

Are Thigh and Calf Bioimpedance Spectroscopy less Susceptible to the Influence of Body Posture during Continuous Applications?

A.H. Ismail¹, C. Castelar¹, S. Leonhardt¹

¹Philips Chair for Medical Information Technology, RWTH Aachen, Pauwelsstr. 20, Aachen, Germany

Contact: ismail@hia.rwth-aachen.de

Introduction

Continuous monitoring of body fluid status especially during hemodialysis (HD) treatment is a crucial task. Several tools have been suggested over the last decades [1], including bioimpedance spectroscopy (BIS), which has shown to be more clinically attractive due to its ease of use and accuracy comparable to gold standards (i.e. dilution methods) [2,3]. However, as BIS is susceptible to the influence of external factors including changes in body posture and orientation [4, 5], application of laboratory standards, i.e. limiting the subject to a supine position, has been recommended. Alternatively, the sum of segmental BIS (sBIS) has been also introduced [6]. Nevertheless, these methods are not very clinically favorable for continuous application over extended period of time, i.e. case of HD. Fixing a subject to a supine position for an average of three to five hours treatment with his arms and legs are being extended, as well as the requirement of extra cables and electrodes (case of sBIS), is uncomfortable and mostly unpractical. Recently, alternative configurations of BIS as thigh and calf BIS have been suggested [7, 8]. These new configurations have a very good correlation with the standard whole body BIS while avoiding the complex implantation procedure imposed by other methods, in which electrodes can be simply attached to a trouser, sock, or short-like clothes while keeping the upper part of the subject completely free. Nevertheless, the susceptibility of the thigh and calf BIS to similar errors raising from body posture has not been yet fully addressed.

This study aims to evaluate the influence of changes in body posture on thigh and calf BIS during hemodialysis treatment within two different scenarios (Sitting and Trendelenburg position). Moreover, a three-pool model, representing the thigh and calf segments, will be applied to simulate the associated changes in extracellular resistance (R_e) with each of the aforementioned scenario.

Materials and Methods

Subjects: twelve outpatients undergoing a five hours hemodialysis treatment were studied at the dialysis unit of the RWTH Aachen University Hospital. All patients submitted a written informed consent and the study protocol was approved by the local medical ethical committee. The inclusion criteria was: in- or outpatients HD patients aged above 18 years. The exclusion criteria were HIV, pregnancy, pacemakers, amputation of a limb, or artificial joints.

Study Protocol: Prior to each measurement, patient's standing height and weight, systolic and diastolic blood

pressure, thigh's and calf's circumferences and lengths, and plasma electrolytes were measured. Post-dialysis, patient's weight, applied ultrafiltration rate (UFR) and collected ultrafiltration volume (UFV) were noted.

Initially, all patients had to be in supine position and treatment was started as planned, without any interference. 90 min through the treatment, three patients (*Scenario A*) were asked to change their position (for one hour) by only raising their upper part by $\sim 90^\circ$ to sitting position while legs remain in the supine position. The other three patients (*Scenario B*) remained in supine position until a medical intervention was required, by which only their legs were lifted by 30° (Trendelenburg position). This occurred in our study at 100 ± 20 min from the start of the treatment.

Measurement: Bioimpedance data were obtained every 15 min using Xitron Hydra 4200 (Xitron Technologies Inc., San Diego, CA, USA) with tetra-polar electrodes are being located according to manufacturer's instructions for thigh and calf BIS measurements; Fig. 1. A distance of 5 cm were always kept between the voltage and current electrodes to ensure reproducibility. For each BIS method, extracellular resistance (R_e) was acquired as reported elsewhere [9-11].

Blood samples were drawn from the arterial line, and patient's plasma solutes concentrations were obtained using an automated blood gas analyzer (ABL800 Basic, Radiometer Medical ApS, Brønshøj, Denmark).

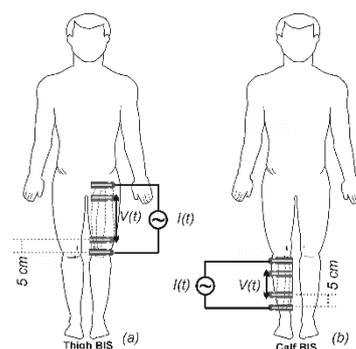


Figure 1: Sketch shows the location of the electrodes for (a) Thigh- and (b) Calf-BIS measurements

Modelling the influence of body posture on R_e : A change in body posture or orientation in space would generate a fluid shift between intracellular (IC), interstitial (IntF) and plasma (PL) compartments due to gravity changing the hydrostatic and osmotic pressure balance between these compartments. This shift could be simulated using a nonlinear

three-pool model modified from Medrano *et al.* [12] and Coli *et al.* [13] as given in Fig. 2.

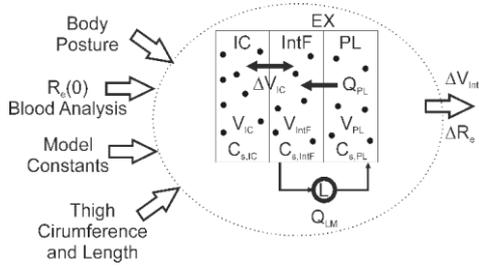


Figure 2: The general concept of the model

As 90% of the injected current in the limbs will only flow through the muscle, which is mainly IntF, IntF was approximated \approx ECF for the limbs. Hence, only change in IntF was considered here. Throughout this section, we were only evaluating changes in variables limited to the thigh and calf segment and not the total body variations.

Initially, thigh IntF volume (i.e. \approx ECF) was calculated from the measured segmental R_e while representing the thigh or the calf as a truncated cylindrical volume (with c_1 and c_2 are the circumference at both ends and l is its length); eqs. (1, 2). The change in interstitial fluid (ΔV_{IntF}) was depicted in eq. (3) as sum of fluid shift to IC ($-\Delta V_{IC}$) due to difference in osmotic activities at cellular membrane, fluid shift from PL through the capillary membrane (Q_{PL}), and the action of lymphatic pump ($-Q_{LM}$).

The difference in osmotic activity was calculated as the sum of all solutes concentrations (C_s) in the corresponding compartment, with k is being a correction coefficient accounts for intermolecular attraction and transmembrane water transfer (eq. (4)). Subscript “s” accounts for sodium (Na^+), potassium (K^+), Calcium (Ca^{+2}), and protein.

$$IntF_{seg} \cong ECF_{seg} = k_G \cdot \left(\frac{\rho_{ECF}}{R_{e,seg}} \right)^{\frac{2}{3}} \quad (1)$$

$$k_G = 0.1434 \cdot \frac{(c_1^2 + c_2^2 + c_1 c_2) \cdot l^{\frac{5}{3}}}{(c_1 c_2)^{\frac{2}{3}}} \quad (2)$$

$$\frac{dV_{IntF}(t)}{dt} = -\frac{dV_{IC}(t)}{dt} + Q_{PL}(t) - Q_{LM}(t) \quad (3)$$

$$\frac{dV_{IC}(t)}{dt} = k \cdot \left[\sum_s C_{s,IC}(t) - \sum_s C_{s,IntF}(t) \right] \quad (4)$$

Using Starling equation and a filtration coefficient (k_f), the fluid shifts from PL (Q_{PL}) was calculated as the difference in both hydrostatic (P) and oncotic (Π) pressures between capillary (subscript “cap”) and interstitial; eq. (5). The action of lymphatic pump (Q_{LM}) was approximated from relationship between interstitial hydrostatic pressure and volume, as the ratio of changes in body segment volume (V_{seg})

to the total body volume multiply with relative lymph flow (Q_R); eqs. (6-7) [14, 15].

$$Q_{PL}(t) = k_f \cdot \left[(P_{cap}(t) - P_{IntF}(t)) - \left(\sum_s (\Pi_{s,cap}(t) - \Pi_{s,IntF}(t)) \right) \right] \quad (5)$$

$$Q_{LM}(t) = 0.0031 \cdot \frac{V_{seg}(t)}{V_{body}(t)} \cdot Q_R \quad (6)$$

$$Q_R = \begin{cases} 0, & P_{IntF} \leq -3 \\ 0.78 \cdot P_{IntF} + 2.9, & else \\ 4.6, & P_{IntF} > 3 \end{cases} \quad (7)$$

The concentration of each solute was described as the ratio of its mass (M_s) to the volume in the corresponding compartment. For solute kinetics, we only considered intracellular and extracellular (subscript “EX”) compartments.

$$C_s = \frac{M_s}{V_s} \quad (8)$$

The change in a solute mass (ΔM_s) in intracellular compartment was defined as the solute mass flux (Φ_s) across the cellular membrane from extracellular compartment plus its production rate (G_s) in IC. For all solutes except protein, Φ_s was defined based on solute concentration balance across the cellular membrane, with k_s is the mass transfer coefficient. Only for protein, Φ_s was considered null.

$$\frac{dM_{s,IC}(t)}{dt} = \Phi_s(t) + G_{s,IC} \quad (9)$$

$$\Phi_s(t) = -k_s \cdot [C_{s,IC}(t) - g_s \cdot C_{s,IntF}(t)] \quad (10)$$

$$\frac{dM_{s,EX}(t)}{dt} = -\Phi_s(t) + G_{s,EX} \quad (11)$$

According to eqs. (9-11), the solute concentration in interstitial compartment is given in eq. (12), where r is the plasma water fraction and D is the Gibbs-Donnan ratio.

$$C_{s,IntF}(t) = \frac{M_{s,IntF}(t)}{V_{IntF}(t)} = \frac{M_{s,EX}(t)}{V_{IntF}(t) + V_{PL}(t) \cdot r/D} \quad (12)$$

Using the baseline measured R_e and blood analysis data, patient’s anthropometric data, and given the capillary hydrostatic pressure at each body position, changes in thigh and calf R_e due to body posture were estimated from the change in IntF volume as a function of time.



Results

Table 1 presents the baseline physical and clinical characteristics of the twelve patients and their treatments. All patients received hemodialysis treatment of 5 hours. Half of the patients were considered hemodynamically stable at pre-dialysis. Two Patients showed sign of pre-dialysis overhydration; yet only one of them showed peripheral pitting edema. Only one patient was considered diabetic. Fig. 1 shows the locations of the electrodes for the thigh and calf BIS, while Fig. 2 presents a graphical representation of the applied three-pool model. BIS measurements during HD and Simulink® simulations of the influence of body posture on R_e for two patients are shown in Fig. 3 and 4, respectively. During supine position, the rate of change in ΔR_e due to ultrafiltration (UFR) was $+0.09 \pm 0.03 \Omega/\text{min}$ (thigh) and $+0.05 \pm 0.03 \Omega/\text{min}$ (calf). However, this was altered to $+0.06 \pm 0.01 \Omega/\text{min}$ (thigh) and $+0.02 \pm 0.02 \Omega/\text{min}$ (calf) post Sitting, and to $+0.12 \pm 0.03 \Omega/\text{min}$ (thigh) and $+0.08 \pm 0.11 \Omega/\text{min}$ (calf) post Trendelenburg. The simulated changes in R_e with body posture were very similar for thigh and calf BIS measurements; R_e decreases during sitting position and increases during Trendelenburg position. However, changes during the latter position were much faster.

Table 1: Baseline physical and clinical characteristics

Baseline Characteristics	
Number of Subjects	12
Gender, % female	33.3
Age, years	59.9 ± 17.9
Height, cm	172.4 ± 8.1
Weight, kg	82.4 ± 9.6
BMI, Kg / m ²	27.9 ± 4.3
UFR, ml / h	502.0 ± 312.6
UFV, L	2.0 ± 1.1
SysBP, mmHg	122.6 ± 22.9
Hemodynamically Stability, %	50.0

Discussion

During hemodialysis treatment, a significant amount of body fluid is removed via ultrafiltration. If no medical intervention or UFR profiling were applied, this can be observed by BIS methods as a continuous increase in extracellular resistance almost till the end of the treatment. However, this is only true if the patient remains in a constant supine position with legs apart and arms away from the body. If a subject changes his body orientation in the space, a fluid redistribution may occur between inter-body compartments, i.e. intracellular, interstitial and plasma. Hence, the extracellular resistance distribution throughout the whole body changes. Fig. 3 points out in this direction, in which a hemodynamically stable patient undergoes HD with constant UFR asked to change his position from supine to sitting. As a result, a significant portion of fluid was shifted to IntF in the thigh and calf segments, which relatively counteracted the effect of UFR on R_e . Accordingly,

the rate of change in measured R_e was altered from $0.09 \Omega/\text{min}$ to $0.02 \Omega/\text{min}$ for the thigh and from 0.10 to 0.05 for the calf, corresponding to this time period. In a different scenario, where patient's legs were raised as a part of required medical intervention, thigh R_e increased very quickly more than that expected from UFR. These observations were held true for all patients in this study. The larger changes in thigh R_e after Trendelenburg position was applied, may suggest that the thigh plays a key role in body refilling during HD, especially since the remaining parts of the leg may contain less amount of fluid.

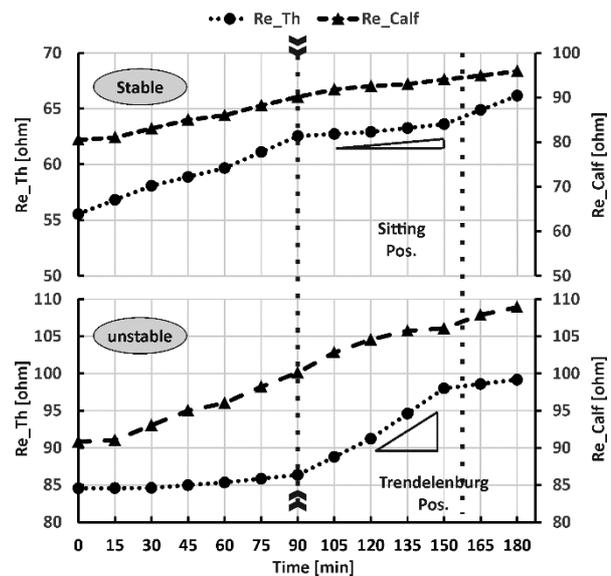


Figure 3: Trends showing the change in Thigh- and Calf- R_e in a stable (with scenario A: Sitting Position) and an unstable (with scenario B: Trendelenburg Position) patient.

To further investigate this observation, a non-linear three compartments model was developed for the thigh and calf body segment. The model allows to reproduce the influence of similar body movements on measured R_e . For the sake of simplicity, the simulations were all done without considering the HD treatment.

Apart from the calf measurements, a good agreement between the simulated results and measured data was found. This could be due to the simplification taken in eq. (1), which may not be very applicable to the calf segment. This simplification was based on the assumption that due to high muscle content, IntF compartment contributes significantly more than PV to the conduction current in the lower limbs. However, as the calf contains much less muscle mass, PV could contribute more to the measured R_e , which explains why simulations were not in fully agreement with measured calf R_e .

Recently, the sum of segmental BIS measurements was suggested to overcome this problem [6]. The method usually divides the body into three or more segments, from which segmental R_e is calculated. The sum of all resistances would represent the total body extracellular R_e . Nevertheless, the method requires extra amount of cable,

electrodes, and care should be given when placing the electrodes at the body. For example, inaccurate distance between electrodes due to mispositioning may produce significant artifacts in measured segmental R_e as reported by Shiffman [16]. Hence, rendering this method in particular unfavorable for daily clinical applications.

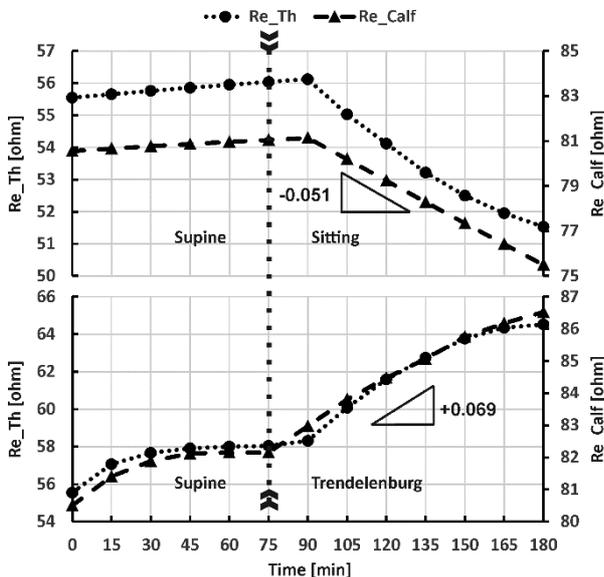


Figure 4: Trends showing the simulated changes in Thigh- and Calf- R_e after switching to sitting Position (upper) and after switching to Trendelenburg Position (lower) position.

Despite the reported results, the study has some limitations, which need to be addressed in further work. Although all applied variables and equations are based on published data, the use of such large amount of variables and simplification in the model could limit its use to research only. Furthermore, the simulated results were not confirmed by real measurements and hence the accuracy of the model is subject to error. Sensitivity analysis suggested that only physiological factors as hydrostatic and oncotic pressure variables and protein concentration have a significant effect on ΔR_e . Fluid shift toward IC during movement had no substantial influence on the model accuracy. However, this held true only if the HD process would not take into account.

Conclusions

Bioimpedance spectroscopy is a very attractive tool for continuous monitoring of body fluid status in clinical practice. However, the accuracy of the method is subject to the influence of external errors and needs to be improved. Hence, the use of BIS is limited so far, to observe changes in body fluid status rather than determining absolute body volumes, and if so (in case of extracellular fluid), then under very cautious. This is also valid for segmental BIS (e.g. thigh, calf, or knee-to-knee). Since the application of laboratory standards is most likely unpractical during some clin-

ical practice as HD treatment, the use of such a mathematical model to filter/correct segmental BIS data in the future is promising. However, further investigations are needed to improve the model accuracy and extend its application.

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