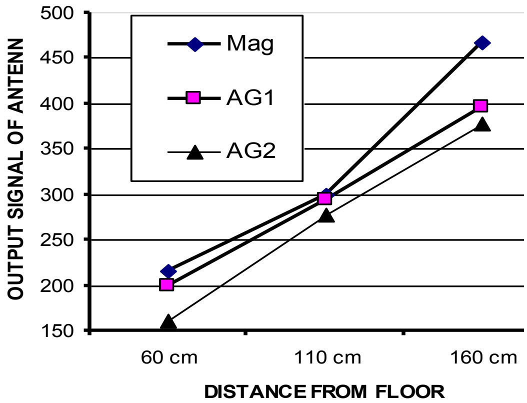
Each antenna is placed into a room center as far as possible from metallic constructions and power-line wires mounted inside the room walls. Output signal is amplified, registered by digital multimeter VOLTCRAFT DMM M-3890D, and stored by software DMM Profi Lab 3.0. Measured data were inputted via USB to computer and averaged, dataset consists of 500 records to achieve high accuracy, see below Fig. 1.



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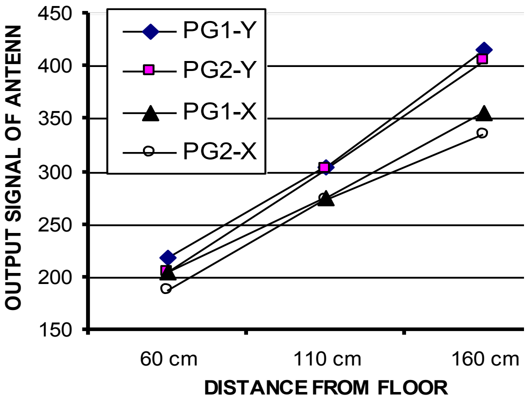

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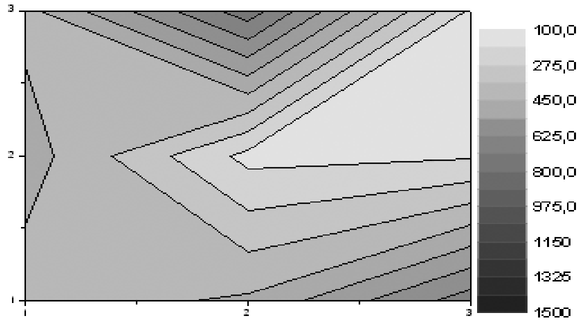
Fig. 1. Dependence of magnetic disturbances from distances to floor: a – axial, b - planar antennas.

From Fig. 1 it is evident tendency of increasing disturbances level with increasing of height for all antennas that suggest deterministic nature of this effect. Reason in that a room is on at ground floor and electric equipment of higher labs gives above disturbances. In addition, massive reinforce-concrete tie-pieces into ceils give the magnetic non-homogeneity. It is clear shown that noise level is decreased with increasing order of antennas, and noise level along the horizontal axis X is less than level along the Y one.

B. Distribution over Room Area

9 examinations were performed by each kind of antennas, so that PG-1 and PG-2 register the gradients of horizontal disturb components (X, Y), but axial antennas AG-1 and AG-2 register vertical component of disturbances (see Fig. 2).

Taking into account that in walls also are metallic constructions and power electric lines, distribution of magnetic disturbances over room area within a square 3X3 m is also studied.



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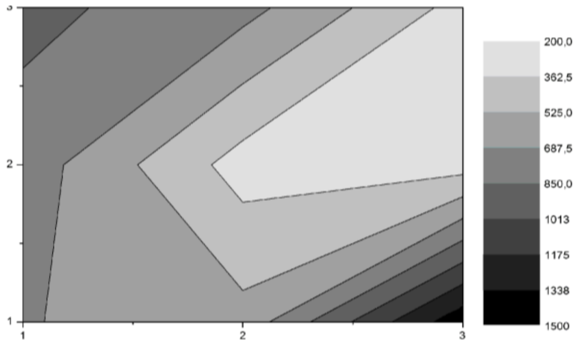

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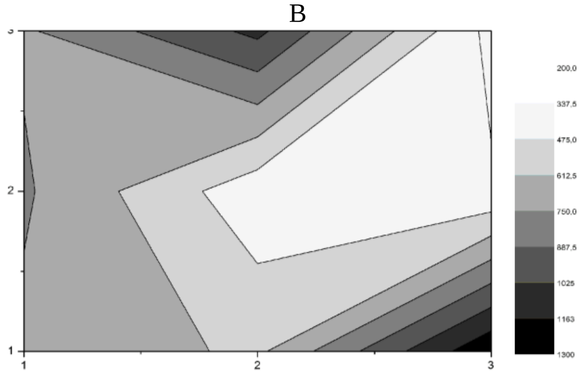

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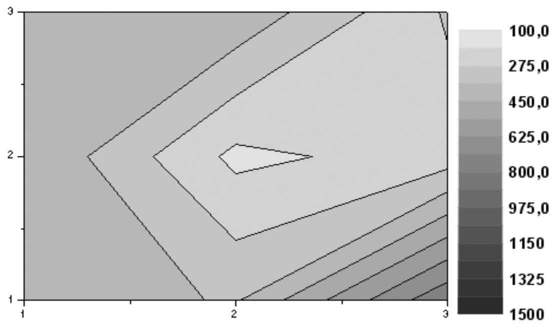

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Fig. 2. Distribution of disturbances at lab room: magnetic field (A), 1st (B), 2nd (C), vertical 2nd (D) gradients.

From Fig. 2 one can see that minimum of all kind of disturbances level existence at the far-right corner of room that is why above corner of room is recommended for installation of SQUID-magnetometers. More detail, vertical component of 2nd gradient reach minimum near room center. Our experiment shows that disturbances can varies more than one order of magnitude.

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IV. IMPROVEMENT OF BIOMAGNETIC APPARATUS

A. Comparison of antennas noise-immunity

Table 1. Noise-immunity of antennas of various kinds

Kind of antenna	Output signal			Relative Signal-to-noise ratio
	Source on	Source off	Difference	
Magnetometer, M	232	90	142	1
Axial, AG-1	230	100	130	1,09
Axial, AG-2	230	112	118	1,20
Planar, PG-1	225	220	5	28,4
Planar, PG-2	220	220	< 1	142

For the study of antennas noise-immunity a test signal is used, a source of which is 10 turns of copper wire placed at distance of 10 cm from the nearest antenna coil, on which a sine-wave signal was given by frequency 5 kHz and amplitude 10 V. Amplitudes of output voltages from antennas under the action of test source are summarized in Table. 1

B. Development 2-channel Adjustable Magnetometer

With the purpose of selection of useful signal from disturbances which penetrates through antennas, it is developed 2-channel SQUID-magnetometer made with possibility of change of distance between antennas. The diameter of cryogenic probe is equal to 50 mm, antennas has 8 mm. The probes of the separate channels are made so that the antennas axes are displaced from the probe axes to 5.75 mm. It allows change distance between antennas with help of rotation of probes. The output signal of such magnetometer is a difference of output signals of both channels [7].

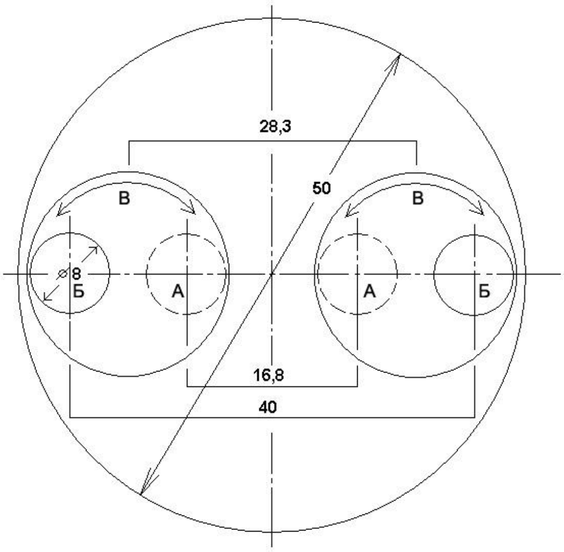


Fig. 3. Chart of 2-channel SQUID-Magnetometer with a Variable Base.

Initial position of probes is A (see Fig. 3) gives minimum distance 16,8 mm, which only in 2 times exceeds the diameter of antennas and no more than distance to the signal sources within studying object. In this case for axial gradiometers of the 2nd order, which register the 2nd derivative of vertical magnetic field component d^2H_Z/dZ^2, an output signal is equivalent to such for a magnetometer with antenna – gradiometer of higher (3th) order, which registers the derivative of $d^3H_Z/dXdZ^3$ (Mode 1).

Finishing position of probes B is chieved by rotation of both probes on 180° and gives maximal distance 40 mm, which exceeds the diameter of antennas 8 mm up to 5 times. Thus, if the field source is under one of given antennas, distance to other antenna assuredly anymore than distance to the field sources into investigated object. In this case the output signal of magnetometer is equivalent as for a magnetometer with the single reference channel (Mode 2).

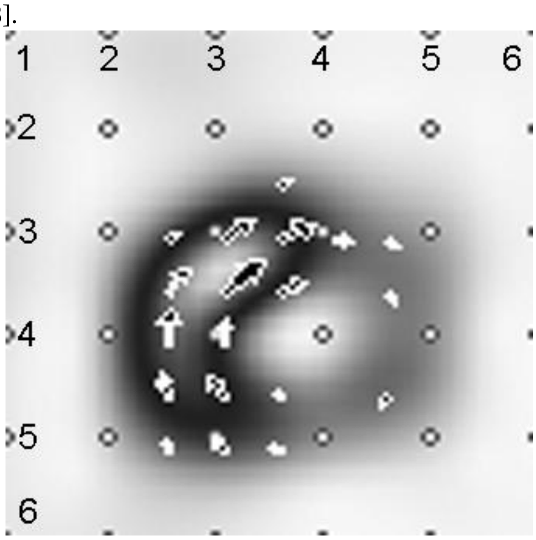
Litera B at Fig. 3. illustrates displacement of each probe from a center at its rotation on 90° angle from initial, when the intermediate variant of middle distance 28,3 mm is realized. This is the mode of differential magnetometer, which close to the Mode 1(2) in the case if both antennas are identical (different) and relatively large (small) distance to the source. Here we consider that large (small) distance means distance, which is more (less) than above middle distance between the antennas, i.e. 28 cm.

V. EXPERIMENTAL STUDY OF MAGNETIC NANOPARTICLES (MNP) AND ANIMALS

A. Registration of Rabbit MCG

Two-stage researches were conducted on laboratory rabbits with age of 6 months and weigh 3 kg. During the 1st stage it was conducted verification of accuracy of IPS for the current sources into the animal body. The 2nd stage verifies the ability (sensitivity) of MCG system to find out the MNP injected into the animal body by an intravenous injection.

They were conducted registration of the MFM by a size 20X20 cm above the animal body at 36 spatial points with a step 4 cm and duration of 4 sec at each point, and here distance from rabbit to bottom of cryostat tail is equal to 0.5 cm. The algorithm of data processing is similar to such one for rats [8].



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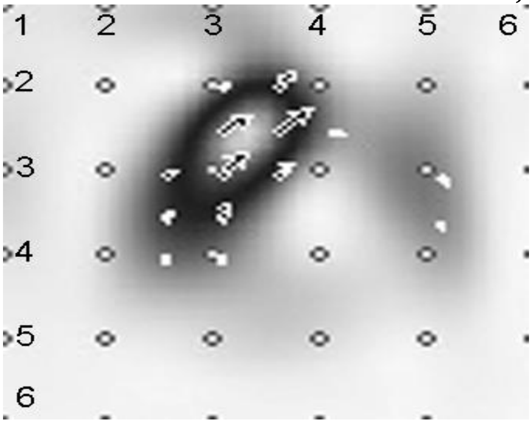

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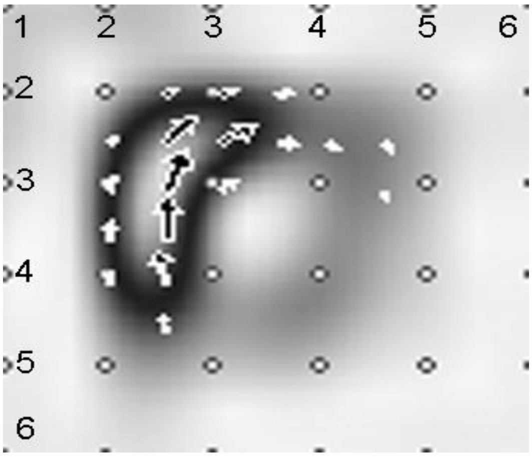

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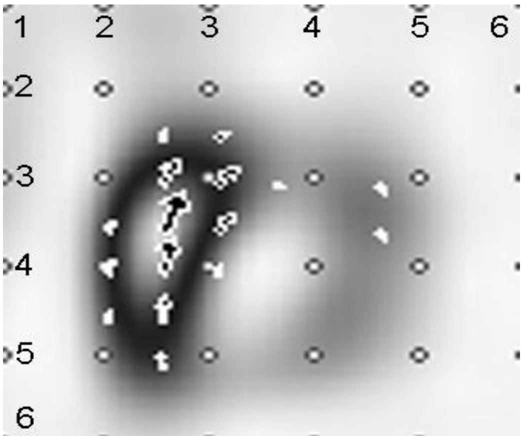

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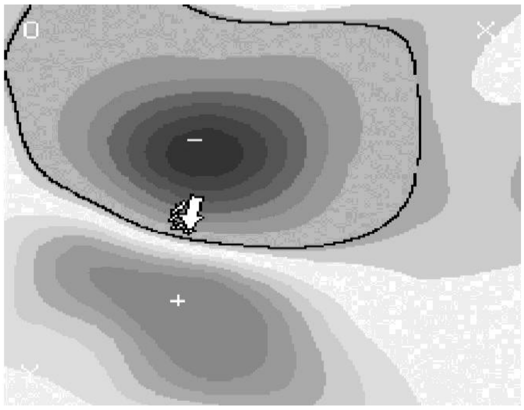
Fig. 4. Distributing of currents above the rabbit body at the R peak: initial position (a), after shift on 2 cm downward (b), to the right (c), and upward (d).

To verification of the IPS accuracy, 4 measurements were conducted with shifts onto corners of quadrate with a side 2 cm. The results of visualization of current density distribution (CDD) maps are resulted at Fig. 4, where area of maximal CDD reflects position of the rabbit heart.

From Fig. 4-a it is clear that at initial position an area of maximal currents mainly localize between the spatial points 3.3-4.3. After shifting on 2 cm downward, currents area is displaced to points 2.3-3.3 (Fig. 4-b). Subsequent shifting to the right resulted in displacement of currents area to the points 2.2-3.3 (Fig. 4-c). Finally, displacement of rabbit upwards resulted in the proper opposite shifting of currents area to points 3.3-4.2 (Fig. 4-d).

B. MNP Influencing on MFM Pattern of the Rabbit Body

During the second stage of rabbit investigation, measurements of MFM from the heart were conducted without and with MNP injection into animal body. For experiments 2 ml suspensions of magnetite are used in physiology solution, which was intravenously injected in a vein of the eye sine. Content of iron in every preparation is 32 mg, and dose of iron – 12 mg/kg weight.



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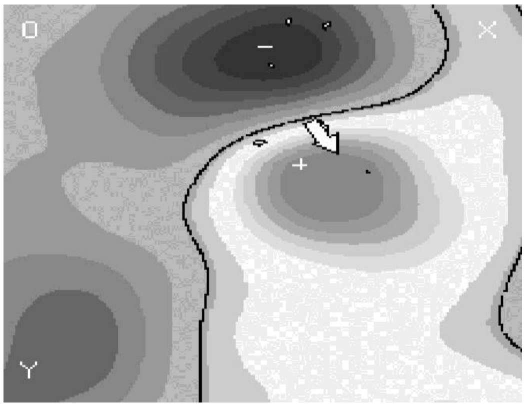

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Fig. 5. MFM above the rabbit body at the R-peak before (a) and after injection of MNP (b).

Presented at Fig. 5 maps demonstrate distributing of the magnetic field above the rabbit body at the beginning QRS of interval. As one can see on Fig 5-a, before injection of MNP the MFM map has dipole-like pattern having two strong field extrema.

Contrary, MNP injection leads to violation of dipole structure, and MFM map has already substantially non-dipole structure (see Fig. 5-b). In detail, additional field sources are take place instead of single strong dipole source. Above changes of the magnetic field distribution is influenced by MNP accumulated into the rabbit body, including specific organ-target other than heart, firstly liver, kidney, spleen.

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VI. CONCLUSION

1. Experimental study of magnetic disturbances suggest that:

a) Optimum height for the SQUID-based measurements in order to reach minimum disturbances level, is 60 cm from room floor, that is further measurements were conducted, as a rule, on this height (Fig.1).

b) Analysis of Fig. 2 data we can see that minimum of disturbances level existence at the far-right corner of room. i.e. near three points (2,2), (3,2) and (3,3), that is why above corner of given room is recommended for installation of SQUID-magnetometers. Our experience shows that disturbances can varies more than one order of magnitude.

2. Analyzing the experimental voltage at the output of scaling antenna models (Tabl. 1), it should be noted that the planar gradiometers PG-1 and PG-2 have the highest noise-immunity. Among axial gradiometers the SNR is increased with increasing the gradiometer order, and that the highest SNR is demonstrate by the axial gradient meter of the 2nd order using in our MCG systems.

3. From the analysis of CDD maps of the rabbit heart at the R-peak (Fig.5), it is shown that areas of maximal CDD are moved in relation to each other on 2 cm accordingly with moving of lab animal. It confirms the quality of realization IPS algorithm, i.e. it means possibility to study of CDD into the rabbit heart based on the human-oriented MCG system at unshielded location.

4. From Fig.5-b it is evident that destroy of dipole structure on MFM map and appearance of additional field minimum at the left-down corner is influenced by accumulation of MNP inside the rabbit body including body organs. More detail, it can be explained by the accumulation of MNP into internal organs below heart (liver and spleen). MNP in these organs are oriented by the Earth magnetic field. As a result, in fact, a signal from MNP is registered together with MCG signal.

Similar parasitic effect was early observed during study of MCG for persons with iron overload [9]. Noise-immunity of SQUID-channels at clinical location was investigated at [10].

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REFERENCES

[1] J.Vrba, "SQUID-gradiometers in real environments", SQUID-sensors: Fundamentals, Fabrication and Applications. Kluwer Academic Publishers, pp.117-178, 1996.

[2] M. Budnyk, O. Zakorchenyi, V. Budnyk et al, "Improvement of small-channel MCG system for unshielded environment", IFMBE Proceedings Series, vol. 28 (Advances in Biomagnetism), Springer Verlag, pp. 66-69, 2010.

[3] M. Budnyk, I. Voytovych, Yu. Minov, et al, "Low-cost 7-channel magnetocardiographic system for unshielded environment", Neurology & Clin. Neurophysiology, 2004:12.

[4] Yu. Minov, M. Budnyk, Patent UA 103062, "Device for mechanical balancing the superconductive gradient meter at unshielded environment", 2013.

[5] C.C. Wu et al, "Animal magnetocardiography using SQUID gradiometers assisted with magnetic nanoparticle injection: A sensitive method for early detecting electromagnetic changes induced by hypercholesterolemia", Applied Physics Letters, vol.90, pp.054111-15, 2007.

[6] A. Brazdeikis, C. Chu, P. Cherukuri et al, "Changes in magne-to cardiogram patterns of infracted-reperfused myo- cardium after injection of super paramagnetic contrast media", Neurology & Clin. Neurophysiology, 2004:16.

[7] Yu. Minov, M. Budnyk, O. Zakorhenyi, Pat. UA 90153, "Two-channel SQUID-magnetometer with changeable base", 2010.

[8] O.Zakorchenyi, M.Budnyk, K.Koronovska, "Studying Squid-magnetometer system at unshielded environment", Electronics and communications, vol. 2-3, part. 1, pp. 172-176, 2009.

[9] V. Sosnitsky, P. Sutkovoj, M. Budnyk et al, "MCG-imaging in iron overload's presence", Biomedizinische Technik, vol. 42, No 1, pp. 285-287, 1997.

[10] M. Budnyk, V.Sosnytskyi, O. Zakorchenyi et al, "Development of 4-channel cardio magnetic scanner and technical requirements for 9-channel scanner to diagnose the heart abnormalities", Proc. 6th IEEE Workshop "Intelligent Data Acquisition & Advanced Comp. Systems (IDAACS'2011), Prague (Czech Republic), pp. 91-96, 2011.

AUTHOR BIOGRAPHY

Oleksandr Zakorchenyi graduated from Shevchenko Natl Univ of Kyiv as Master in Applied Physics, Dept. Med. Radio physics (2008), engineer in Glushkov Institute of Cybernetics (2007-2009). Post-graduate student (2008-2011). Currently he working in Ukrainian branch of company "Materialize", activities are focused in biomedical instrumentation and data processing. He has over 20 publications and few Ukrainian patents; he participated in some research projects. Awards: Prize for Young Scientists, NAS of Ukraine (2011), Winner of All-Ukr. Competition "Invention-2012" (3rd place in absolute nomination).

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Winner of Ukr. Contests: “Invention-2012” (1st place in two nomination, 3rd place in absolute nomination), Ministry of Defense “The Best Invention of Year” (1st place in nomination “Medicine”, 2013).