

In-vivo blood characterization system

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Blood-impedance characterization system is presented. It is intended for measuring hematocrit and blood viscosity in-vivo. Using specially designed central venous catheter, it examines blood online by measuring inside the right atrium where strong ECG signal is recorded as well. Additionally, temperature compensation of the acquired results is performed and patient temperature is monitored with a tiny thermistor incorporated alongside with the impedance sensor. Sweeping in the frequency range from 20 kHz to 1.2 MHz, the measurement system derives various blood-impedance components, e.g. plasma resistance, cell membrane capacitance, cell interior resistance. Proper catheter positioning and processing of the measured impedance components is helped by the ECG signal measured with the same impedance sensor. Hence, sufficient measurement accuracy and repeatability is achieved.

1. INTRODUCTION

Blood impedance (Z_b) and particularly plasma resistance (R_p) and cell membrane capacitance (C_m) may be of a great importance for the medicine. They are related to hematocrit (H_t), which is the most valuable determinant of blood viscosity [1,2]. By measuring blood viscosity various heart-related thrombotic events such as heart infarcts or strokes can be prevented. During animal experiments, a reduction of arterial thrombosis has been obtained by hemodilution therapy, which results in lower hematocrit as several studies have reported that an optimal hematocrit for tissue perfusion exists. Fibrinogen, another determinant of blood viscosity, affects Z_b as well. In the view of the above-mentioned considerations our goal is to explore the diagnostic

potential for measuring blood viscosity, hematocrit and fibrinogen levels and other blood parameters in-vitro and in-vivo by means of impedance measurement techniques.

Blood is a suspension of red cells, white cells, and platelets in plasma. A simplified three-element circuit model describes its properties (Fig. 1) [3,4]. The concentration of red cells is called hematocrit and in this electrical structure is represented by R_p . R_i represents the cell interior resistance, as C_m is a measure for the cell membrane capacitance. The total complex impedance measured by a sensor includes the polarization effect of the electrodes (Z_e) too [5].

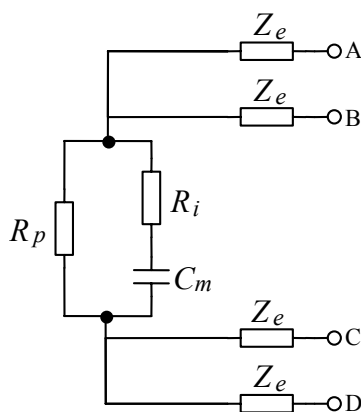


Figure 1. Three-element model of blood including electrode polarization impedance Z_e .

Though R_p is an accurate measure of H_t and therefore good indicator for the viscosity, it does not reflect fully viscosity because of the non-Newtonian characteristics of blood. The non-Newtonian behavior of blood means that it has higher viscosity at lower shear rate. Therefore, viscosity varies with the flow and shear rate eventually. To compensate for this, accurate measurement of C_m is needed. At a certain shear rate C_m is determined by the amount of cells (this is H_t), nevertheless approximately 10% of C_m is affected by the presence of plasma macromolecules between the cells. Consequently, R_p is considered to be measure for H_t and the combination of R_p and C_m is to be used to determine viscosity.

2. MEASUREMENT SYSTEM

Dedicated impedance-measurement system was designed to perform the characterization of blood. It works with sinusoidal signal in the frequency range from 20 kHz to 1.2 MHz and applies 10 uA current through the sensor. Figure 2 shows the measurement system named HemoCard Vision[®] (HCV). Its specially developed catheter can be seen in Fig. 3. It has four-electrode setup and a thermistor located at the distal end, near the tip. With the existing three lumens for administering of infusion solutions and/or measuring atrial pressure it enables all characteristic features of a central venous catheter (CVC) alongside with the impedance and temperature measurement capabilities.



Figure 2. HemoCard Vision measurement system.



Figure 3. Catheter for in-vivo characterization of blood in the right atrium.

Four stainless steel electrodes, 0.8 mm wide, positioned equidistantly 2 mm center-to-center, sense the impedance. The outer pair is the excitation one and the inner is the sense pair.

The thermistor is placed in a lumen, next to the electrodes. UV resin fills the cavity around the thermistor for better thermal contact.

Three triaxial cables, 0.49 mm in diameter, and one coaxial cable, 0.33 mm in diameter, connect the electrodes to the interface electronics.

The equivalent electrical model of blood is shown in Fig. 1. Fricke has established it back in 1925 [6]. Since then results have been reported for various blood samples as the specific resistance and capacitance of whole blood have been measured. Based on this experience we set the following ranges for the HCV interface electronics: 20Ω to 70Ω for R_p and 0.2 nF to 2 nF for C_m . The applied current is limited by electromagnetic compatibility regulations to $10 \mu\text{A}$. No DC current is allowed.

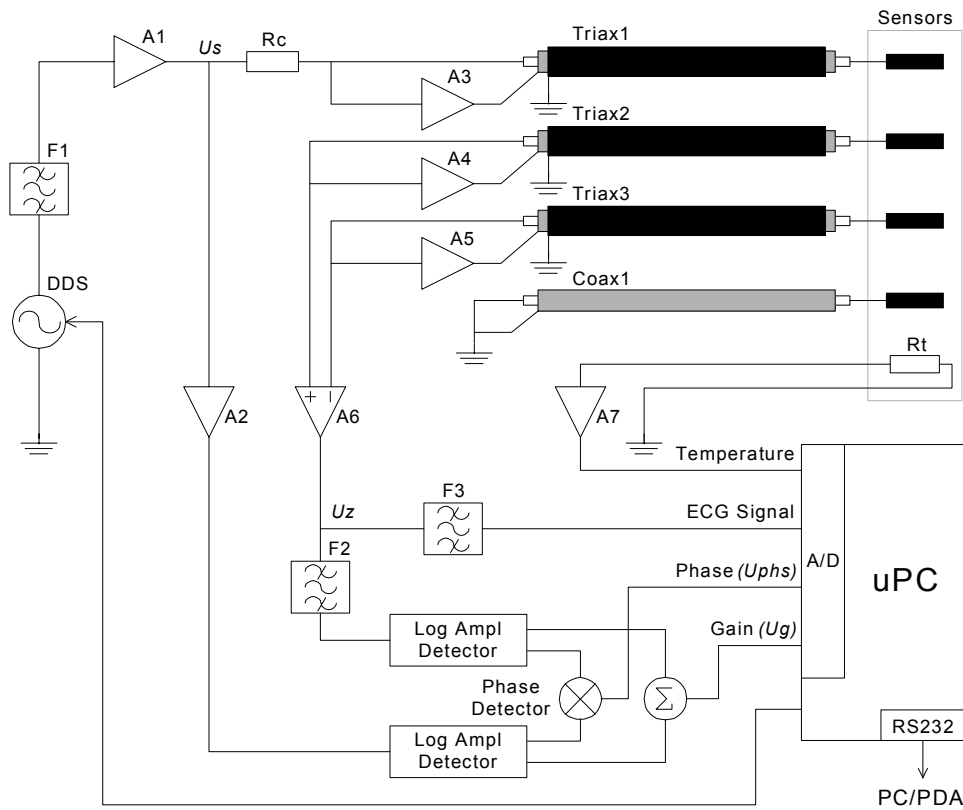


Figure 4. Block diagram of the HCV interface electronics.

Figure 4 shows the block diagram of the interface electronics. It is battery-powered device using 3.7 V Li-Ion cell. Internal memory collects the measured data, which on later stage is transferred to a PDA or PC for further processing. The RS232 connection is optically decoupled for safety reasons.

An excitation signal is generated by a direct digital synthesizer (DDS). Five discrete frequencies, 20 kHz , 200 kHz , 400 kHz , 600 kHz , and 1.2 MHz , are applied consecutively in the time. The excitation signal is filtered by F1, buffered by A1 and applied to the “high-potential” excitation electrode via clamp resistor R_c . The “low-potential” excitation electrode is connected to ground via decoupling capacitor (not shown in Fig. 4). Stray capacitance of 75 pF can be measured with each of the cables that connect the sensors to the electronics. Therefore, active guarding is applied in order to avoid phase and gain errors (A3, A4, A5). Additionally, third, grounded shield prevents emission or penetration of undesired signals.

High input-impedance differential amplifier (A6) senses the voltage, U_z , between the measurement electrodes. This signal is rather complex due to the presence of ECG component. Figure 5 shows the cardiac conduction system. The tip of the catheter is located inside the right atrium, between the sinoatrial node (SAN) and the atrioventricular node (AVN). Consequently, the measured signal is a mixture of weak impedance and strong ECG signals. The ECG component covers the frequency range from 0.5 Hz to 250 Hz, while the lowest impedance-signal frequency is 20 kHz. Two band-pass filters F2 and F3 ensure proper separation of the ECG and impedance signals.

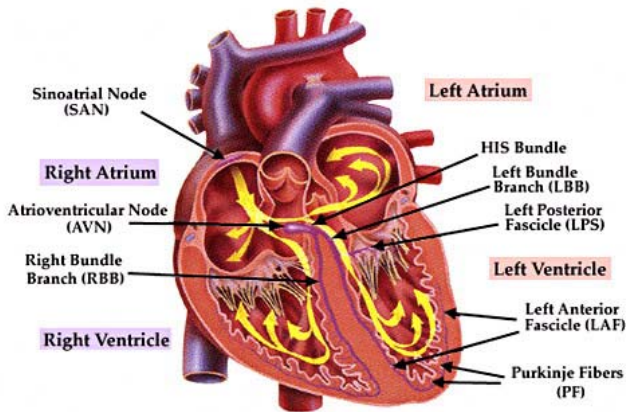


Figure 5. Cardiac conduction system diagram.

Already filtered, the impedance signal is then compared with the source signal U_s by a phase gain analyzer and Z_b is calculated accordingly [7, 8].

3. EXPERIMENTAL RESULTS

Swine and sheep are known to have cardiovascular system similar to this of human, therefore these are used regularly during in-vivo experiments. Three animal trials have been performed with two swine and two sheep. The aim of the procedure was to measure Ht and viscosity in-vivo by means of R_p and C_m measurements. Separately, in-vitro experiments in human blood were performed for validation of the in-vivo results.

Change in Ht and viscosity was induced by hemodilution and blood temperature variation between 27 °C and 38 °C. Heart-lung machine was connected through surgery with the sheep and open-heart surgery with the swine in order to speed up the measurement procedures. *Vena jugularis* in the neck is used to introduce the catheter, which is then advanced to the right atrium through *vena cava superior* (Fig. 6).



Figure 6. Animal experiment with sheep.

Figure 7 shows the measured R_p , C_m and ECG in-vivo in a sheep. It is assumed that the effect of the atrial wall over the measured impedance is negligible during the diastole phase of the cardiac cycle when the ventricles are relaxed and the right atrium is wide open. This is during the so-called T -top (lowest ECG extremum).

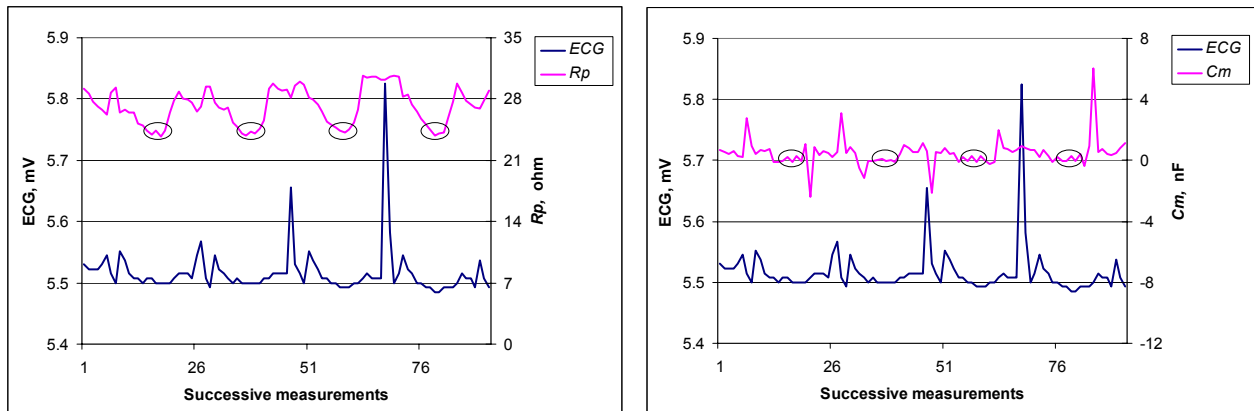


Figure 7. R_p , C_m and ECG, measured in-vivo.

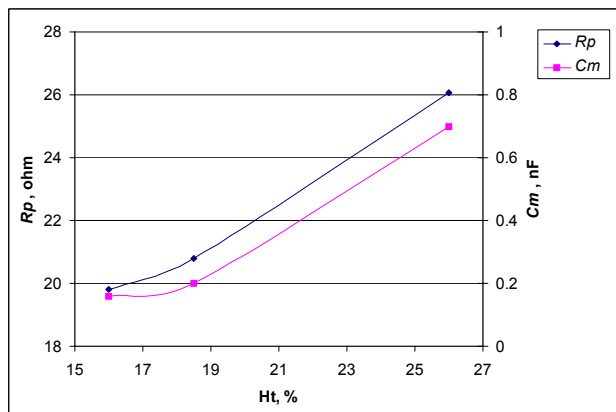


Figure 8. In-vivo measurements of R_p and C_m versus Ht.

As mentioned already, hemodilution is applied for inducing Ht and viscosity variations. Two sheep were administered with Voluven as R_p and C_m were measured versus the resultant Ht (Fig. 8). Good match between the measured in-vivo R_p and C_m and previously obtained in-vitro results has been found. However, these results are considered to be irrelevant, due to extremely low viscosity and Ht (about 20%) measured with the selected animals. In humans the normal hematocrit is about 40-42% in men and 39-41% in women. Furthermore, these sheep had smaller heart then expected since they were young and had a weight of 40 kg only. It was also impossible to perform proper experiments in presence of a heart-lung machine, which diverts partly the blood flow through the heart and reduces even further its size. In humans with a 2 times higher weight the heart volume will be twice as much.



Figure 9. Endothelium bio layer.

It is assumed that the obtained results are strongly affected by the presence of endothelium bio layer that was discovered on the electrodes (Fig. 9). The lack of sterilization is likely to be the main reason for the fast growing bio layer. This is to be seriously investigated during future trials when the stainless steel electrodes will be replaced by platinum electrodes, considered to be more biocompatible.

4. CONCLUSIONS

A new technology to determine hematocrit and blood viscosity by direct impedance measurement in the right atrium of the heart is developed. It enables fast clinical examination of patients with high thrombotic and heart infarct risks. Dedicated measurement device is created for online monitoring of patient's blood properties, ECG and temperature using specially designed central venous catheter. Various in-vitro and in-vivo trials have been performed to test the functionality and safety of the new device as well as to verify the accuracy and repeatability of the measured parameters. Despite the biocompatibility problems, e.g. presence of bio layer, it is assumed that this new technique may soon be applied for on-line detection of red blood cell aggregation tendency and as such be used as a reliable inflammation marker.

5. REFERENCES

- [1] G.A.M. Pop, W.J. Hop, et al., *Blood electrical impedance closely matches whole blood viscosity as parameter of hemorheology and inflammation*, Applied Rheology, Vol 13, Issue 6.
- [2] T. X. Zhao, B. Jacobson, *Quantitative correlations among fibrinogen concentration, sedimentation rate and electrical impedance of blood*, Medical & Biological Engineering & Computing, May 1997.
- [3] R. Pething: *Dielectric properties of body tissues*. Clin. Phys. Physiol. Meas., 1987, Vol. 8, Suppl. A, UK.
- [4] L. A. Geddes, L. E. Baker, *Principles in applied biomedical instrumentation*, A Wiley-interscience publication 1989.
- [5] H. P. Schwan, *Electrode polarization impedance and measurements in biological materials*. The more school of electrical engineering, Electromedical division, University of Pennsylvania, Philadelphia, 1988, Pennsylvania.
- [6] Hugo Fricke and Sterne Morse, *The electric resistance and capacity of blood for frequencies between 800 and 4½ million cycles*, The Journal of General Physiology, Vol 9, 153-167, 1925.
- [7] Blagoy P. Iliev and Gerard C. M. Meijer, *An impedance-measurements system for electrical characterization of rockwool substrates*, Sicon/04 - Sensors for Industry Conference New Orleans, Louisiana, USA, 27-29 January, 2004.
- [8] Tian-xian Zhao, Bertil Jacobson and Tommy Ribbe, *Triple-frequency method for measuring blood impedance*. Physiol. Meas., Vol. 14, 145-156, 1993, UK.