IN VIVO ASSESSMENT OF HAEMATOCRIT CHANGES BY ELECTRICAL IMPEDANCE MEASUREMENTS

P. J. Riu, O. Surkhy and P. Bogonez

Catalonian Reference Center for Bioengineering (CREBEC), Technical University of Catalonia (UPC), Barcelona, Spain

priu@eel.upc.edu

Abstract: Electrical impedance techniques are currently used to assess body fluids under several conditions, including hemodialysis. We propose to use the same methods to assess haematocrit in-vivo, thus allowing a better assessment of adverse effects during dialysis sessions. A pressure cuff is placed on the upper part of the arm and pressure pulses are generated using a computer-controlled air pump resulting in a total or partial closure of the upper arm veins and hence an increase in the distal arterial blood volume due to the compliance of the arteries and the elasticity of the surrounding tissues. By producing cycles in the applied pressure, a range can be found where the mechanical compliance of the arteries (C) is essentially constant, thus changes in H_t can be monitored even without knowing the value for the compliance C. If an initial value of H_t is obtained by an independent method, then the on-line in-vivo assessment of H_t will be possible by measuring the electrical impedance. Both, changes in H_t and changes in body fluids can be assessed using the same technique.

Introduction

Recent data estimated that 400,000 people suffer from kidney failure in the USA only; the lives of many of these patients depend on dialysis (BioMed Central Nephrology, October 2003). Patients can suffer from adverse side effects during dialysis such as hypotension, headache and vomiting. Most of these irritating symptoms are related to the excess shift of fluids between the extracellular and intracellular areas, and due to the rapid changes of the chemical balance during dialysis.

Haematocrit (*Ht)* -defined as the volumetric ratio of the packed-cell (erythrocyte) in blood- is a very useful clinical indicator to estimate the fluid shift between the extracellular and intracellular areas. Significant changes in the blood Haematocrit are recorded during artificial dialysis resulting in remarkable changes in the blood conductivity that can reach to 20% [1]. The changes in the Haematocrit and blood conductivity reflect the change in the blood volume due to the fluid removal from plasma assuming conservation of erythrocyte volume. Several attempts for monitoring the Haematocrit based on impedance or optical approaches have been introduced in the recent years. In [2] a continuous measurement of Haematocrit and plasma volume variation during dialysis based on impedance measurements is proposed, using Hanai model for suspension of non conducting cells (erythrocyte in this case):

$$\rho_b = \rho_p \left(1 - Ht\right)^{\frac{-3}{2}} \qquad (1)$$

where ρ_b and ρ_p are the blood and plasma resistivity and Ht is the Haematocrit expressed as a decimal number. An expression relating the instantaneous Haematocrit and the instantaneous impedance is also obtained in [2]:

$$Ht = 1 - \left(1 - Ht_0\right)\left(\frac{Z_0}{Z}\right)^{\frac{2}{3}} \qquad (2)$$

Where Ht and Ht_0 are the measured and initial values of the Haematocrit.

This approach can only be performed directly on blood by using an impedance measurement cell connected to the arterial line of the heamodialyser. It also requires taking a blood sample before starting the dialysis procedure and measuring the initial Haematocrit Ht_0 using traditional laboratory methods.

We will introduce a new approach for monitoring the blood Haematocrit based on the electrical admittance of a parallel compartment model. The admittance variations will be measured on the surface without direct contact between the blood and the electrodes

The continuous and totally non-invasive measurement of the blood Haematocrit is considered an essential key to monitor and reduce dialysis side effects and thus improving dialysis quality.

Theory

I. Tissue Modeling

The biological tissue in vivo can be modeled by an electrical circuit to describe the behavior of

ISSN: 1727-1983

extracellular and intracellular fluids in response to an injected current with different frequencies. A parallel conductors model shown in (Fig. 1) consists of the resistance of the extracellular fluid $R_{(EC)}$ in parallel with the resistance of the intracellular fluid $R_{(IC)}$ and the cell membrane capacitance C_m.

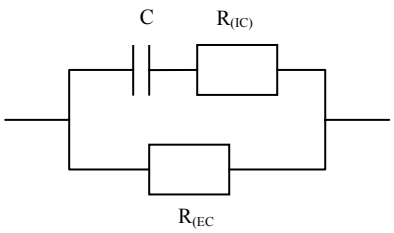

Fig. 1. Tissue model. Two parallel conductors $R_{(EC)}$ // $(R_{(IC)} + 1/j\omega C_m)$

Extracellular fluid consists of interstitial fluid (containing lymph fluid) as well as blood which is a suspension of non conducting cells-erythrocytes and relatively conducting fluid –plasma, therefore the model in Fig. 1 can be expanded into more detailed model shown in Fig. 2. It is generally assumed that at high frequency, the injected current will penetrate both intracellular and extracellular areas while at low frequency the current will pass through extracellular area only since the cell membrane will act as insulator.

The body geometry consists of complex and diverse elements with different dielectric properties; however, in the presence of non conducting elements (skin ,fat, bones) one can assume that at low frequency the current will penetrate only the interstitial and plasma regions and thus the model shown in Fig. 2 can be represented using the electrical admittance in a simpler model shown in Fig. 3 :

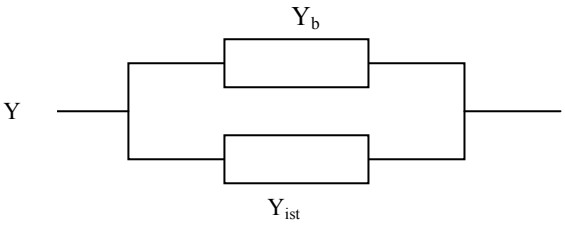

Figure 3. Simplified body model at low frequencies

When a current is injected by electrodes placed on the body surface and separated by a distance L, the measured admittance Y is

$$Y = Y_b + Y_{ist} = \sigma_{eq} \frac{V_{EC}}{L^2} \qquad (3)$$

where L is the distance between the electrodes, V_{EC} is the sample volume, and σ_{eq} is the equivalent complex conductivity of the sample volume .

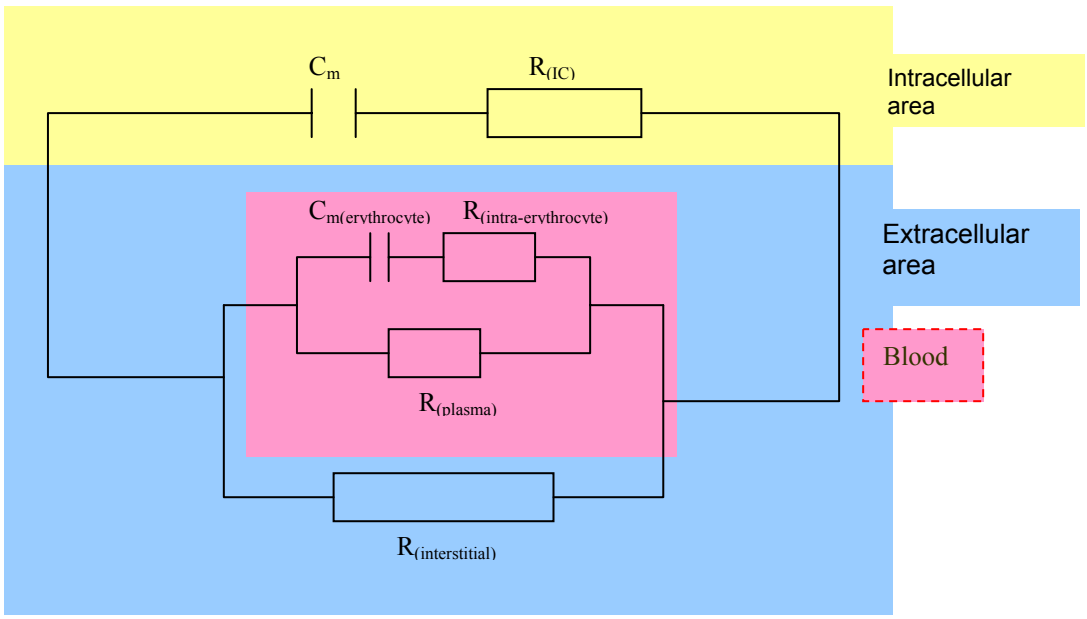

Fig. 2. Expanded tissue model. Extracellular area includes interstitial fluid and blood, modeled as a cell suspension as well.

ISSN: 1727-1983

From Eq(3) we can write :

$$Y = \sigma_{eq}\frac{V_{EC}}{L^2} = \sigma_b\frac{V_b}{L^2} + \sigma_{ist}\frac{V_{ist}}{L^2} \qquad (4)$$

$$\sigma_{eq} = \sigma_b\frac{V_b}{V_{EC}} + \sigma_{ist}\frac{V_{ist}}{V_{EC}} \qquad (5)$$

II. Conductivity of the Extracellular fluid

From Eq(5) we can see that the equivalent (measured) conductivity is equal to the summation of the blood conductivity and the interstitial fluid conductivity each multiplied by the volumetric ratio to the extracellular fluid. We also know that the extracellular fluid consists of the interstitial fluid and blood volume, thus we can also write:

$$V_{EC} = V_b + V_{ist} \qquad (6)$$

Zhu et al [3] present some values of the extracellular volumes in different segments of the body calculated in 11 healthy males

Table (1). The average segmental volumes and the extracellular fluid volumes calculated by Zhu et al. [3]

Segment	Segment length(cm)	Seg.Cross sectional area(cm^2)	V_{EC} (10^3 cm^3)
Arm	56.1±3.18	48.1±10.4	1.31±0.25 .
Trunk	50.9±3.73	647.7±170	10.08±1.65
Leg	91.1±5.77	121.01±22.6	2.80±0.82

In the arm sections the average extracellular fluid volumetric ration to the section ratio is V_{EC}/V_{arm}=48.1% (range 30.4%-77.3%). For healthy adults, the blood volume ratio in the body is approximately equal to 1/13 of the total body volume.

If we assume that the blood is distributed equally in all the body segments we can write V_b=0.077 V_{arm} and Eq(4) can now be written:

$$V_{EC} = V_b + V_{ist}$$

$$\left(\frac{V_b}{V_{EC}}\right) = 0.16 \qquad (7)$$

$$\left(\frac{V_{ist}}{V_{EC}}\right) = 0.84 \qquad (8)$$

And Eq(5) becomes:

$$\sigma_{eq} = 0.16\sigma_b + 0.84\sigma_{ist} \qquad (9)$$

III. Blood conductivity and Blood Volume.

Measuring the admittance using electrodes attached to the surface can be useful in order to determine the conductivity of the extracellular fluid which is a function of the blood conductivity and the interstitial fluid conductivity each multiplied by the volumetric ratio to the extracellular fluid as shown in Eq.(9). However, using the local surface measurement directly is not helpful in evaluating the partial blood conductivity. A short-term increase of the arterial blood volume and a measurement of the volume-dependent admittance can be the solution. Total or partial closure of the upper arm veins (brachial vein, cephalic vein, and basilic vein) will produce an increase in the arterial blood volume due to the known compliance of the arteries.

Typical volume-pressure and compliance–pressure curves for a normal artery are shown in Fig.4.

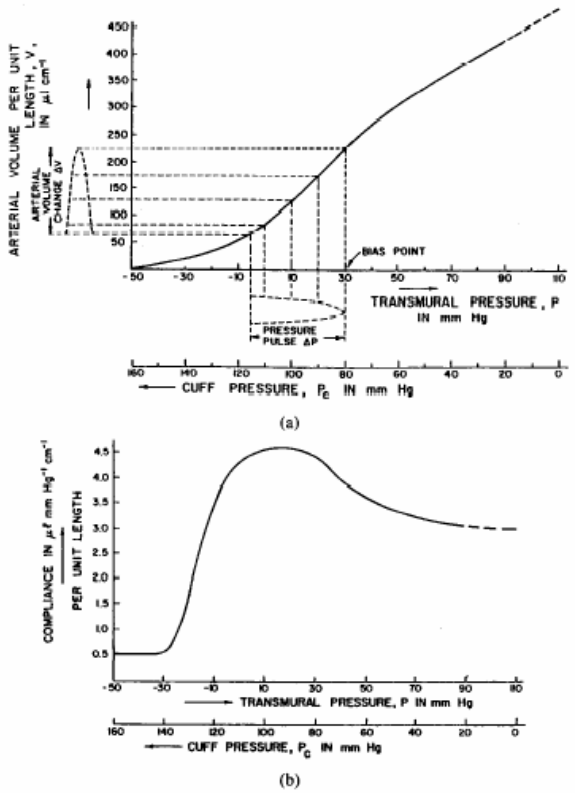

Fig. 4. Typical volume-pressure and compliance–pressure curves for a normal artery. Ref [4]

ISSN: 1727-1983

The measured admittance before closing the upper arm veins can be written as:

$$Y_{(i)} = \sigma_{eq} \frac{V_{(i)EC}}{L^2} = \sigma_b \frac{V_b}{L^2} + \sigma_{ist} \frac{V_{ist}}{L^2} \qquad (10)$$

The measured admittance after closing the upper arm veins is:

$$Y_{(ii)} = \sigma_{eq} \frac{V_{(ii)EC}}{L^2} = \sigma_b \frac{V_b + \Delta V_b}{L^2} + \sigma_{ist} \frac{V_{ist}}{L^2} \qquad (11)$$

In Eq.11 we assume that for a short term closure of the upper arm vein the interstitial fluid will not change.

The admittance difference can be calculated by subtracting Eq.10 from Eq. 11. We can write the change in the admittance:

$$\Delta Y = Y_{(ii)} - Y_{(i)} = \sigma_b \frac{\Delta V_b}{L^2} \qquad (12)$$

Admittance - compliance relationship: Mechanical compliance of the artery is defined as the ratio of blood volume change (ΔV) to blood pressure change(ΔP):

$$C = \Delta V / \Delta P \quad [\mu L / mmHg / cm] \qquad (13)$$

From Eq.12 the change in admittance produced by the applied cuff pressure is:

$$\Delta Y = \sigma_b \frac{\Delta V_b}{L^2} = \sigma_b \frac{C \Delta P}{L^2} \qquad (14)$$

Admittance- haematocrit relationship: The relationship between the blood conductivity and the haematocrit is given by:

$$\sigma_b = \sigma_p (1 - Ht)^{3/2} \qquad (15)$$

where σ_p is the plasma conductivity. Eq. 12 can thus be written as:

$$\frac{\Delta Y}{\Delta P} = \frac{C}{L^2} \sigma_p (1 - Ht)^{3/2} \qquad (16)$$

This shows that the change in the measured admittance is a function of the blood conductivity and the compliance-dependent increase in the arterial blood volume.

Methods and materials

A pressure cuff was placed on the upper part of the arm and pressure pulses were generated using a computer-controlled air pump resulting in a total or partial closure of the upper arm veins and hence an increase in the distal arterial blood volume due to the compliance of the arteries and the elasticity of the surrounding tissues.

The response of the electrical admittance to the applied pulsatile pressure was measured by a self-designed local impedance analyzer with SNR 45dB,imapedance range(40-1KΩ), and frequency range (1KHz-1MHz) . Both the admittance and the pressure signals were analyzed using Matlab. The value for C was calculated by measuring the admittance in response to step changes in the pressure and using an initial value of Ht measured by an independent method. The measurement setup is shown in figure 5. Two approaches were used: the first approach was to apply pressure pulses (6 pulses per min) using the pressure cuff and recording the admittance waves . The second approach was to apply a relatively slow single pressure pulse with inflation time approximately 25 sec and longer deflation time. In booth approaches the admittance response was recorded using surface electrodes (3M Red Dot (TM) Ag/AgCl 2560) with single injection frequency of 100KHz.

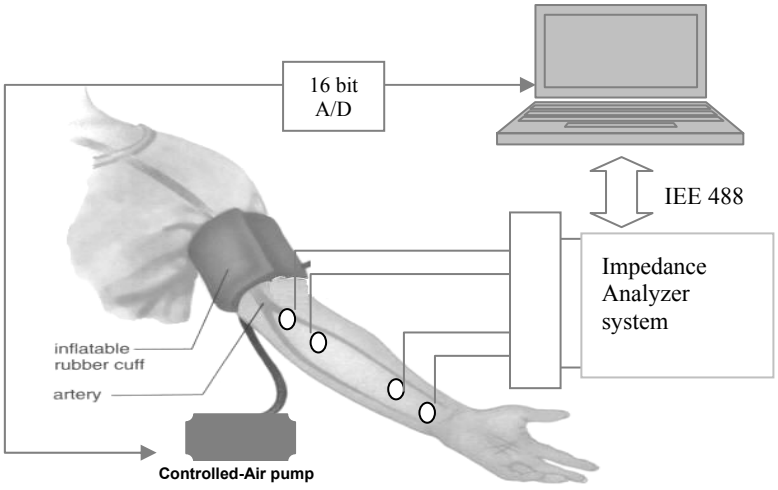

Fig.5. Computer controlled system for impedance and cuff pressure measurements

ISSN: 1727-1983

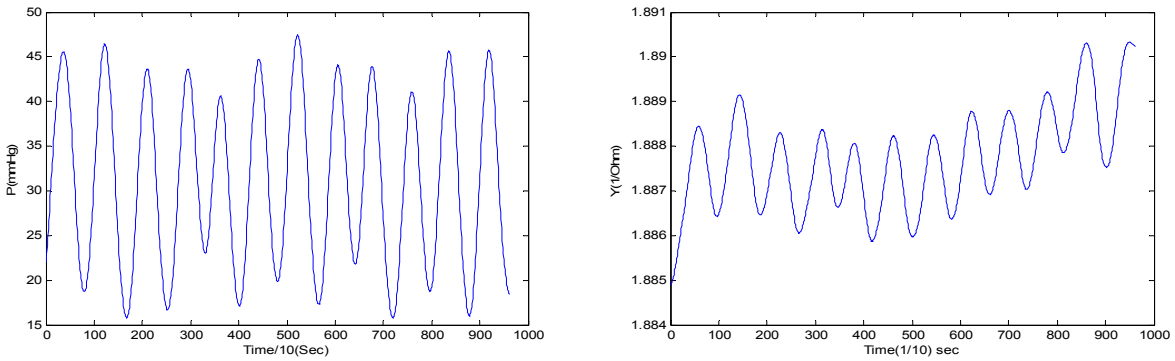

Figure 6. The applied pressure pluses (left) and the recorded admittance signal (right)

Results

*Approach 1 pressure pulses :*Figure 6 shows the recorded admittance and the applied pressure in a healthy volunteer displaying several inflation/deflation cycles. The pressure and admittance signals were processed using Matlab in order to detect each pulse. The pulses were separated and saved in a matrix form and averaged (Figure 7-a , 7-b). A mean admittance wave and pressure pulse were calculated. After a phase shift correction the derivative dY/dP was calculated and plotted against P (Figure 7-c). It is observed that it remains constant for pressures between 20 and 45 mmHg, indicating that the compliance is constant in this pressure range (assuming that H_t and σ_p have not changed in such a short period). H_t is then estimated from Eq. 5, using the calculated value of C.

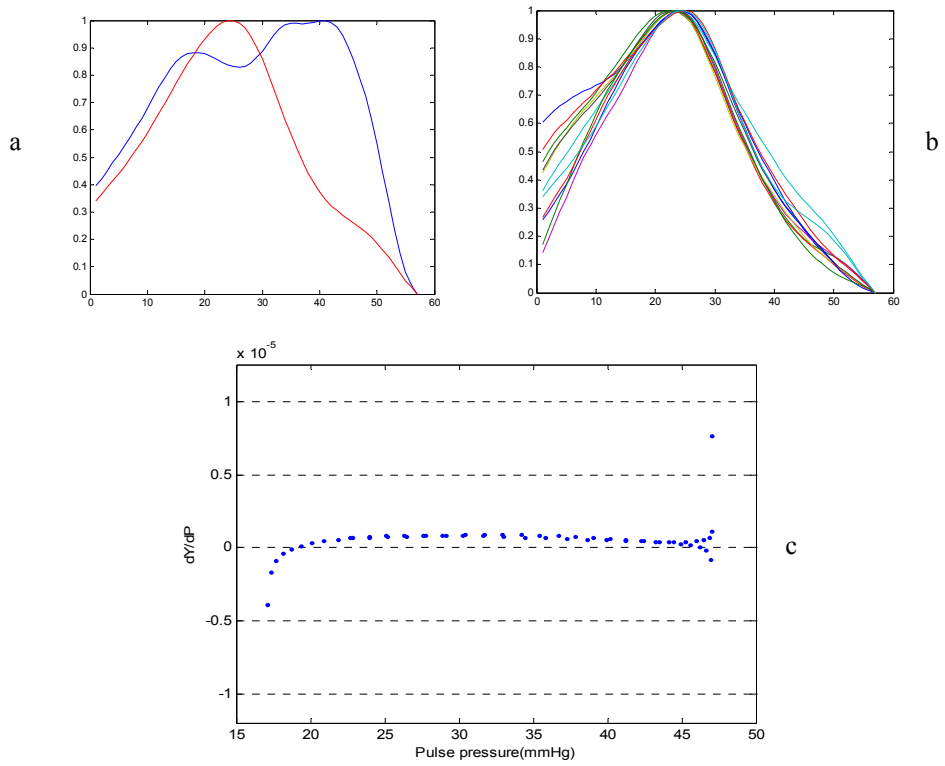

Figure 7. Analysis of the pressure and admittance signals-Approach 1

ISSN: 1727-1983

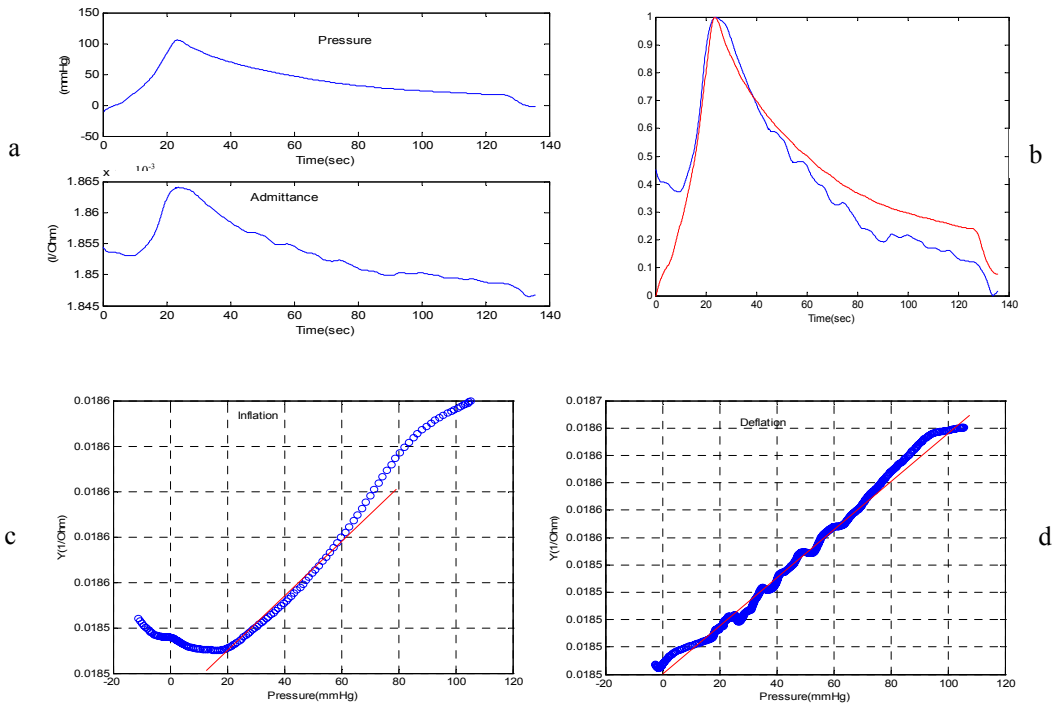

Figure 8. admittance response to a single pressure pulse.

Approach 2.Single pressure Pulse: Figure (8-a) shows the applied pressure pulse and the recorded admittance response. The admittance values for the inflation cycle were separated and plotted against the values of P (Figure 8-c), the same was repeated for the deflation cycle (Figure 8-d).

It is noticed that the Y P graph behaves almost linearly in the pressure range 20-40 mmHg. i.e., dY/dP is constant in this range.

Sensitivity of heamatocrit changes to dY/dP: The relation between dY/dP was derived in eq.16. The relative sensitivity in the Y-P slope is defined as the relative change in the dY/dP values to ΔHt. For a given Ht value and assuming that C will be constant in the pressure range between 20-40 mmHg we can write:

$$\Delta\left(\frac{\Delta Y}{\Delta P}\right) = \frac{C}{L^2}\sigma_p \times -\frac{3}{2}(1-Ht)^{1/2}\,\Delta Ht \qquad (17)$$

$$\Delta\left(\frac{\Delta Y}{\Delta P}\right)\left(\frac{\Delta P}{\Delta Y}\right) = \frac{\frac{C}{L^2}\sigma_p \times -\frac{3}{2}(1-Ht)^{1/2}\,\Delta Ht}{\frac{C}{L^2}\sigma_p (1-Ht)^{3/2}} = -\frac{3}{2}(1-Ht)^{-1}\,\Delta Ht \qquad (18)$$

Discussion and Conclusions

By producing cycles in the applied pressure, a range can be found where C is essentially constant, thus changes in H_t can be monitored even without knowing the value for the compliance C. If an initial value of H_t is obtained by an independent method, then the on-line in-vivo assessment of H_t will be possible by measuring the electrical impedance. Both, changes in H_t and changes in body fluids can be assessed using the same technique.

References

[1] SAKAMOTO, K. et al (2004) 'Electrical admittance method for estimating fluid removal during artificial dialysis'. *Med. Biol. Eng. Comput.*, **42**:3, pp. 356-365

[2] MAASRANI, M., JAFFRIN, M.Y. (1997): 'Continuous measurements by impedance of haematocrit and plasma volume variations during dialysis', *Med. Biol. Eng. Comput.*, **35**:3, pp. 167-171

[3] ZHU F. et al (1998): 'Dynamics of segmental extracellular volumes during changes in body positions by bioimpedance analysis', *J Appl. Physiol.*, **85**:2, pp. 497-504

[4] KIM D.W., KIM S.C. (1999), 'Measurement of leg arterial compliance of normal subjects and diabetics using impedance plethysmography', *Annals N Y Acad. Sci.*, **873**, pp. 112-120

ISSN: 1727-1983