25 YEARS OF IMPEDANCE PLETHYSMOGRAPHY

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In the year 1978, exactly 25 years ago, the first Impedance Plethysmograph (IPG) System, developed at Electronics Division, BARC, was taken to Department of Surgery, Seth G.S. Medical College & K.E.M. Hospital and Department of Medicine, Grant Medical College & J.J. Hospital, Mumbai, for the assessment of central and peripheral blood flow in the human body. The literal meaning of Impedance Plethysmography is “Recording of instantaneous volume (of an object) by measurement of electrical impedance”. It has, however become a synonym for “indirect assessment of blood volume changes in any part of the body from changes in the electrical impedance of the body segment”.

A typical impedance measuring system is comprised of a sine-wave oscillator followed by voltage to current converter. This converter outputs sinusoidal current of constant amplitude (1-10 mA) which can be passed though the body segment with the help of two band electrodes called the current electrodes I1 and I2. Voltage signal developed along the current path is sensed with the help of another pair of
electrodes called the sensing electrodes or voltage electrodes V1 and V2 as shown in Fig. 1.

The amplitude of the signal thus obtained is directly proportional to the electrical impedance of the body segment between the electrodes V1 and V2. The amplification and detection of this signal yields an output signal, which is proportional to instantaneous impedance $Z$ of the body segment. Initial value of the impedance, also known as basal impedance $Z_0$ is obtained from a sample and hold circuit and is numerically displayed on the panel.

Small changes in the impedance of the body segment caused by physiological processes like blood circulation, respiration etc, are obtained by subtracting the initial value of the impedance from the instantaneous impedance and is called the $\Delta Z(t)$ waveform. The $Z$ is also differentiated with respect to time to get the rate of change of impedance or the $dZ/dt$ waveform. By convention $-\Delta Z(t)$ and $-dZ/dt$ are recorded on a strip chart recorder to relate these waveforms with blood volume changes directly and are colloquially called $\Delta Z(t)$ and $dZ/dt$ waveforms.

Since $\Delta Z(t)$ and $dZ/dt$ are produced by the physiological processes, it is possible to extract the changes produced by one particular process by either suppressing the other process or by signal processing techniques. For example to extract the signal produced by blood circulation, the subject under investigation can be instructed to hold his breath. On the other hand a low pass filter can suppress the changes caused by blood circulation and give the changes produced by respiration. Nyboer's equation, derived from parallel conductor theory, relates the blood volume changes ($\Delta V$) with the changes in electrical impedance ($\Delta Z$) as follows (Nyboer J. 1960):

$$\Delta V = \rho_b \frac{L^2}{Z_0^2} \Delta Z$$

where $\rho_b$ is the resistivity of blood in ohm-cm, L is the length between sensing electrodes and $Z_0$ is the gross electrical impedance and the body segment.

This equation is modified appropriately to obtain stroke volume/cardiac output from $dZ/dt$ waveform (Kubicek et al 1966) and peripheral blood flow from $\Delta Z$ waveform with the help of venous occlusion principle (Kubicek et al 1974). With joint efforts of BARC and KEM Hospital, a new method for estimating peripheral blood flow from $dZ/dt$ waveform was developed. This method was not only simple but also yielded peripheral blood flow in real time in several segments of the limb, unlike systems available from abroad (Parulkar et al 1981). With this new method, blood flow index (BFI), differential pulse arrival time (DPAT) and pulse termination time (PTT) could be estimated in different segments of the limb, such as, upper arm, elbow, forearm and wrist in the upper extremity and upper thigh, knee, calf and ankle in the lower extremity, from the basal impedance value and $dZ/dt$ waveform.
recorded from the respective segment. Also coefficient of venous stasis (CVS) can be estimated by ratio of BFI in elevated position and that in supine position of the limb. Venous capacitance and maximum venous outflow can be estimated from $\Delta Z(t)$ waveform using venous occlusion principle for detecting diseases of the veins.

Extensive clinical trials on 100 normal subjects and 10,000 patients with peripheral vascular occlusive diseases at KEM Hospital and J.J. Hospital during 1978 to 1990 and comparison of IPG observations with angiography observations in more than 500 subjects revealed the sensitivity and specificity of the indigenously developed technique to be 96% and 98% for the diagnosis of peripheral arterial occlusive disease (Jindal et al 1990 (a)) and more than 80% for the diagnosis of deep vein thrombosis (Jindal et al 1990 (b)). Typical data is shown in Figs 2 and 3.

Fig. 2: ICVG waveforms in a patient (RKP-30-M) with femoral artery occlusion in the left leg. The amplitude of the waveform on right side gives normal appearance. Left thigh shows a marginal decrease in the amplitude of the waveform, which becomes moderately lower at knee level and markedly lower at calf and ankle levels. The BFI and DPAT values in this patient are as follows:

<table>
<thead>
<tr>
<th>Location</th>
<th>Right Side</th>
<th></th>
<th>Left side</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>BFI</td>
<td>DPAT (ms)</td>
<td>BFI</td>
</tr>
<tr>
<td>Thigh</td>
<td>1.48</td>
<td>70</td>
<td>1.13</td>
</tr>
<tr>
<td>Knee</td>
<td>2.12</td>
<td>50</td>
<td>0.85</td>
</tr>
<tr>
<td>Calf</td>
<td>1.64</td>
<td>-</td>
<td>0.29</td>
</tr>
<tr>
<td>Ankle</td>
<td>1.68</td>
<td>40</td>
<td>0.23</td>
</tr>
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</table>
All the BFI values in the right leg give normal appearance. Though DPAT at thigh is very marginally decreased and that at knee is very marginally increased, in view of normal BFI values, right leg is considered normal and minor changes in DPAT are attributed to measurement error. In the left leg there is marginal decrease in BFI at thigh level and moderate decrease at knee level with increase in DPAT at knee level, thus indicating an occlusion at iliac or femoral level. Since the decrease in BFI and increase in DPAT at knee is smaller in this case as compared to that of figure 5.6, the occlusion is more likely to be in the femoral artery than the iliac artery. Below the knee there is marked decrease in the value of BFI and increase in DPAT at ankle level indicating a further block at calf level with few collaterals.

Aortogram in this patient has shown left femoral artery to be narrow and irregular, profunda femoris to be markedly dilated and complete occlusion of the superficial femoral artery. Distal part of the femoral, popliteal and leg branches are not seen to be opacified. This data illustrates that in certain cases aortography is not in a position to give information about post-occlusion blocks, which is well detected by impedance cardiovasography.

![Image](image_url)

**Fig. 3: ICV G and OIP observations in a patient (RA-32-M) with pain and swelling in both the legs. The presentation of the waveforms a similar to that of figure 5.11. The amplitude of the waveforms is seen to increase significantly on elevation of the legs at all the locations indicating varicosity of the veins. Amplitude of the OIP waveform on both the sides appear to be within normal range with mild decrease in the descent of the curve. The values of ICV G and OIP parameter in this case are given in following table. BFI is seen to be reduced moderately at all the locations in both the legs which increases appreciably on elevation of the legs giving rise to higher values of coefficient of venous stasis. These observations suggest secondary varicosity in both the legs. OIP observations show normal values of venous capacitance. There is a slight decrease noted in the values of MVO in both the legs. ICV G and OIP observations together therefore, suggest chronic deep vein thrombosis in both the legs. Venography in the patient has shown patchy opacification of deep veins and muscular veins of the calf in both the legs. Proximal portion of popliteal vein, superficial femoral vein, and external iliac vein are seen to be inadequately opacified bilaterally. Secondary varicosity of great and short sapaneous veins has been observed in both the legs. These observations are thus in full agreement with ICV G diagnosis.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Right Leg</th>
<th>Left Leg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Knee</td>
<td>Calf</td>
</tr>
<tr>
<td>Zo</td>
<td>49.5</td>
<td>51.0</td>
</tr>
<tr>
<td>BFI(s)</td>
<td>0.73</td>
<td>0.89</td>
</tr>
<tr>
<td>BFI(e)</td>
<td>1.56</td>
<td>1.31</td>
</tr>
<tr>
<td>CVs</td>
<td>2.13</td>
<td>1.47</td>
</tr>
<tr>
<td>PTT</td>
<td>480</td>
<td>490</td>
</tr>
<tr>
<td>VC</td>
<td>-----</td>
<td>0.80</td>
</tr>
<tr>
<td>MVO</td>
<td>-----</td>
<td>0.10</td>
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The technique has undergone several renovations during the past 25 years such as development of microprocessor based impedance plethysmograph system, introduction of simple and reliable calibration for \( \frac{dZ}{dt} \) waveform (Jindal et al., 1985). Correction of formula for estimating peripheral blood flow (Jindal et al., 1994), introduction of normalised \( \frac{dZ}{dt} \) waveform for easy assessment of peripheral blood flow (Jagruti et al. 2000) and development of PC-based impedance cardiovasograph system (Jindal et al., 2001).

The microprocessor based impedance plethysmograph system employed ensemble averaging technique to minimize respiratory artifacts, external pick up and internal noise of the system. The patient did not have to hold his breath during investigation as the respiratory artifacts were taken care of. The procedure thus became very simple and user/patient friendly. The technical know-how of this system was transferred in 1989 through Notional Research & Development Corporation.

![Diagram of the system](image-url)
Fig. 4 shows schematic block diagram and photograph of the latest PC-based impedance cardiovasograph developed at BARC. It is comprised of an EPROM driven sine-wave current generator which passes the user selectable sine-wave current of constant amplitude at 50 KHz frequency through the body segment in patient mode with the help of isolation transformer and a relay. The same generator passes modulated sine-wave current (1% amplitude modulation with triangular wave at 1 Hz frequency) through the calibration network of fixed resistance values in calibration mode (Jindal et al 1985). The voltage signal developed along the current path is sensed with the help of sensing electrodes and amplified using a differential amplifier. The high Q band-pass filter removes the superimposed noise and the output of the filter is rectified, filtered and buffered to obtain a voltage signal Z, which is proportional to the instantaneous electrical impedance of the body segment under investigation.

The Z signal is used to obtain \( \Delta Z(t) \) signal with the help of a differential amplifier. The inverting input of this amplifier is fed by the Z signal and the non-inverting input is fed by the Zo signal, obtained with the help of 12-bit DAC from PC, so as to obtain \( \Delta Z(t) \) at the output. Z is also differentiated with the help of an electronic differentiator to obtain dZ/dt signal. For obtaining normalized dZ/dt signal, i.e. the dZ/dt signal normalized with respect to the impedance value \( \text{NdZ}/dt \), log Z is obtained with the help of a log amplifier, which is subsequently differentiated by using another electronic differentiator. \( \Delta Z(t) \), dZ/dt and NdZ/dt signals are then multiplexed with the help of an analog multiplexer. Either of these waveforms can be selected at the output by the operator through the user interface panel. The multiplexed impedance signal is filtered with the help of a 2nd order low pass filter having a cut off at 40 Hz for smoothening the waveform. The output of the filter is amplified with a programmable gain amplifier implemented by using a multiplying DAC. The amplified output is given to dual analog switch which gives Z signal at the output during the sync pulse and function of Z i.e. \( \Delta Z(t) \), dZ/dt or NdZ/dt during rest of the cardiac period. The multiplexed output from the analog switch is connected to a 12 bit ADC for digitization and to be read by personal computer, through interface unit.

The isolated ECG amplifier senses the ECG voltages from the body surface and amplifies by a gain of 60 dB. The output of this amplifier is given to an adaptable threshold R-wave detector and a multiplexer for giving the synchronization pulse to be used by PC for time sequencing the impedance data. A spike, synchronous with the negative phase of the triangular wave, is used to generate the sync pulse in place of ECG in the calibration mode, and is multiplexed with the ECG signal.

Fig. 5 shows typical user interface panel for IPG investigation. It provides facility to enter personal information of the patient, select the desired investigation, acquire data from the patient or load/display/print the data of a patient acquired earlier. On selecting the investigation, the relevant list of leads appears in the list box, to aid the user. At the end of data acquisition, parameters such as BFI, PAT, PTT etc. are automatically computed and displayed below the graph. For specific application of continuous cardiac output monitoring, the system has been simplified into a small module, called Cardiac Output Monitor (COM). Fig. 6 shows typical user interface panel for COM. The know-how of both the units has been transferred to Larsen & Toubro Ltd., in 2000 for mass production. The clinical applications of impedance plethysmography do not end with measurement of central and peripheral blood flow but more important applications are in advance stages of development at several institutes. For instance, the fluctuations in peripheral blood flow or cardiac output are being explored to study the effect of different diseases on the autonomous nervous system (ANS). In this application, continuous IPG signal is recorded from a body segment for a period of five minutes. BFI values
are then obtained as a function of time from this signal and interpolated to get equi-spaced values. Fourier transform of this time series then gives the periodicity with which the fluctuations are taking place. Fig. 7 shows typical blood flow fluctuations in time and frequency domain obtained from a normal subject. The peak at 0.012 Hz. represents activity of thermo-regulation/baro-receptor reflex/sympathetic nervous system and those at 0.189 Hz. and 0.236 Hz. represent activity of parasympathetic nervous system and respiration, respectively (Deepak et al 1996).
The Medical Analyzer system developed at BARC is the continuation of the work carried out during past 25 years, for studying the activity of ANS under the influence of different diseases (Jindal et al. 2003). The unique feature of this system is that it yields heart rate variability, respiration rate variability, cardiac output variability and stroke volume variability/peripheral blood flow variability (Left/Right) from a single data acquisition from the subject which is not feasible with any other commercial instruments. Preliminary study carried out on 300 subjects show that ANS activity gets selectively modified which is specific for the disease. To converge this application into a diagnostic tool, data collection on large no. of subjects is in progress.

The workshop on “Non-invasive Measurement of Peripheral Blood Flow and Cardiac Output” organised at All India Institute of Medical Sciences, New Delhi, during April 15-17, 2003, witnessed an overwhelming response from the medical community from all over the country. Two units each of impedance cardiovasograph and cardiac output monitor from Electronics Division, BARC, were used to give live demonstration on peripheral blood flow estimation and cardiac output monitoring and

Fig. 7 Typical peripheral blood flow fluctuations in time (lower) and frequency domain (upper) in the right wrist of a normal subject. Presence of multiple peaks indicates more noise in the power spectral density; however, two peaks are prominently centered around 0.012 and 0.236 Hz. The mid-frequency peak at 0.189 Hz is smaller in magnitude.

Fig. 8: Second panel discussion sitting from left to right: Dr. Alaka K. Desphande, JJ Hospital, Mumbai, Prof. Vinod Kumar, Electrical Engineering, IIT Roorkee, Prof. Sheh Anand, Biomedical engineering, IIT, Delhi, Dr. K. Mohandas, Director, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram, Prof. A. S. Paintal, V.P. Chest Institute, Delhi, Dr. I. B. Singh, Advisor, Instrumumentation and development, Deptt. of Science and Technology, Delhi, Dr. G. D. Jindal, Electronics Division, BARC, Mumbai and Dr. Ashima Anand, V. P. Chest Institute, Delhi, Dr. Madhuri Behari, Neurology, AIIMS, Dr. K. K. Deepak, Addl. Prof, Deptt. of Physiology, AIIMS deliberating on “ Developing our own Electro-diagnostic Techniques”.
provide hands-on experience to all the participants in the workshop.

Panel discussion on ‘Rheography by Impedance Plethysmography in Medicine’, moderated by Dr. P.K. Banerjee, Director, Defence Institute of Physiology and Allied Sciences (DIPAS), Delhi, concluded with the following remarks:

“Let us congratulate Bhabha Atomic Research Centre for bringing out state of the art technology on Impedance Plethysmography. It is probably the first indigenous technology to come in final usable form. The use of the same in continuous monitoring of cardiac output is beyond doubt. As far as its applications in the diagnosis of peripheral vascular occlusive diseases are concerned, BARC has conducted extensive studies on clinical validation in collaboration with KEM Hospital and J.J. Hospital, Mumbai. Their experience is more than satisfactory, as second block some times missed on arteriography is sensed by this technique and the information not available in Colour Doppler investigation on collateral circulation and distal arterial run off is readily provided by this technique. It is for the medical fraternity to come forward and carry out adequate trials to make it a routine clinical investigation”.

During the second panel discussion of the workshop on “Developing our own Electro-diagnostic Techniques”, moderated by Dr. K. Mohandas, Director, Sree Chitra Tirunal Institute for Medical Sciences & Technology (SCTIMST), Thiruvananthapuram, road map for the objective was shown. It was emphasized that there is need to establish institutions for drawing specification, issue certifications and regulate the products. Greater participation from industry and medical fraternity was also stressed. Also need for distinguishing basic research and import substitution programme and promotion of both was highlighted. Director, SCTIMST, also expressed his happiness on their proposed collaboration with BARC in the field of Biomedical Engineering.

References

