Summary of Clinical Investigations ES Teck Complex system

EIS System in adjunct to Treatments' monitoring and to diagnosis with the conventional methods

Dr. V. G. Alexeev, Dr. L. V. Kuznekova, Dr E.A. Markelova . Botkin Hospital Moscow
September 25, 2009

Abstract

Clinical investigations were conducted at the S.P. Botkin Hospital from May 20, 2006, to September 1, 2006, in order to evaluate the Bioimpedance parameters provide from a device named Electro Interstitial Scan (E.I.S), we performed drug administration studies.

Two hundred fifteen (215) test subjects (Age 54 $\pm$ 16) were recorded with the EIS System. These patients presented affections diagnosed by conventional examinations (hypothyroidism, hypertension, atherosclerosis or thrombosis risk, and Major depression) and were undergoing no treatment.

The treatments corresponding to the diseases were decided by the conventional examinations results, and a follow-up being undertaken on one hand with the EIS System and on the other hand by conventional methods.

Hypothesis

1. Could the drugs 'administration affect the Bioimpedance parameters estimated from the 3 measured parameters of the EIS system and therefore the EIS can be used in adjunct in treatments' follow up?

2. Could the EIS parameters be used in diagnosis of the diagnosed affections?

The hypothesis 1 was validated according to the raw data analysis:

Thyroid treatment monitoring

The findings show that SDC 11/12 and TSH has a significant negative correlation to each other ($r = -0.975$, $p = 0.005$). It shows that, SDC 11/12 shares approximately 95.1% (that is $(-0.975)^2$x100% or 0.951x100%) of its variability with TSH. Thus, a high value of SDC 11/12 corresponds to low TSH or low value of SDC 11/12 corresponds to high TSH.

The findings show that EPA-SPA11/12 and TSH has a significant positive correlation to each other ($r = 0.926$, $p = 0.024$). It shows that, EPA-SPA11/12 shares approximately 85.7% (that is $(0.926)^2$x100% or 0.857x100%) of its variability with TSH. Thus, a high value of EPA-SPA11/12 corresponds to high TSH or low value of EPA-SPA 11/12 corresponds to low TSH.

Beta blockers treatment monitoring

The findings show that SDC 2/4/15/17 and Diastolic Pressure has a significant positive correlation to each other

($r = 0.975$, $p = 0.005$). It shows that, SDC 2/4/15/17shares approximately 95.1% (that is $(0.975)^2$x100% or 0.951x100%) of its variability with Diastolic Pressure. Thus, a high value of SDC 2/4/15/17 corresponds to high Diastolic Pressure or low value of SDC 2/4/15/17 corresponds to low Diastolic Pressure.

The findings show that ESGHF/VLF and Diastolic Pressure has a significant positive correlation to each other

($r = 0.977$, $p = 0.004$). It shows that, ESGHF/VLF shares approximately 95.4% (that is $(0.977)^2$x100% or 0.954x100%) of its variability with Diastolic Pressure. Thus, a high value of ESGHF/VLF corresponds to high Diastolic Pressure or low value of ESGHF/VLF corresponds to low Diastolic Pressure.

ACE inhibitors treatment monitoring

The findings show that EPA-SPA6/8/19/21 and Diastolic Pressure has a significant negative correlation to each other ($r = -0.892$, $p = 0.042$). It shows that, EPA-SPA6/8/1921/ shares approximately 79.6% (that is $(-0.892)^2$x100% or 0.796x100%) of its variability with Diastolic Pressure.

Anticoagulant treatment monitoring

The findings show that SDC 6/13/19 and PI (Prothrombin Index) has a significant positive correlation to each other
($r = 0.998$, $p < 0.001$).

The findings show that EPA-SPA 6/13/19 and PI (Prothrombin Index) has a significant positive correlation to each other ($r = 0.961$, $p = 0.009$).

The findings indicate that ESG HF/VLF and PI (Prothrombin Index) has a significant positive correlation to each other ($r = 0.994$, $p = 0.001$).

SSRI treatment monitoring

The findings indicate that there were a significant positive correlations between SDC 9/10 and the treatment Response at D+30 ($rho = 0.484$, $p < 0.001$) and D+45and D+60 ($rho= 0.557$, $p < 0.001$).

The findings indicate that there were a significant positive correlations between EPA-SPA 9/10 and the treatment Response at D+45 ($rho = 0.709$, $p < 0.001$) and D+60 ($rho= 0.804$, $p < 0.001$).

2. Could the EIS parameters be used in diagnosis of the affections diagnosed?

The hypothesis 2 was NOT validated according to the raw data analysis:

Only the following correlations had been showed:

The Hypertension group 2A data shows the significant positive correlation between EPA-SPA and Diastolic pressure before the treatment (D).

The major depression group 4 data shows the significant positive correlations between SDC 9/10 and the treatment response (R) for D+ 30 and it also provide evidence of significant positive correlation between ESG HF/VLF and the treatment response (R) for D+45 and D+60 measurements.

New Approach of Bioimpedance technology concerning Attention Deficit/Hyperactivity Disorder (ADHD) in Children

Dr Frederique Caudal (France) , Pr Andrew Stoll USA (Statistical Analysis of the Pre study and power and sample size), Minimax Consulting USA (Statistical analysis of the raw data).

Abstract

Clinical trials were conducted at the office of Dr. Frederique Caudal, paediatrician and specialist in Attention-Deficit/Hyperactivity Disorder (ADHD) in children.

Symptoms of this disorder are related, in the current literature, to a low level of cerebral neurotransmitters.

The diagnosis of ADHD children is almost symptomatic, which leads to the dramatic possibility of error and treatment (Ritalin®, or SSRI or catecholamine's) with medications associated with numerous side effects in particular for the age of the population.

For this reason, a new, measurable, and therefore objective marker was proposed using the Electro Interstitial Scanner (EIS) Bioimpedance measurement device, in adjunct to the conventional diagnoses and treatment monitoring of the ADHD children.

From 10.04.2006 to 05.16.2007, data from 59 children (age 12 ± 5) presenting ADHD diagnostic and not undergoing treatment were recorded with the EIS System. This database was compared with another control group database (age 14 ± 6) of non-hyperactive children also recorded with the same EIS System.

Hypothesis tested

The hypothesis tested was:

- Can the EIS device with reference to its ESG (Electro Scan Gram) graph be used as a marker for ADHD children and therefore as adjunct to the conventional diagnosis of ADHD children?

This hypothesis was validated by statistical analysis.

Independent Sample T-test

In order to determine the differences between ADHD and the control group in the values of v9/v10, v2/v4/v15/v17 and v1/v3/v16/v18 comparison of means via independent samples t-test was conducted. Table 1.1 presented the t-test results for v9/v10 scores at ADHD and the control group. It shows the number of cases per group used in the analysis, the means, the standard deviation, degrees of freedom, t value and the significance of the test (p-value). The findings in Table 1.1 indicate that the mean of v9/v10 at ADHD (M=78.38) was significantly ($p<0.001$) higher than the mean of v9/v10 at the control group (M=21.75). Thus, the score of v9/v10 at ADHD was expected to be higher than the scores of v9v10 at control group.

Table 1.1

Independent Sample T-test for v9/v10 between ADHD and Control

	N	Mean	Std. Deviation	DF	T	P-value
ADHD	104	78.38	30.062	224	19.309	0.000
Control	122	21.75	11.166			

Table 1.2 shows the t-test results for v2/v4/v15/v17 between ADHD and the control group. Accordingly, the mean of v2/v4/v15/v17 at ADHD (M=52.96) was significantly ($p=0.003$) higher than the mean of v2/v4/v15/v17 at the control group (M=47.96). Thus, the score of v2/v4/v15/v17 at ADHD was expected to be higher than the scores of v2/v4/v15/v17 at the control group.

Table 1.2

Independent Sample T-test for v2/v4/v15/v17between ADHD and Control

	N	Mean	Std. Deviation	DF	T	P-value
ADHD	208	52.96	19.981	450	3.031	0.003
Control	244	47.96	47.96			

T-test results for v2/v4/v15/v17 between ADHD and the control group were presented in Table 1.3. the findings shows that the mean of v1/v3/v16/v18 at ADHD (M=30.34) was significantly ($p<0.001$) higher than the mean of v1/v3/v16/v18 at the control group (M=16.75). Thus, the score of v1/v3/v16/v18at ADHD was expected to be higher than the scores of v1/v3/v16/v18 at the control group.

Table 1.3

Independent Sample T-test for v1/v3/v16/v18between ADHD and Control

	N	Mean	Std. Deviation	DF	T	P-value
ADHD	208	30.34	1.016	450	12.931	0.000
Control	244	16.57	0.481			

Sensibility and specificity:

Based upon the statistical data analysis, ADHD was correctly predicted at 69% in the group ADHD, and no ADHD was correctly predicted at 89% in the group no ADHD.

Comparing the Accuracy of the Electro Interstitial Scan-Body Composition (EIS-BC) Device between a BC Module and a Valid Assessment of BC and between an EIS Module and a Standard Assessment of Heart Rate Variability

John E. Lewis, Angelica B. Melillo, Evan Long, Yaima Alonso, Elizabeth Ko, Soyona Rafatjah, Janet Konefal, and Judi M. Woolger
Department of Psychiatry and Behavioral Sciences and Department of Medicine University of Miami Miller School of Medicine, Miami, FL 33136

Abstract

The Electro Interstitial Scan-Body Composition (EIS-BC) device consists of two modules: (1) the BC module and (2) the EIS module. The objective of this study was to compare the BC module to a standardized, valid assessment of BC and to compare the EIS module to a standardized assessment of heart rate variability (HRV). Fifty subjects between 20 and 62 years of age were assessed for body composition by the BC module (total body water, fat-free mass, and fat mass) on one hand and dual x-ray absorptiometry (DXA; total fat mass and fat-free mass). On the second hand, spectrum analysis of the EIS module and HRV as measured by a standard HRV device (ES Teck PEMS) to estimate sympathetic nervous system activity were assessed. Height, weight, blood pressure (BP), and pulse were also measured. The results of the study indicated that the correlation between DXA and EIS-BC body fat percent measurements was very high ($r=.92$, $p < 0.001$). The correlation between the EIS spectrum analysis and HRV variables was also very high ($r=.76$, $p < 0.001$), suggesting that the high conductivity ratio has predictive capability on the sympathetic nervous system activity. The results of the study suggest that the EIS-BC device has a significant level of reliability in estimating body composition and sympathetic nervous system activity.

Bioelectrical impedance analysis EIS –BC* versus Quantum II RJL and comparison measurements results and predictive equations used for the 2 devices.**

Dr. V. G. Alexeev, Dr. L. V. Kuznetsova. Botkin Hospital Moscow July, 26 2009

Abstract

Raw Data BC (N=65)

In order to compare the measurements of R, Xc, TWB, FFM and EWC between RJL and EIS-BC paired sample t-test was performed. This test is appropriate when the objective is to compare whether two scores that are taken from the same sample are significantly different. Table 3.3 shows the results of the paired sample t-test for RJL and EIS-BC data, it shows the compared means of each study variables, standard deviation, t-value and the significant value of the test (p-value).

Findings from the paired samples *t* tests in Table 1 were as follows:

- The mean of R at RJL (*M*=508.80) and the mean of R at EIS-BC (*M*=509.02) do not significantly differ. Thus, the scores of R at RJL and R at EIS-BC were statistically equal.
- The mean of Xc at RJL (*M*=66.23) was significantly higher (p<0.001) than the mean of Xc at EIS-BC (*M*=62.92). Thus, the scores of Xc at RJL were expected to be higher than the scores of Xc at EIS-BC.
- The mean of TWB at RJL (*M*=40.80) was significantly (p<0.001) higher than the mean of TWB at EIS-BC (*M*=30.72). Thus, the scores of TWB at RJL were expected to be higher than the scores of TWB at EIS-BC.
- The mean of FFM at RJL (*M*=52.26) was significantly (p<0.001) higher than the mean of FFM at EIS-BC (*M*=49.59). Thus, the scores of FFM at RJL were expected to be higher than the scores of FFM at EIS-BC.
- The mean of EWC at RJL (*M*=40.80) was significantly (p<0.001) higher than the mean of EWC at EIS-BC (*M*=30.72). Thus, the scores of EWC at RJL were expected to be higher than the scores of EWC at EIS-BC.

Table 1

Paired Samples T-Test for RJL and EIS-BC data

	Mean	SD	T	P-value
RJL R	508.8000	71.71868	-0.445	0.658
EIS-BC R	509.0154	71.58616		
RJL Xc	66.2308	11.26495	19.170	0.000
EIS-BC Xc	62.9231	10.70238		
RJL TWB	40.8046	9.63366	25.643	0.000
EIS-BC TWB	30.7185	7.44830		
RJL FFM	52.2569	10.96801	7.634	0.000
EIS-BC FFM	49.5923	10.27891		
RJL EWC	16.9769	3.32936	14.279	0.000
EIS-BC EWC	15.5815	2.93991		

In Conclusion:

Test under raw data BC shows that the scores of Xc, TWB, FFM and EWC for the data RJL were significantly higher than the scores of Xc, TWB, FFM and EWC for the data EIS-BC. Whereas, it also shows that the scores of R for both RJL and EIS-BC data do not show significant difference.

Bioimpedance dispersion width as a parameter to monitor living tissues.

Antoni Ivorra, Meritxell Genesca, Anna Sola, Luis Palacios, Rosa Villa , Georgina Hotter and Jordi Aguilo . Physiol. Meas. 26 (2005) 1–9

Abstract

In the case of living tissues, the spectral width of the electrical bioimpedance dispersions (closely related with the α parameter in the Cole equation) evolves during the ischemic periods. This parameter is often ignored in favor of other bioimpedance parameters such as the central frequency or the resistivity at low frequencies. The object of this paper is to analyze the significance of this parameter through computer simulations (in the α and β dispersion regions) and to demonstrate its practical importance through experimental studies performed in rat kidneys during cold preservation. The simulations indicate that the dispersion width could be determined by the morphology of the extra-cellular spaces. The experimental studies show that it is the unique parameter able to detect certain conditions such as a warm ischemia period prior to cold preservation or the effect of a drug (Swinholide A) able to disrupt the cytoskeleton. The main conclusion is that, thanks to the α parameter in the
Cole equation, the bioimpedance is not only useful to monitor the intra/extracellular volume unbalances or the inter-cellular junctions resistance but also to detect tissue structural alterations.

Keywords: dispersion width, cytoskeleton, monitoring, morphology, Cole, bioimpedance

Electrical Bioimpedance Cerebral Monitoring:

.

Fernando Seoane artinez Department of Signals and Systems
Division of Biomedical Engineering Göteborg, Sweden, 2007& School of Engineering Borås, Sweden, 2007

Abstract

Neurologically related injuries cause a similar number of deaths as cancer, and brain damage is the second commonest cause of death in the world and probably the leading cause of permanent disability. The devastating effects of most cases of brain damage could be avoided if itwere detected and medical treatment initiated in time. The passive electrical properties of biological tissue have been investigated for almost a century and electrical bioimpedance studies in neurology have been performed for more than 50 years. Even considering the extensive efforts dedicated to investigating potential applications of electrical bioimpedance
for brain monitoring, especially in the last 20 years, and the specifically acute need for such non-invasive and efficient diagnosis support tools, Electrical Bioimpedance technology has not made the expected breakthrough into clinical application yet. In order to reach this stage in the age of evidence-based medicine, the first essential step is to demonstrate the biophysical basis of the method under study. The present research work confirms that the cell swelling accompanying the hypoxic/ischemic injury mechanism modifies the electrical properties of brain tissue, and shows that by measuring the complex electrical bioimpedance it is possible to detect the changes resulting from brain damage. For the development of a successful monitoring method, after the vital biophysical validation it is critical to have available the proper electrical bioimpedance technology and to implement an efficient protocol of use. Electronic instrumentation is needed for broadband spectroscopy measurements of complex electrical bioimpedance; the selection of the electrode setup is crucial to obtain clinically relevant measurements, and the proper biosignal analysis and processing is the core of the diagnosis support system. This work has focused on all

these aspects since they are fundamental for providing the solid medico-technological background
necessary to enable the clinical usage of Electrical Bioimpedance for cerebral monitoring.
Keywords: Electrical Bioimpedance Spectroscopy, Hypoxia, Ischemia, Stroke, Brain Monitoring, Impedance Measurements, Biomedical Instrumentation, Non-invasive Monitoring.

Assessment of Vasoactive Agents and Vascular Aging by the Second Derivative of Photoplethysmogram Waveform

Hypertension: Volume 32(2) August 1998pp 365-370
Takazawa, Kenji; Tanaka, Nobuhiro; Fujita, Masami; Matsuoka, Osamu; Saiki, Tokuyu; Aikawa, Masaru; Tamura, Sinobu; Ibukiyama, Chiharu
Received January 24, 1998; first decision February 8, 1998; revision accepted April 7, 1998.
From The Second Department of Internal Medicine, Tokyo Medical College, Tokyo, Japan.

Abstract

To evaluate the clinical application of the second derivative of the fingertip photoplethysmogram waveform, we performed drug administration studies (study 1) and epidemiological studies (study 2). In study 1, ascending aortic pressure was recorded simultaneously with the fingertip photoplethysmogram and its second derivative in 39 patients with a mean +/- SD age of 54 +/- 11 years. The augmentation index was defined as the ratio of the height of the late systolic peak to that of the early systolic peak in the pulse. The second derivative consists of an a, b, c, and d wave in systole and an e wave in diastole. Ascending aortic pressure increased after injection of 2.5 [micro sign]g angiotensin from 126/74 to 160/91 mm Hg and decreased after 0.3 mg sublingual nitroglycerin to 111/73 mm Hg. The d/a, the ratio of the height of the d wave to that of the a wave, decreased after angiotensin from -0.40 +/- 0.13 to -0.62 +/- 0.19 and increased after nitroglycerin to -0.25 +/- 0.12 ($P<0.001$ and $P<0.001$, respectively). The negative d/a increased with increases in plethysmographic and ascending aortic augmentation indices ($r=0.79$, $P<0.001$, and $r=0.80$, $P<0.001$, respectively). The negative d/a reflects the late systolic pressure augmentation in the ascending aorta and may be useful for noninvasive evaluation of the effects of vasoactive agents. In study 2, the second derivative of the plethysmogram waveform was measured in a total of 600 subjects (50 men and 50 women in each decade from the 3rd to the 8th) in our health assessment center. The b/a ratio increased with age, and c/a, d/a, and e/a ratios decreased with age. Thus, the second derivative aging index was defined as b-c-d-e/a. The second derivative wave aging index (y) increased with age (x) ($r=0.80$, $P<0.001$, $y=0.023x-1.515$). The second derivative aging index was higher in 126 subjects with any history of diabetes mellitus, hypertension, hypercholesterolemia, and ischemic heart disease than in age-matched subjects without such a history (-0.06 +/- 0.36 versus -0.22 +/- 0.41, $P<0.01$). Women had a higher aging index than men ($P<0.01$). The b-c-d-e/a ratio may be useful for evaluation of vascular aging and for screening of arteriosclerotic disease. (Hypertension. 1998;32:365-370.)

Noninvasive Cardiac Output Estimation Using a Novel Photoplethysmogram Index

L. Wang, Emma Pickwell-MacPherson, Y. P. Liang and Y. T. Zhang

31st Annual International Conference of the IEEE EMBS Minneapolis, Minnesota, USA, September 2-6, 2009

Abstract

Cardiac output (CO) monitoring is essential for indicating the perfusion status of the human cardiovascular
system under different physiological conditions. However, it is currently limited to hospital use due to the need for either skilled operators or big, expensive measurement devices. Therefore, in this paper we devise a new CO indicator which can easily be incorporated into existing wearable devices. To this end, we propose an index, the inflection and harmonic area ratio (IHAR), from standard photoplethysmographic (PPG) signals, which can be used to continuously monitor CO. We evaluate the success of our index by testing on sixteen normotensive subjects before and after bicycle exercise. The results showed a strong intra-subject correlation between IHAR and COimp measured by the bio-impedance method in fifteen subjects (mean $r = 0.82$, $p<0.01$). After least squares linear regression, the precision between COimp and CO estimated from IHAR (COIHAR) was 1.40 L/min. The total percentage error of the results was 16.2%, which was well below the clinical acceptance limit of 30%. The results suggest that IHAR is a promising indicator for wearable and noninvasive CO monitoring.