Design and Development of an IPG System Without an Occlusive Cuff to Detect Deep Vein Thrombosis

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Abstract. Deep Vein Thrombosis (DVT) is a condition that leads to the formation of blood clots in the deep veins. Swelling or pain inthe lower limb is a common symptom thatgenerally affects the deep veins in the leg. Pulmonary Embolism (PE) is the most dangerous complication of DVT. It occurs when blood clots migrate from the deep veins of the legs to the lungs. Various invasive and non-invasive methods can be utilized to detect DVT. Among them, Impedance Plethysmography is one of the non–invasive methods, which uses an occlusive cuff. This could cause separation of possible thrombus due to downstream venous pressure, resulting in PE. Hence, this paper aims to design and develop an Impedance Plethysmography (IPG) System without an occlusive cuff to detect DVT. Also, the proposedcost-effective systemaims to provide noise-free IPG signals. These signals will be further processed to identify the DVT through Matlab software.

The observations on subjects have shown an increasing impedance withreduced blood volume due to limb rise. However, the impedance decreases when the limb is returned to its resting position. While the limb is returned to its initial position, the subjects with DVT have a longer blood-filling timethan expected, especially for the affected leg. Moreover, the proposed methodology is validated with 30 subjects, and its efficacy is endorsed by calculating performance measures like sensitivity and specificity.

Keywords: Deep Vein Thrombosis · Impedance plethysmography · Occlusive cuff

1 Introduction

Intraluminal clotting is one of the most critical complications affecting the peripheral veins. The most frequent life-threatening peripheral vascular disease is Venous Thromboembolism (VTE), which is caused by the incorporation of DVT and PE conditions. DVT is the development of blood clots in the deep veins, most commonly in the legs. PE is a potentially fatal consequence of DVT. PEoccurs when a clot breaks (embolizes) and

B. Raj et al. (Eds.): ICETE 2023, AER 223, pp. 26–35, 2023.
https://doi.org/10.2991/978-94-6463-252-1_5

travels to the lungs or the coronary arteries. It is caused by a combination of two or three following conditions inclusive of slow blood flow through deep veins, the tendency for a person's blood to clot quickly, and irritation, inflammation, or injury to the vein's inner lining. The primary symptoms of DVT are a feeling of warmth on the affected leg, pain, swelling, soreness or cramping, and changes in skin color on the leg [1].

This paper is organized as follows. The literature survey is explained in Sect. 2, the methodology is described in Sect. 3, results and discussions are presented in Sect. 4, and finally, conclusions are drawn in Sect. 5.

2 Literature Survey

Various non-invasive techniques have been developed to detect and analyze DVT and PE. Impedance Plethysmography (IPG) is one of the techniques for measuring blood flow volume variations in various areas of the human body caused by the presence of blood clots. It is a non-invasive approach to identifying the blood clots in the arms or legs, which indicates the presence of DVT [2–3].

IPG is invented by Nyboer in 1939, and by the 1970s, various IPG devices are commercially available to diagnose DVT [4]. IPG measures the differences in bio-impedance between the electrodes implanted on the body surface [5–6]. IPG offers a good advantage compared to venography which is invasive and requires much skill [7–8].

Glew D et al. discussed that an unrestricted outflow of venous blood results in a rapid shift in impedance, but the obstruction in outflow affected by a DVT causes a more gradual change in impedance. For 30 suspected DVT participants, this technique had a sensitivity of 100% and a specificity of 61%. The authors concluded that IPG delivers erroneously positive results in people with no DVT diagnosed by venogram [9].

P.S. Wells et al. have analyzed the accuracy of clinical prediction in conjunction with IPG, especially in out-patients with conjecture DVT. However, IPG is substantially more sensitive but less specific [1].

Harriet Heijboer et al. investigated 494 patients with DVT using the cuff inflation IPG technique and 491 patients with DVT using the ultrasonography approach using venography as a reference. The author found that abnormal ultrasonography has a 94%positive predictive value whereas IPG has 83% positive predictive value. Serial ultrasonography is recommended over IPG in the diagnosis of DVT due to its better performance in detecting venous thrombosis [10].

Erika Pittela et al. proposed a method for assessing the functioning of the peripheral vascular system, emphasizing the lower limbs, that combines IPG and spectrometry. This technology uses an electrical bio-impedance sensor to detect changes in blood volume to monitor venous flow. Such measurements do not require the deployment of an occlusive cuff, which might result in the separation of possible thrombus due to downstream venous pressure; however, motion artifacts influence the measurement of DVT [11].

Russell Hull et al. studied 346 suspected DVT patients utilizing the Occlusive IPG technique and found that the approach had a 93% of sensitivity and a 97% of specificity when compared to a venogram. The test is unable to differentiate between DVT and other factors such as arterial insufficiency, and failure of muscle relaxation [12].

David R. Anderson et al. re-evaluated the accuracy of occlusive IPG for the detection of DVT using 384 consecutive out-patients and found that IPG has much-reduced sensitivity for proximal-vein thrombosis [13].

D K Swanson et al. designed a basic IPG system for vascular disease diagnostics that is accurate, economical, easy to use, and simple to manufacture [14].

Rogers, Frederick B., et al. discusses that venography is a gold standard technique and it is an invasive technique, not suitable as a screening study because it takes a long time and there are essential risks and impediment associated with its use [15].

Thomas, S. M., et al. concluded CT Scan has become the standard approach for evaluating DVT in suspected patients [16].

Heijboer., et al. concluded a series of ultrasound tests that may be performed for several days to further evaluate whether the blood clot is developing or a new blood clot is formed [17].

The research gaps identified from existing research works motivated us to develop an IPG system that is portable, low-cost, and has the best sensitivity and specificity, without using an occlusive cuff.

3 Methodology

The methodology was divided intothe design of electrodes, instrumentation for IPG, and measurement procedure. To summarize, the IPG system produces a continuous sinusoidal signal which passes through a limb segment via a pair of stimulating electrodes. A second pair of electrodesplaced nearby measures the potential caused by the current's interaction with the tissue components. Accordingly, an inexpensive instrument was developed, in which each electronic circuit on board performs specific tasks, such as wave generation, current injection, and sensing.

The Arduino Mega 2560 was used as a DAQ card, and the waveforms were captured and displayed using MATLAB software. The information was used for further investigation.

Electrodes play a significant part in signal detection, and hence they were designed appropriately. A measurement procedure was used to record the IPG signal. An explanation regarding the design of the electrodes is given below.

3.1 Design of Electrodes

Several types of electrodes are available in the market. Though some of these electrodes are suitable for detecting the IPG signal of subjects with different limb sizes, the electrodes need adjustability. The electrodes were designed to meet the needs of a wearable item. The following specifications were listedhere, (i) adaptability- to adapt to different body types, (ii) accurate and consistent signalcapturing- it must be equivalent to electrodes presently used in the prosthetic market, and (iii) lightweight nature - the weight of medical equipment is one of the reasons for prosthesis rejection.

The designed electrodes are composed an elastic textile structure consisting of 40% elastane, and 60% polyester, with a length of 30 cm to suit the required adjustability. A 12 cm touch fastener was utilized, which allows the same electrodes to be tested

on volunteers with forearm widths ranging from 21 to 30 cm. The designed electrode dimensions are round, with a diameter of 10 mm and length of 20 cm, and 99% pure silver plating.

The quadrupole design was used for the electrodes, with two stimulation electrodes (S1, S2) positioned outside, injecting the current and two measuring electrodes (M1, M2) placed internally concerning the predicted route of the current in the body. These measuring electrodesacquire the related potential variations caused by blood flow changes.

Instrumentation for IPG. The basic components of the IPG systemare shown in Fig. 1. It consists of three sections which include the stimulating section, the measuring section, and the interfacing section. The stimulating section includes an electronic oscillator circuit, voltage-to-current converter, and isolation circuit. The measuring section comprises a voltage follower, instrumentation amplifier, and filter circuit. The interfacing section (processing) consists of a level shifter, clamping circuit, analog-to-digital converter, serial communication, and Personal Computer (PC).

In the stimulating section, a sine wave oscillator is designed using a Wein Bridge Oscillator to generate a 16 kHz sinusoidal signal with an amplitude of 10 V peak to peak which is applied to voltage to current converter to convert it into 1 mA current signal. This current is applied to the affected leg using two stimulating electrodes (S1 and S2) through an isolation circuit. Here, isolation circuits will safeguard circuits, equipment, and people from shocks and short circuits, while producing accurate readings.

A measuring section consists of two measuring electrodes M1 and M2, which are applied to detect the changes in electrical potential generated due to blood flow. The corresponding potential is amplified through an instrumentation amplifier. The voltage follower circuit is designed for impedance matching between the skin, electrode, and instrumentation amplifier circuit. The amplified signal is applied to the high pass filter circuit, with a cut-off frequency of 0.01 Hz, and intended to remove the low-frequency noise signal. The output of this filter circuit is applied to the PC for additional processing through an interface unit.

The interfacing unit consists of a level shifter to shift the voltage levels from negative to positive at the output of the filter circuit and a clamping circuit to shift the voltage levels from 0 V to 3.3 V. With the assistance of the Data Acquisition (DAQ) system, Arduino Mega 2560 detectedanalog signals generated from clamping circuits and convert them to digital integers, which were processed by a computer with MATLAB software. Finally, MATLAB software saved digital data in a file for subsequent processing. The ratio of the measured signal voltage to the stimulated signal current's amplitude was used to determine the IPG signal's impedance. The developed IPG system is shown in Fig. 2.

Measurement Procedure. The measurements were taken using four designed strip electrodes attached to the affected area of the thigh using electrode gel. Electrode gel carries an electric current from the skin to a measuring instrument and vice versa. A 1mA alternating current with a frequency of 16 kHz was delivered through two stimulating electrodes (S1, S2), and a potential difference was monitored across measuring electrodes (M1, M2). For the impedance plethysmography test, there is no cuff on the patient thigh to measure the blood flow. Instead, the following steps were used to determine how much the impedance changes.

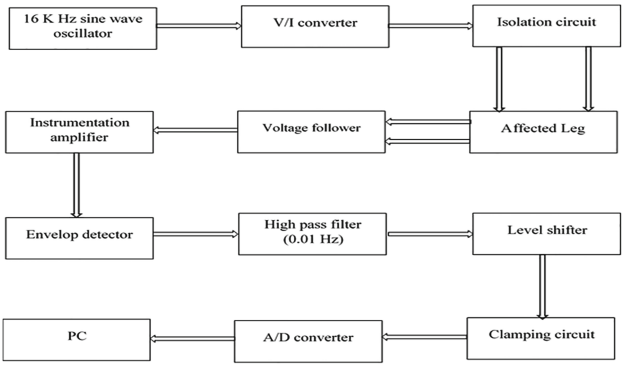

Fig. 1. Basic components of the IPG system.

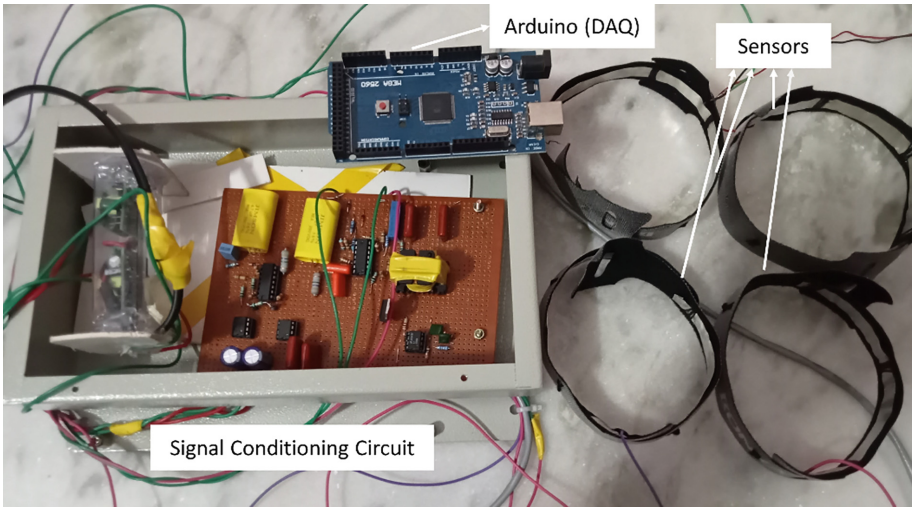

Fig. 2. Developed IPG system.

The subjects were instructed to lie in a supine position while the signal was acquired from the lower limb, maintaining the lower limbs straight and relaxed. The lower leg was manually lifted to a 45-degree angle after 5 s. The leg was then returned to its starting position after being held in this condition for 10 s. The data was collected during the process and supplied to the computer for the next step.

4 Results and Discussions

The designed IPG system was validated using 30 subjects. Subjects wereconsidered with the criteria of above the age of 20 years, male and female subjects including healthy, and DVT-affected persons. According to theseobservations on human subjects, limb elevation causes blood volume reductions, which were accompanied by an increase in

impedance, and a matching decrease in impedance as the limb was brought back to its restingposition. DVT-affected legs havemore blood filling time as shown in Figs. 4 and 6. The IPG waveforms of healthy subjects are shown in Figs. 3 and 5. And for DVT-affected subjects are shown in Figs. 3 and 5. CT-Scan was the reference standard for comparison.

The designed IPG system was applied to 30 subjects for testing purpose, and the results were compared with the CT-Scan test result for the same subjects. According to the comparison, the IPG test & CT Scan results for 22 of them were negative, while the results for 6 were positive. One individual had a negative IPG test but a positive CT Scan result, while another had a positive IPG test but a negative CT-Scan result. By considering the above discussion, a confusion matrix was designed and represented in Table 1.

Performance parameters like sensitivity and specificity of the designed IPG systemare calculated based on the confusion matrix values. Sensitivity is the proportion of true positives correctly detected by the system mentioned in Eq. (1), while specificity is the proportion of true negatives correctly detected by the system depicted in Eq. (2).

$$Sensitivity = \frac{TP}{(TP + FN)} \tag{1}$$

$$Specificity = \frac{TN}{(TN + FP)} \tag{2}$$

Substituting Table 1 values into Eqs. (1) & (2), gave specificity and sensitivity of 95.65% and 85.7% respectively.

The proposedIPG system's Pros and Cons are mentioned in Table 2 by comparing other methodologies.

Table 1. Confusion matrix

	CT-Scan test result-positive	CT-Scan test result-negative
IPG test positive	True Positive (6)	False Positive (1)
IPG test negative	False Negative (1)	True Negative (22)

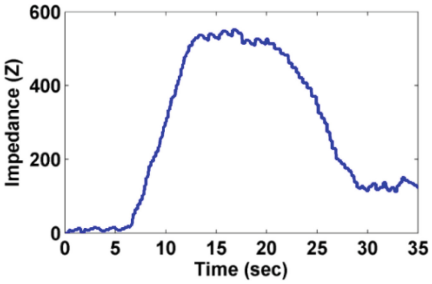

Fig. 3. IPG signal of healthy subject 1

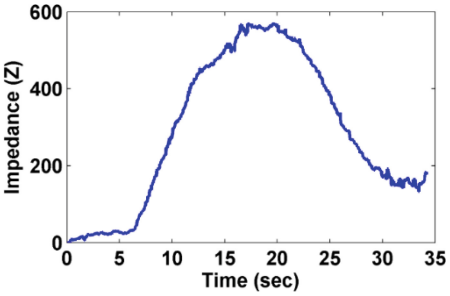

Fig. 4. IPG signal of DVT-affected subject 2

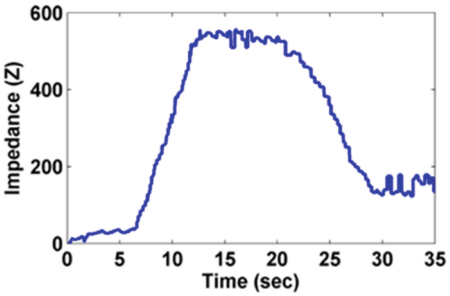

Fig. 5. IPG signal of healthy subject 3

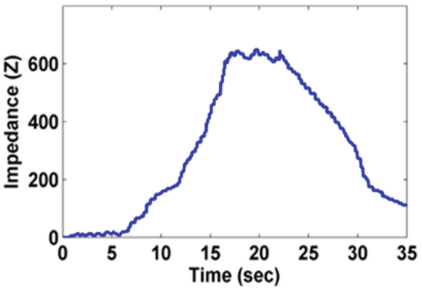

Fig. 6. IPG signal of DVT-affected subject 4

5 Conclusions & Future Scope

A portable, low-cost, and noise-free IPG system was developed, which has been used to measure DVT without using an occlusive cuff to overcome PE by venous pressure. The designed electrodes have the following properties of adjustability, lightness, and constant signal acquisition to pick proper signal variations. The IPG system is validated with 30 subjects, all above the age of 20 years, male and female, healthy and DVT affected showing a sensitivity of 85.7% and a specificity of 95.65%. In future work, the proposed IPG system can be validated with more subjects and will be used to detect other peripheral vascular diseases.

Table 2. The proposed IPG system's Pros and Cons by comparing other methodologies.

S.No	Methodology	Pros	Cons
1	Ultrasonography	Noninvasive, safe, sensitivity, and specificity 96% for diagnosing DVT.	Expensive, operator-dependent, non-portable, unavailability in the primary health center
2	Venography	It is the gold standard method. high sensitivity and specificity.	Invasive, painful, risk of an allergic reaction.
3	CT-Scan	Non Invasive, sensitivity and specificity 95% for diagnosing DVT	Costly, pelvic radiation, non-portable, and unavailability at the primary health center.
4	Impedance plethysmography using Occlusive cuff	Noninvasive, sensitivity and specificity 85% for diagnosing DVT, inexpensive.	Due to downstream venous pressure the chances of occurring Pulmonary Embolisms. More validation is required.
5	**Proposed system (Design and Development of an IPG system without an Occlusive cuff to detect Deep Vein Thrombosis)**	Noninvasive, inexpensive, portable, overcome PE by venous pressure due to occlusive cuff. Due to the low cost, the likelihood of availability in primary health centres is increased..	More validation is required.

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