Tetrapolar Impedance Plethysmograph for assessing peripheral venous congestion

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Abstract. It has been suggested that venous congestion would be an independent and fundamental stimulus for the onset of decompensated cardiac heart failure. Early detection of congestion could be assessed by venous occlusion plethysmography. In this context, we propose to develop a tetrapolar impedance plethysmograph and method for evaluating the drain venous capacity after a 60sec cuff occlusion by analyzing changes in limb impedance. Occlusion maneuver avoids venous return; therefore, blood accumulates in limbs changing its impedance. The device comprises of a 50KHz stabilized current generator that provides a sinusoidal current of 2mA that flows through the limb to produce an amplitude modulated voltage which is appropriately amplified and filtered. Then, the signal is demodulated and stored using a sample and hold circuit. Finally, the basal impedance is separated from impedance variations due to volume changes by means of a suppression circuit. The whole plethysmograph has proven to be highly linear ($R^2 = 0.998$) while the current shows stability in repeated measurements with different loads (from 6 to 412 $\Omega$). Frequency response curve shows a typical low-pass pattern with a cut-off frequency of 7Hz. Finally, as an example, a temporary record of an occlusive maneuver in a healthy volunteer is presented.

1. Introduction
Impedance plethysmography is one of the tools to evaluate volume changes in a limb. Through the recording of tissue impedance, the peripheral circulation can be studied including both arterial and venous systems. It is based on the fact that the impedance of body segments reflects the filling state of the blood vessels contained [1].

Moreover, venous occlusion plethysmography (VOP) [2] is the most widely used method to perform limb’s blood circulation evaluation which has been used in a variety of conditions, i.e. during exercise [3], reactive hyperemia [4] and cardiac heart failure (CHF) [5]. The latter is characterized by abnormalities of left ventricular function and neurohormonal regulation, which is accompanied by dyspnea (breathlessness), fatigue, exercise intolerance, fluid retention and reduced longevity. Still
today, CHF is of great interest to medical researchers because of its implications in quality of life, morbidity, mortality and the associated costs of these, both economic and human [6].

Furthermore, the early vascular effects of CHF have not yet been fully elucidated; there is evidence from clinical trials that a large number of hospitalizations for decompensated CHF is produced due to symptoms and signs of venous congestion with varying degrees of severity [7-8]. A recently evaluated implantable device to monitor fluid accumulation in chest (congestion) -using measurements of intrathoracic impedance, OptiVol, Medtronic Inc- showed that it is possible to detect pulmonary congestion between 7 and 14 days before being triggered the patient’s decompensation [9].

Some research groups have postulated that body weight gain detected in patients with heart failure before hospitalization could be due to peripheral venous congestion with fluid retention in the lower limbs [10-11], and also, this process would occur before pulmonary congestion. Therefore, the detection of symptoms of venous congestion would predict decompensated heart failure.

To evaluate this hypothesis, our group proposes to assess changes in volume limbs by means of a based-impedance VOP system.

Finally, the purpose of this paper is to present the design of a tetrapolar impedance plethysmograph and a procedure to evaluate the limbs veins response when a sub-diastolic occlusion maneuver is applied.

2. Block diagram of a tetrapolar impedance plethysmograph

The most common method for measuring limbs impedance involves an ac constant current generator applied to the analyzed limb segment and measures the potential difference developed across the tissue [12]. In this case, a general-purpose tetrapolar impedance plethysmograph is designed including four main blocks showed in figure 1.

The first one is a constant current generator that injects, by means of two electrodes, E1 and E2, a stabilized alternating current in the biological element. This current produces -over the tissue- a voltage difference modulated in amplitude by the impedance changes. The voltage is picked up by another pair of electrodes, E3 and E4, placed between the electrodes E1 and E2. Tetrapolar electrode configuration reduces errors due to the nonlinear potential differences generated in the area near the injecting-electrodes observed in the bipolar configuration due to the electrode-tissue interface polarization impedance [12]. That amplitude-modulated signal is recorded and processed by the second block (figure 1), which includes of an instrumentation amplifier, a second order high-pass active filter and an inverting amplifier.

Third block is responsible for providing a continuous signal ($V_{DC}$) proportional to the potential difference obtained between E3 and E4. This is achieved with a full wave rectifier, an envelope detector and a second order low-pass active filter.

As mentioned previously, VOP is a method that, among other parameters, allows non-invasive measurement of volume changes in a segment of the limbs during an occlusive maneuvers. Distal to the recording site, a cuff is mounted on the limb. Before the veins are occluded through inflation of this cuff, the limb volume enclosed between the impedance plethysmograph inner electrodes, remains constant at rest. After occlusion, venous drain of the limb is suddenly stopped and only arterial inflow is maintained; thus, limb impedance shows the changes in total volume. So, limbs impedance ($Z_b$) has two components; the first, related to the tissues does not vary with time under identical conditions, is called basal impedance ($Z_{basal}$), and the second component ($\Delta Z$) is due to blood pulsations and changes in veins volume.

The equipment described in this work has been designed to measure changes in volume due to the accumulation of blood in limbs veins by means of impedance variations. In a first step, limbs of healthy volunteers will be evaluated and subsequently, the same assessment will be made in subjects with acute and chronic venous diseases, especially peripheral venous congestion. In this context, despite the plethysmograph can measure the variation due to blood flow, it is not used.

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Third block produces an output proportional to \((Z_{basal} + \Delta Z)\) but the useful information in limbs is frequently \(\Delta Z\). Furthermore, usually \(\Delta Z << Z_{basal}\).

In order to obtain \(\Delta Z\) variations, a fourth block is designed which is responsible for recording and storing the voltage value corresponding to the basal impedance \((V_{basal})\) and re-inject it into a subtracting circuit (figure 1). The potential obtained results,

\[
V_{\Delta Z} = V_{DC} - V_{basal}
\]

\[\text{(1)}\]

**Figure 1.** Plethysmograph General Diagram.

3. **Design of the tetrapolar impedance plethysmograph**

A Wien-Bridge oscillator with controlled amplitude generates a 50 KHz sine wave oscillation (carrier). The amplitude control is achieved by introducing two diodes in the oscillator’s negative feedback loop (figure 2). Additionally, its output is filtered using a band-pass filter -with a center frequency of 50 KHz and a bandwidth of 6 KHz-, in order to remove any carrier harmonic component.
Figure 2. Wien-Bridge oscillator.

Figure 3 presents a constant current source that converts voltage signal –delivered by oscillator plus band-pass filter – to an ac current with an intensity of 2 mA. The carrier’s specifications (50 KHz and 2 mA) are used to avoid current perception and to achieve adequate signal-noise relation, respectively [13]. Furthermore, the current, controlled by the voltage signal from the previous stage, is given by,

\[ i = \frac{V_{osc}}{R_5} \]  \hspace{1cm} (2)

where resistance \( R_5 \) defines the current flowing through the tissue to ground through the resistance \( R_{control} \) (see figure 3).

Figure 3. Constant Current Source.

The current source circuit has the ability of injecting a highly stabilized current into a load with a ground terminal, independently of the load value. In fact, this is possible if the oscillator amplitude remains unchanged when load varies. Then, the current generator performance depends on the oscillator performance.

When the current \( i \) flows through the tissue, a voltage obtained between electrodes E3 and E4 results proportional to the impedance \( Z_b \). This voltage is picked up by an instrumentation amplifier (AD620, Analog Devices) which has high input impedance and high common mode rejection ratio (CMRR) features (figure 4). The gain of this amplifier was set to 3 times.
In order to eliminate interferences due to electrodes movements and polarization, an active one-op-amp high-pass filter is coupled to the instrumentation amplifier. The filter has a cutoff frequency of 16 KHz which also provides a good filtering for line frequency.

Demodulation is achieved using a full wave rectifier, an envelope detector and active second-order low-pass filter with a cut-off frequency of 13 Hz (figure 5). This block provides an output voltage which is proportional to the biological tissue impedance.

AD620 input is an amplitude modulated signal where modulation is caused by the accumulation of blood in the limb veins when the occlusive maneuver was performed. These changes are very slow defining the cut-off frequency of the last filter (figure 5).

Figure 6 presents a sample and hold circuit (S/H) that stores $V_{basal}$ voltage. The capacitor C is designed to maintain the stored voltage during the occlusive maneuver, approximately 60 sec; so a circuit with a discharge time of 6000 sec was designed, thus minimizing the effect of the capacitive discharge on the output signal.
Finally, S/H output circuit is then subtracted from the total signal $V_{DC}$ obtaining $V_{IZ}$ which shows the changes in the impedance during the occlusive maneuver. Subtracting circuit output is then amplified by an inverting amplifier (not shown in figure 6) with a gain of 11 times.

4. Results

4.1. Bench testing

To evaluate the equipment performance, the linearity of the whole device, the stability of the current source and the frequency response of the third-stage low-pass filter were assessed. Furthermore, a calibration curve -output voltage as a function of the load impedance- was made.

4.1.1. Linearity. Knowing that the relationship between load impedance and output voltage define the success of an impedance plethysmograph, linearity is evaluated simulating biological tissue by means of different values commercial resistors ($Z_c$) and the output voltage $V_{DC}$ was measured using a Tektronix TSD 1001B digital oscilloscope. Results are shown in figure 7.

![Figure 7. Relationship between $V_{DC}$ and $Z_c$. Regression line equation is presented. $R^2$ - correlation coefficient.](image)

From figure 7, the relationship between these two variables is highly linear ($R^2=0.998$) where the equation relating these two variables is,

$$V_{DC} = 0.031Z_c - 1.157$$

From (3), limb impedance can be calculated.

4.1.2. Current Stability. The current delivered by the generator was evaluated varying its load (simulating biological tissue by resistances). Load values are varied between 6 to 412 $\Omega$. Current stability -flowing through the load- was evaluated by measuring the voltage difference ($V_{control}$) over a resistance ($R_{control}$), which had a fixed value (1500 $\Omega \pm 1\%$) (see figure 3). Results are shown in figure 8. Voltage is measured using a digital oscilloscope (Tektronix TSD 1001B).
Figure 8. Voltage difference over $R_{\text{control}}$ vs load impedance $Z_c$. Note that $Z_c$ are only resistances varying between 6 to 412 $\Omega$.

From figure 8, the equation of the line that best fits the distribution of data obtain is shown. In fact, the slope of this line is very small ($0.00012 \text{ V/}\Omega$) and indicates that the control voltage is practically independent of load impedance. The intercept gives an approximation of the average value obtained in the different measurements (2.95 V). Current value (designed) is 2 mA. So, calculated current is:

$$i = \frac{V_{\text{control}}}{R_{\text{control}}} = \frac{2.95976 \text{ V}}{1500 \Omega} = 1.97 \text{ mA} \quad (4)$$

4.1.3. Third block’s low-pass filter response. Presented in figure 1, this block defines the frequency response of the equipment output. A voltage signal generator (INSTEK GFG-8215A) is connected directly to the filter input varying the frequency between 0.05 to 2000 Hz, approximately. Input and output signals were recorded with a digital oscilloscope (Tektronix TDS 1001B). From these data, gain ($A_v$), in decibels, was calculated. Figure 9 presents these results.

The filter has a cut-off frequency of 7 Hz. Clearly, 50 KHz carrier signal suffers an attenuation of about 70dB. Although the filter’s cutoff frequency was calculated at 13 Hz, the actual response still fulfills our expectations.
4.1.4. **Calibration curve.** It assesses the performance of the whole plethysmograph plotting the output voltage $V_o$ (fourth block, figure 1) versus resistances $Z_c$ [Ω] placed instead the limb impedance. More, biological tissue is simulated with a 500 Ω trimpot (multi-turn variable resistor) where 100 Ω basal impedance is seted. Voltage corresponding to this basal impedance is stored by the sample and hold circuit (see figure 6). Besides, changes in limb volume are simulated by means of small incremental resistances of 0.5 Ω that increases up to a total increment of 5 Ω. Finally, output voltage $V_o$ is recorded with a digital oscilloscope (Tektronix TSD 1001B) (figure 10).

![Figure 10. Output voltage (Block 4 in figure 1) vs load impedance $Z_c$.](image)

From figure 10, the calibration curve results in highly linear response ($R^2=0.998$) where the slope indicates the voltage gain of the whole system. This gain allows us to discriminate small increases in biological tissue impedance $\Delta Z$ during the occlusive maneuver.

4.2. **Experimental test**

To evaluate the plethysmograph performance, impedance measurements are made on the upper limbs of healthy volunteers. The protocol used consist, first, in placing a cuff on the patient’s arm, then, connect the four electrodes in the middle segment of the volunteer’s forearm, so that the recording electrodes (E3 and E4) are placed between the current injection electrodes (E1 and E2) (see figure 3 for details). Type-electrocardiographic disposable electrodes (3M) are used.

The procedure for VOP evaluation includes the following steps: 1- the subject is at rest for 30 sec and then, basal impedance is registered, 2- occlusive cuff is rapidly inflated to a pressure of 50 mmHg causing a forearm venous occlusion during 60 sec and 3- the cuff pressure is quickly released and changes in voltage output are recorded for 30 sec. All process is registered as a function of time with a digital oscilloscope (Tektronix TSD 1001B).

![Figure 11. Changes in plethysmographic signal during a venous occlusion maneuver in a 23-years old healthy volunteer.](image)
Throughout the maneuver, the patient must remain at rest avoiding any movement that might interfere with measurement. Figure 11 presents the time varying signal obtained during VOP procedure.

Figure 11 shows a pre-occlusion stage with an approximately constant impedance value, an suddenly increase of the output signal after venous occlusion and finally, a stage of decline that occurs with the occlusion release. Clearly, occlusion produces an accumulation of blood in the forearm’s venous system; the ratio of rise gradually decreases until the curve reaches a plateau that indicates the maximum venous blood capacity. When the cuff is released, the time-varying output voltage decreases and its shape depends on the draining venous capacity returning near to the basal level prior occlusion.

5. Discussion and Conclusion
The developed impedance plethysmograph complies with previously proposed specifications. The current source is stable and independent of the load, thus fulfilling an essential feature for this device.

In healthy subject measurements, impedance changes due to accumulation of blood in forearm veins were clearly observed. Despite having made measurements in several subjects, these records are not yet sufficient to assess repeatability. Our group is currently working on it. The electrode type and positioning during experimental measurements became an important factor to control in order to obtain repeatable records. In this regard, a new custom-made array of electrodes will be tested in a near future.

Although this device was preliminary evaluated only in upper limbs, it has shown to be capable of recording temporal changes of limb impedance. However, to prove that the device is capable of measuring peripheral venous congestion in temporal evolution of decompensated cardiac heart failure, lower limb measurements will be required in the near future in healthy subjects as well as in patients with peripheral venous congestion.

As future prospects, our research group expects to calibrate the device with a plethysmograph based on a closed chamber pressure measurement, and finally, determine whether it can predict future decompensation in patients with CHF as a warning prevention system.

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References
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