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Leg electrical resistance predicts venous blood viscosity and hematocrit.
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We previously reported that whole body bioelectrical impedance analysis (BIA) measurements are correlated to some hemorheologic factors, suggesting a relationship between viscosity factors and electric properties of flowing blood not only *in vitro* but also *in vivo*. Recently we reported that with segmental BIA (analyzing the body considered as composed of 5 cylinders) predictive equations for various determinants of blood viscosity were closer than for the whole body. Another widely used BIA technique uses leg-to-leg impedance measurements so that two cylinders (the two legs) are analyzed. We investigated whether impedance measured with this technique (Tanita TBF-300) is also a predictor of blood viscosity factors. From viscometric measurements performed on venous blood drawn in recreative athletes over the range of shear rates 1 to 6000 s⁻¹ (RHEOMETRE Anton Paar CP 50-1), we found a correlation between leg-leg resistance at 50 kHz (Rx[50kHz]) and blood viscosity at 1000 s⁻¹ ($\eta_{1000} = 0.0051 \text{ Rx}[50\text{kHz}] + 1.3265$; $r=0.521$ $p=0.028$ yielding a prediction of η_{1000} (Bland Altman plot : bias 0.05 [RANGE -0.24; 0.34]). Neither plasma viscosity nor the red cell rheology index « k » of Quemada's model are correlated with Rx[50kHz], but hematocrit (Hct) does ($\text{Hct} (\%) = 0.0217 \text{ Rx}[50\text{kHz}] + 33.783$; $r=0.480$ $p=0.044$) yielding a prediction of Hct (Bland Altman plot : bias -0.11, [range -1.67; 1.45]). The discrepancy between actual and predicted Hct is also correlated with resistance at 50 kHz ($r=0.575$ $p=0.031$) as does the discrepancy between actual and predicted Hct /viscosity ratio ($r=-0.651$ $p=0.006$). Therefore, as other previously studied methods, leg to leg BIA predicts viscosity, suggesting that blood rheology may influence the passage of an electric current in the legs.

Running title:

Keywords: segmental bioelectrical impedance, hematocrit, Myrenne aggregometer, Red blood cell aggregation, electrical conductance, light transmission

1. Introduction

Bioelectrical impedancemetry (BIA) can be used *in vitro* to evaluate hematocrit [5] and red cell aggregation [1]. This technique is also widely applied in medicine for the assessment of body composition [2, 6, 7, 10, 15].

Actually, recent research on BIA has shown that this technique was able to measure an even wider range of parameters. We repeatedly reported with whole body impedance measurements correlations between electrical properties of the whole body (impedance, resistance, reactance) and some hemorheologic factors (hematocrit, whole blood viscosity and plasma viscosity, red cell rigidity and RBC aggregation) [3, 19].

One of the limits of such studies investigating the links between whole body impedance and the rheological properties of blood was the shape of human body, which barely can be modeled as a cylinder. By contrast, on cylindrical segments *i.e.*, arms, legs or trunk studied separately, these relationships can be more clearly evidenced, as we recently reported with newly developed BIA devices [20].

Another widely used BIA is leg to leg, which actually measures the circulation of electricity through the two legs, *i.e.*, a cylindrical model of a part of the body [4]. Whether this simple and usual measurement provides a reflect of hemorheological parameters as previously shown with other techniques is unknown.

Therefore this study was undertaken in order to investigate whether the electric properties of the two legs are correlated to measurements of blood viscosity.

2. Subjects and methods

2.1. Study subjects

Characteristics of subjects are shown in Table 1. The study was approved by the local Institutional Ethics Committee and the competent European authority (N°EudraCT: 2016-002742-23). Written informed consent was obtained from each volunteer prior to his enrolment in the study. They were included in a study aiming at investigating whether simultaneous administration of low doses of epoetin-alpha (Binocrit) and growth hormone (Genotonorm) have an effect on erythropoiesis or on the aerobic performance. Consequences for the anti-doping screening are also studied.

2.2. Bioelectrical impedance measurements

Bioimpedance analysis as performed with the Tanita TBF-300A body composition analyzer which utilizes "foot-to-foot" BIA technology (Bio-electrical Impedance Analysis) to make determining internal body composition. This device measures impedance of the body to an alternative electric current of a frequency of 50 kHz and an intensity of 500 μ A. It can measure impedances ranging from 150 to 900 ohms [16].

2.3. Hemorheological *in vitro* measurements

Venous blood samples for hemorheological measurements (7 ml) were drawn in the cubital fossa with a large needle, with potassium EDTA as the anticoagulant in a vacuum tube (Vacutainer).

Viscometric measurements were then performed over the range of shear rates 1 to 6000 s^{-1} with the RHEOMETRE Anton Paar CP 50-1 (Anton Paar Germany GmbH, Hemuth-Hirth-Strasse 6, D-73760 Ostfildern / Germany) [11-13].

Hematocrit was measured together with other hematological markers with the Coulter analysis.

2.6. Statistics.

Results are presented as mean \pm the SEM. A value of $p < 0.05$ was considered as significant. Comparisons were made with nonparametric tests. Pearson coefficients of correlation were tested by least square fitting.

3. Results

As shown on Fig. 1 there was a correlation between leg-leg resistance at 50 kHz ($R_x[50\text{kHz}]$) and blood viscosity at 1000 s^{-1} ($\eta_{1000} = 0.0051 R_x[50\text{kHz}] + 1.3265$; $r=0.521$ $p=0.028$ yielding a prediction of η_{1000} . The Bland Altman plot (Fig. 2) of this relationship shows an agreement with a bias of 0.01 and range of ± 0.2 .

As shown on Fig. 3, hematocrit is also correlated to leg-to-leg resistance at 50 kHz.

($\text{Hct} (\%) = 0.0217 R_x[50\text{kHz}] + 33.783$; $r=0.480$ $p=0.044$) yielding a prediction of Hct (Bland Altman plot : bias -0.11, [range -1.67; 1.45]). The discrepancy between actual and predicted Hct is also correlated with resistance at 50 kHz ($r=0.575$ $p=0.031$) as does the discrepancy between actual and predicted Hct /viscosity ratio ($r=-0.651$ $p=0.006$).

Neither plasma viscosity nor the red cell rheology index « k » of Quemada's model are correlated with $R_x[50\text{kHz}]$.

4. Discussion

This study evidences correlations between BIA crude leg-to leg measurements at 50kHz, and both hematocrit and whole blood viscosity at high shear rate.

These results are in line with our preceding papers cited in the introduction. They lead to think that those previously reported correlations between BIA and viscosity factors were not spurious, because they are regularly found again with various devices and on various populations. We assume that in a narrow cylinder such as the leg the structure of circulating blood (hematocrit, whole blood viscosity) may influence the passage of an electric current by increasing reactance. Whether this may provide a reliable window on hemorheology remains of course to be studied, because the correlation is not so close.

BIA instruments based on leg-to-leg impedance are attractive alternatives to the whole-body BIA model, but studies have shown discrepancies in the evaluation of fat mass compared to reference techniques (around ± 2 kg) [8-9, 14, 17-18].

The reason for this reported poor reliability is obvious: only one part of the body is assessed, and no information about the electric properties of trunk and arms is given. Therefore, a recent review concludes that these individual prediction errors are too great for the methods to be used accurately at the individual level for assessing body fat [4].

Actually we previously performed a comparison of fat mass measurements with this method compared to DEXA and found a not so bad agreement ($r=0.95$ $p<0.001$), which leads to think that the simplicity of the method, although it is accompanied by a moderate loss in precision, does not make it invalid. In addition correction parameters developed for this device can improve its accuracy [16].

By contrast this limitation which is presented as a flaw for body composition assessment is an advantage for our purpose to detect a relationship between the electric properties of a cylindrical segment of the body and blood rheology. Leg-to leg impedance measurements are very easy and inexpensive. This approach is simpler than the multifrequency segmental one presented in one of our previous studies. It can be thus easily tested on large samples.

Further testing of this approach is needed. This study suggests that the previously reported correlations between whole body BIA and viscosity factor were probably not spurious, and that in a narrow cylinder such as the arm the structure of circulating blood (hematocrit, red cell aggregation) may influence the passage of an electric current by increasing reactance. Whether this may provide a reliable window on hemorheology remains of course to be studied.

5. Conclusions

Therefore, as other previously studied methods, leg to leg BIA predicts viscosity, suggesting that blood rheology may influence the passage of an electric current in the legs.

The fact that we regularly observe these relationships between viscosity factors and *in vivo* body impedance with various methods of viscometry and BIA suggests that these findings are not spurious and have physiological relevance.

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List of symbols: Hct: Hematocrit; RBC: red blood cell; SEM: standard error on the mean.

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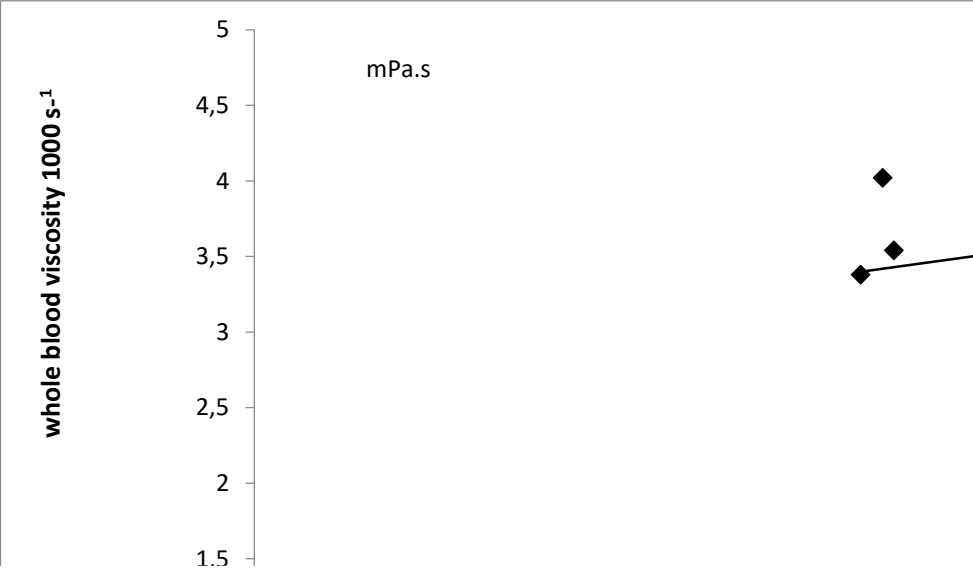
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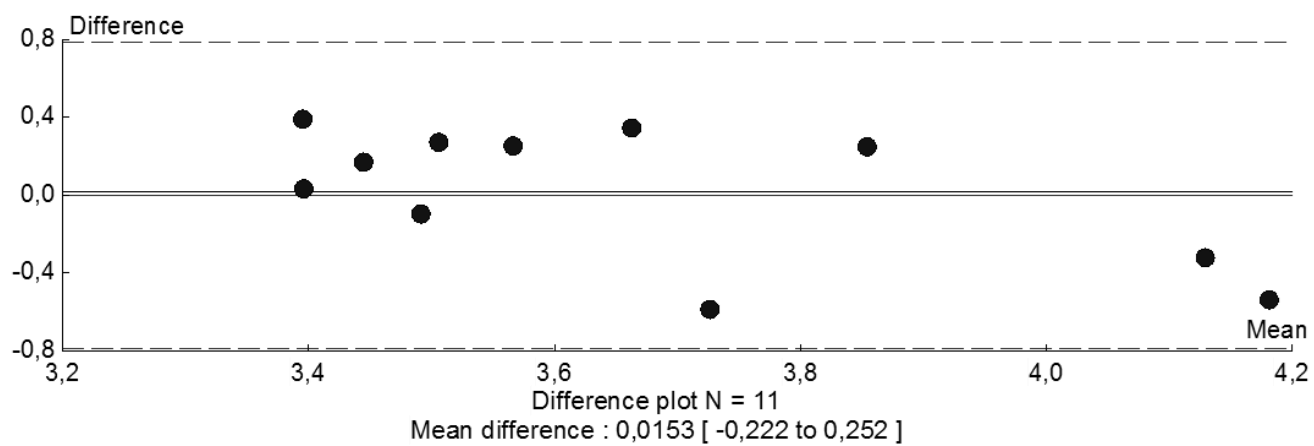
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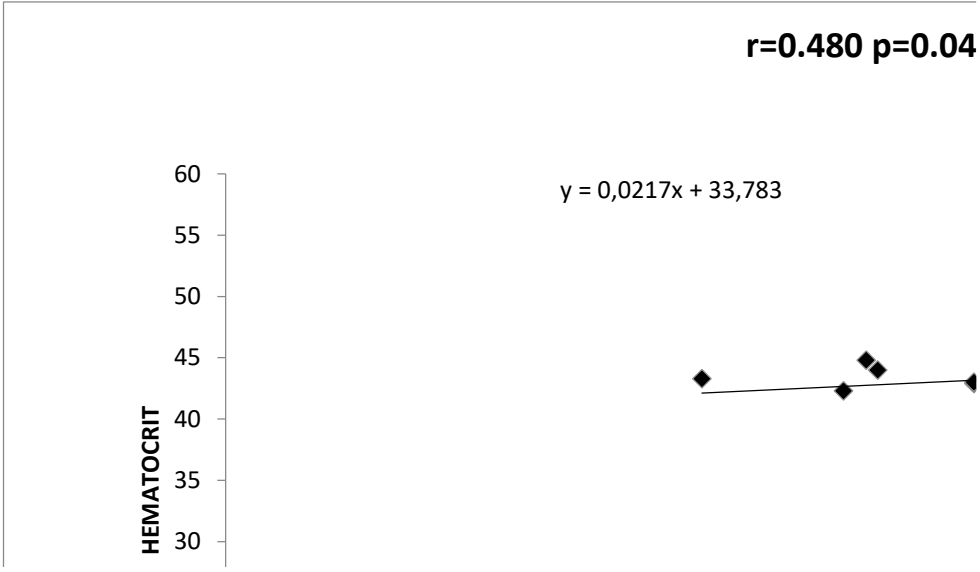
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Table 1. Clinical characteristics of the 11 subjects of the study (mean + SEM).

age (years)	22.20±2.82
weight (kg)	78.77±9.53
height (cm)	175.62±5,91
body mass index (kg/m ²)	25.4±2.35
hematocrit (%)	43.71±2.13







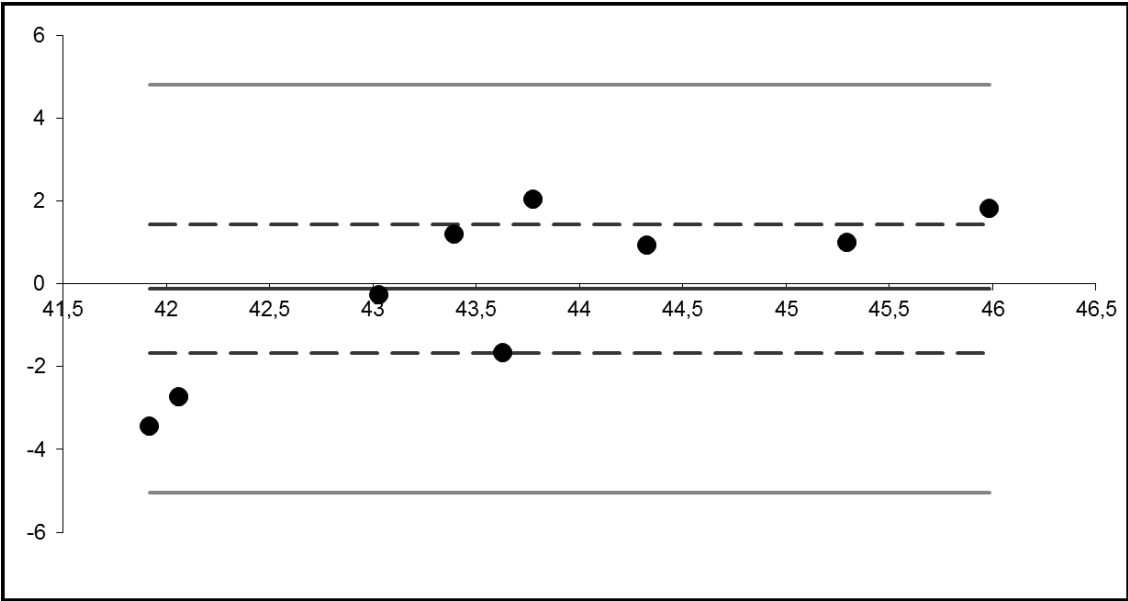


Fig. 1. Correlation between blood viscosity at 1000 s^{-1} and leg-to-leg resistance at 50 kHz.

Fig. 2. Bland Altman graph showing the agreement between blood viscosity at 1000 s^{-1} and leg-to-leg resistance at 50 kHz.

Fig. 3. Correlation between hematocrit and leg-to-leg resistance at 50 kHz.

Fig. 4. Bland Altman graph showing the agreement between hematocrit and its prediction from the correlation with leg-to-leg resistance at 50 kHz presented on Fig. 3. Bias -0.11 ; [range -1.67 ; 1.45].