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Rheology and BIA

To cite this article: M Piquemal and J C Zanotti 2012 *J. Phys.: Conf. Ser.* **407** 012031

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Rheology and BIA

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Abstract. Is it possible to link erythro sedimentation to a global monofrequency of 50KHz bio impedance analysis parameters? Two populations, Control (N=20, average age of 38 ± 18 years, 55% female predominance) versus neopathology undergoing chemotherapy treatment (N=10, average age of 51 ± 10 years, 70% female predominance) were exposed to two simple tests: Blood composition and erythro sedimentation and global Bio Impedance mono frequency (50 KHz) assessment analysis. The Results of simple statistical tests (average, anova) show that the two populations were significantly different (1%), using both biological blood tests or BIA. Only the neopathological group showed a significant correlation between the erythro sedimentation the bio impedance parameters such as Phase angle or Xc (ratio - 0.93 and - 0.93)

Keywords: Erythro sedimentation, phase angle, Xc, blood composition

1. Introduction

The circulation of erythrocytes in the blood (GR) is made possible thanks to a control of blood viscosity. From a mechanical point of view, there is, an interaction between the blood flow, the axial force of the sanguineous current and the rate of deformation of the red cells. While the erythrocytes travel through the vascular system, they have a tendency to restructure themselves in cylindrical forms. This conformity prevents phenomenon such as internal abrasion, turbulence within the vascular system which, without said conformity, could destroy these carriers of hemoglobin.

This cellular behavior is due to the effects of long sanguineous proteins', such as fibrinogen, which maintains the cells in this cylindrical structure. The anticoagulated blood, later pipetted in a thin Westergreen graduated pipet and placed vertically, shows an alignment of the erythrocytes, in the form of a long cylinder: the rolls. The time during which the erythrocytes deposit at the bottom of the vertical pipet is referred to as erythro sedimentation speed.

The results of this test are measured in millimeters of sedimentation of red blood cells (mm) per minute. The mechanism behind this cylindrical conformity of the erythrocytes is related to the presence of fibrinogen or any other sanguineous molecule of an anisometric structure with a high axial quotient [1]. The distance between stacked erythrocytes also affects this process, being thinner than between red blood cell flowing in the bloodstream [2]. There is, therefore, reduction of the repulsive electrical force between the red blood cells. The erythro sedimentation represents an indicator of the inflammation without being an absolute indicator of the inflammation, since this process can also depend on the geometry of the red cells. Given the previously stated information, we would like to know if the measurement of the global cutaneous bioimpedance of a body can relate, to the state of the sanguineous composition and specifically, to erythro sedimentation. Therefore, two populations are

subjected to this concept. The first group consists of subjects considered biologically and clinically healthy (control group). The second is made up of subjects undergoing treatment for neo pathologies (test group). Would it be possible to show that the variation of the angle alpha (marker of capacitive aspect of the cellular membrane), is equivalent, in blood, to an increase of the erythro sedimentation and a possible thrombosis?

2. Methods and material

2.1. Material

A blood sample is taken in fasting, after a 20 minute rest in a reclined position. This sample is analysed to determine: blood count and erythrocyte sedimentation rate. The reading of the blood count is performed manually, with microscopic observation of the lamina.

This entire procedure is performed following a bioimpedance measurement of coetaneous skin, with a single frequency of 50 kHz, in a tetrapole setup (right hand and foot) using the BIA 2000s device from the InputData Company, Germany) [3]

2.2. Method

The experiments population consists of 30 people from different socio-cultural origins, with an average age of 43 ± 17 years, predominantly female (60%). This main population is divided into two groups. The first group consists of 20 individuals without clinical or biological manifestation of disease ($N = 20$, average age of 38 ± 18 years, 55% female predominance). The second group is made up of 10 people with neoplasia: 50% breast cancer and 50% intestinal cancer ($N = 10$, average age of 51 ± 10 years, 70% female predominance), undergoing chemotherapy. Before the experiment all subjects were adequately informed and gave their written consent to participate in the measurement of the bio-impedance signals. All measurements were performed in compliance with the ethical principles set forth in the Declaration of Helsinki [4]. BIA electrodes are applied as follows:

-Hand (first electrode: placed in the middle of the union between the two styloids, at the back of the hand; second: placed in the middle of the space between the second and third metacarpal, 7 cm between the two)

-Feet: (first electrode: anterior side of the tibia-fibula; second: between second and third metatarsal, 7 cm between the two)

The bio-impedance measurement is performed three times, patient resting on supine position, each consecutive measurement taken 2 minutes apart. The presented data represents the average of three individual measurements.

Analysis of the blood is performed manually, as a recount, in a biochemical analysis laboratory.

3. Results

Two simple statistical studies were performed, based on the average, standard deviation and variance analysis of the two data sets from these two populations, namely data originating from electrical properties (with the following five parameters: impedance, reactance, resistance at the hand and foot, Alpha angle) and biological data from the blood samples. The results of these test statistics are as follows:

3.1. Data originating from electrical studies

3.1.1. Simple statistical analysis

Bio impedance data are gathered in table 1.

Table 1. Basic statistical results regarding a monofrecuencial analysis of global coetaneous impedance. a) the clinically and biologically healthy population b) neopathological population. (Z, R, Xc in ohms, and alpha in °).

a)

Healthy subjects	Z 50kHz	Xc	R-Hand	R-Foot	Alpha
Average	518.30	61.15	148.70	128.75	6.80
Standard deviation	66.14	9.40	39.35	24.12	1.17

b)

Neopathological subjects	Z 50kHz	Xc	R-Hand	R-Foot	Alpha
Average	424.20	32.60	207.10	239.20	4.36
Standard deviation	35.22	6.85	56.59	25.21	0.69

A significant variation is noticed between BIA parameters throughout the coetaneous tissue of both groups. Would this data be discriminative?

3.1.2 Analysis of variance between the two populations, from an electrical perspective:

Table 2. Analysis of variance.

Indicators	Value of p
Z 50 kHz	0.00025377
Xc	2.9834E-09
R-Hand	4.0607E-12
R-Feet	2.9792E-12
Alpha	1.0787E-15

All 5 parameters are discriminative data regarding the overall bioimpedance between the two populations. [5, 6, 7]

3.2. Biological blood data

3.2.1. Simple statistical analysis (Table 3).

Table 3. Simple statistical results of the blood data a) for the group of clinically and biologically healthy subjects, b) subjects with neopathologies.

a)

Healthy Subject	Hemoglobine	Red Cells	White Cells	Segmented neutrophils	Lymphocytes	Monocytes	Eosinophils	Erythroced. 1st hour
Average	12.82	4240500	5439	54%	43%	0 %	3%	21
Standard deviation	1.08	357734	838	12%	11%	0%	5%	15.5

b)

Subjects with neopathologies	Hemoglobine	Red Cells	White Cells	Segmented neutrophils	Lymphocytes	Monocytes	Eosinophils	Erythroced. 1st hour
Average	11.20	3724000	4249	67%	27%	3%	3%	39
Standard deviation	1.22	420270	1657	9%	11%	1%	4%	21. 5

3.2.2. *Analysis of variance between the two populations, blood perspective.* The variance analysis shows us that on the following blood parameters the two types of populations can be differentiated, see table I4.

Table 4. Value of the probability of the test between the two populations, regarding biological blood values.

Indicators	P-value
Hemoglobin	0.00093119
Red Blood Cells	0.0015001
White Blood Cells	0.0135427
Segmented Neutrophils	0.00513489
Lymphocytes	0.00106837
Monocytes	3.2515E-12
Eosinophils	0.74358988
Eritrosed 1 st hour	0.01281566

Therefore, out of 8 biological indicators, only the rate of eosinophils would appear not to discriminate between these two populations. The reason probably comes from the data paths in a country of parasitological endemic (giardiasis).

The consistency of the results obtained by these two different methods (bio impedance and biology), leads us to think of a possibility of cross-correlation between these two sources of information (blood biology and overall bio impedance). Would each of these two populations intrinsically retain a similar pattern among biological data and those of bio impedance?

To answer this question, we performed a cross correlative study in each of the two subject groups, including biological datasets (8 parameters) and the impedance (5 parameters).

3.2. Correlative study in each of this population: bio-impedance data, versus biological blood data.

Table 5. shows the correlation coefficients between these two types of data. A) Healthy population, b) Population with neoplasia. (Abbreviations: RBC: red blood cells, WBC: white blood cells, Neutseg. polynuclear Neutrophil, erythro-sedimentation 1st hour. Rate of erythro-sedimentation in the first hour, erythro-sedimentation. 2nd hour. Rate of erythro-sedimentation at the second hour).

a) Healthy population

	Hemo -globin	Hema- tocrit	GR	GB	Neut. Seg.	Lymph -ocytes	Eosin -ophils	Eritrosed. 1st Hour	Eritro -sed. 2nd Hour	MCV	MCH	MCHC
R												
50kHz	-0.52	-0.52	-0.52	0.23	0.17	-0.05	-0.24	0.07	0.12	0.31	-0.32	0.14
XC	-0.17	-0.16	-0.16	0.21	0.09	0.09	-0.38	-0.03	-0.14	0.21	-0.28	-0.02
R- Hand	-0.34	-0.34	-0.34	-0.07	0.12	-0.04	-0.13	-0.05	-0.09	-0.20	0.34	-0.02
R-Foot	-0.15	-0.15	-0.15	-0.03	0.21	-0.06	-0.27	0.21	0.11	0.04	0.12	0.13
Alpha	0.35	0.35	0.35	-0.03	-0.08	0.17	-0.17	-0.13	-0.29	-0.07	-0.02	-0.14

b) Population with cancer

	Hemo -globin	Hema- tocrit	GR	GB	Neut. Seg.	Lymph -ocytes	Eosin -ophils	Eritrosed. 1st Hour	Eritro -sed. 2nd Hour	MCV	MCH	MCHC
R												
50kHz	0.82	0.81	0.35	-0.35	0.30	0.82	0.18	-0.80	-0.18	-0.12	0.03	0.18
XC	0.90	0.91	0.32	-0.63	0.65	0.90	-0.13	-0.93	-0.13	-0.43	-0.33	-0.13
R- Hand	0.00	-0.06	0.38	0.43	-0.38	0.00	0.20	-0.14	0.37	0.56	0.39	0.20
R-Foot	0.57	0.52	0.51	0.18	-0.16	0.57	0.22	-0.61	0.21	0.37	0.35	0.22
Alpha	0.88	0.89	0.32	-0.73	0.76	0.88	-0.25	-0.93	-0.13	-0.56	-0.49	-0.25

A weak correlative relation of data from biological and electrical origin can be identified within the clinically and biologically healthy population. The correlation coefficient is negative and only points to the red cell blood count, as reverse dependency factor of the overall body impedance. However, there is no evidence of dependency between the erythrocyte sedimentation rate and biophysical parameters obtained.

This pattern is modified in the case of neoplasms. Here are strong correlative relationships between the sedimentation rate, red cell count, the white cell blood count, with four of the electrodes applied to the tissue: capacitive effect of the cell membrane and ionic modification of the surrounding tissues.

4. Interpretation

The rate of sedimentation depends on several factors. In vitro, once pipetted, the density change of blood cells versus plasma is one of the major factors of a high erythro-sedimentation rate. The increase

of high axial ratio proteins (e.g. fibrinogen), usually present during inflammatory processes, accelerates this process. Another factor such as the change of structure of the red cell membrane and the reduction of its electrical charge allow the erythrocytes to form ever longer cylindrical structures. Hence, these floating red blood cell structures in the plasma, will precipitate more rapidly, due to increased density, in relation to liquid medium in which they are initially present.

The use of 5 fluorouracile, (responsible for the destruction of the cellular cytoskeleton) and the paclidal (which acts upon DNA replication), active chemotherapy principles, present in these patients, weaken the cellular membrane. The loss of cellular membrane capacitance, identified from an electronic perspective, through the alpha angle at an impedance of 50 KHz. On table 5b, a change of capacitive property is evident via a high correlation ratio affecting red blood cells and white cells associated with the overall reduction of the alpha. This correlative statistical relationship is direct: decreased value of the angle alpha in patients with neoplasia, increased repulsive charge between the red blood cell membranes, thereby increasing the acceleration of erythrocyte sedimentation. However, such a phenomenon is not observed in the control group (weak correlation = 0.51 and inverse), always referring to the red blood cells, where an increase of the capacitive effect of the red cell membranes can be identified which in turn leads to an increase of the repulsive charges between membranes and therefore to a reduction of erythro sedimentation rate (reduction of length of cellular structures).

5. Conclusion

Two groups of patients were subjected to the same protocol, in order to correlate the two types of measurements. The first set of data comes from the biology of the blood. The blood count and erythrocyte sedimentation are contemplated. The second one explores the bodily electrical properties under a single frequency of 50 kHz. This is the case of bio-impedance. The relation between the erythrocyte sedimentation process, by which red blood cells are pooled, in vitro into stacks or rolls of erythrocytes thus precipitating the test tube that contains it, and the properties of the cell membrane body captured by external electrical measurement is sought. Previous studies have shown that the electrical indicator of the bio-impedance, angle alpha, is related to the change of capacitive properties of the cell membranes.

A statistical analysis of a population of young people ($N = 30$, average age 43 ± 17 years old, predominantly female: 60%) divided into two sub groups, control group of subjects with normal biological results ($N = 20$, average age 38 ± 18 years, 55% female predominance) versus the neo pathological group undergoing chemotherapy ($N = 10$, average age 51 ± 10 years, 70% female predominance), has produced the following results. Between these two assessment techniques (biological and corporal bioimpedance), there is a correlation which could become a possibility to differentiate the two groups significantly to within 1% ($P < 0.01$). Regarding the healthy population, the error found in the chemotherapy-treated population is marked by a reduction from 22% of the value of the impedance at 50kHz (R_{50KHz}), 88% of the reactance X_c , of 56% of the alpha angle. The skin resistance in the hand and foot has increased respectively by 28% and 26% compared to the control group.

The correlative study between the two sets of parameters of the two measurement techniques: biological (12 parameters) and electrical (5 parameters) shows that the correlative pattern between these two sources, changes according to the state of health of the studied group. When it comes to healthy subjects, there is only a weak inverse relationship (-0.52) linking biological data to the bio-

impedance. In the case of subjects with neopathology, the following electrical parameters are very strongly correlated with the rate of correlation: R 50 KHz (ratio: -0.8,); Xc (ratio: -0.98); Alpha (ratio : -0.93). These ratios indicate a great dependency between these electrical parameters (weakening effect of the cellular membrane capacitance and ESR).

This correlation could be useful as it would enable the oncologist to evaluate the risk of thrombosis during chemotherapy, through a measurement by BIA. The measurement is non intrusive, it can be done fast, safely and can provide important preventative information regarding the patient's immediate needs.

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