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## Using photoplethysmography to assess for venous insufficiency and screen for deep vein thrombosis (DVT)

### A review of the literature on the use of photoplethysmography (PPG) as an assessment tool to identify the presence of venous insufficiency and in screening for DVT

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#### Plethysmography and PPG

Plethysmography is the term given to the recording of changes in limb size due to tissue fluid or pooled blood within the veins. This measurement can be undertaken in a variety of ways, fluid displacement, electrical impedance, electronic strain gauge, gravimetric methods and PPG<sup>1</sup>. Historically, the diagnosis of venous insufficiency was performed by invasive ambulatory venous pressure measurements (AVP), which has been described as the ideal diagnostic standard<sup>2,3</sup> or as the 'gold standard'<sup>4</sup>. Early investigations using infra-red radiation to identify fluctuations in dermal blood flow resulted in the introduction of PPG. Hertzman<sup>5</sup> described the method of measuring circulation through the skin using Photoelectric Plethysmography by relating the blood content of the skin to the amount of light reflected. AVP is a comparatively invasive technique, as it involves cannulation of the dorsal foot vein. It has been described as painful and cumbersome<sup>6</sup>, associated with complications such as bleeding or haematoma formation<sup>7</sup> and unsuitable for repeated use on the same patient or for screening purposes<sup>8</sup>. In contrast PPG is described as easy to undertake, without risk and user-friendly<sup>9</sup>. PPG has increased in popularity due to the ease and speed of the investigation; this method depends on the absorption of light by haemoglobin in the red cells. Increasingly this was developed to investigate the venous haemodynamics of the lower limb and was renamed light reflection

rheography (LRR). A light emitting diode is placed 10cm above the medial malleolus to measure the speed at which the capillary bed becomes filled with blood following calf muscle exercise, Fig 1. In the normal subject refill time may take between 25 and 45 seconds and a reduction in this refill time identifies degrees of venous insufficiency. More recently this equipment has been used to assess for the absence of DVT where a refill time of greater than 20 seconds would suggest that a DVT is highly unlikely,



Figure 1  
PPG sensor on leg during exercise

#### Using Photoplethysmography to identify venous insufficiency

Ineffective venous return from the lower legs leads to a condition of venous hypertension in the superficial venous system<sup>10,11,12</sup>, which frequently results in ulceration<sup>11</sup>. It has been reported that 1% of the adult population suffer from leg ulcers<sup>10</sup>, which has placed a large financial burden on the health service<sup>13</sup>. Since pioneering work at the Riverside Health Authority and Charing Cross

Hospital Vascular Services<sup>14</sup>, where effective methods of assessment and management of patients with venous leg ulcers were developed, nurses play a substantial role in caring for these patients. As the appropriate treatment for venous insufficiency is the application of compression therapy<sup>15</sup> it is of paramount importance that patients are screened for arterial disease. Failure to identify underlying arterial disease and the subsequent inappropriate use of compression therapy may result in tissue necrosis<sup>16</sup>. The Riverside assessment involved using Doppler Ultrasound, which has now been widely adopted to identify patients with arterial disease that require specialist management<sup>17</sup>. However, this does raise certain questions regarding the interpretation of the assessment, not least that the exclusion of arterial disease does not automatically indicate venous insufficiency<sup>18</sup>. Patient assessments currently rely on past medical history and clinical observations of the limb but in the absence of a clear clinical picture and visible trophic skin changes, venous insufficiency may prove difficult to diagnose if other techniques of investigation are not used. Another significant point is that the majority of services currently provided are for patients who have already gone on to develop ulceration. This would suggest a very reactive service and resources are needed to provide screening programmes where PPG could be used in order to identify individuals with venous insufficiency who may be more at risk of developing ulceration. Furthermore,

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this technique of investigation could be employed in screening for DVT, which is also a significant risk factor for the development of a venous hypertension. Fig 2.



Figure 2  
A combined Doppler and PPG system

### Photoplethysmography to screen for Deep Vein Thrombosis (DVT)

A thrombosis is the formation of a solid mass in the circulation, which has developed from the constituents of the blood<sup>19</sup>. A process of endothelium damage takes place, which triggers a cellular reaction and results in the formation of a haemostatic plug. Following this, fibrin is deposited and the plug is then replaced by fibrin. The development of the thrombus could have resulted from stasis, changes in vessel walls or hypercoagulability. DVT has been described as a common condition among the general population<sup>20</sup>. In its lesser form it may pass unnoticed, however in its major form causes severe illness with the possibility of a life threatening pulmonary embolism or rarely the development of a venous gangrene in the limb. A DVT may also lead to seemingly lesser problems with venous return of blood flow but if left untreated this will contribute significantly to the development of venous hypertension with subsequent ulceration. It is suggested that only 40% of patients with a DVT have any clinical signs of the disorder and detection by clinical means is reported as unreliable with suggestions that in 50% of cases it is incorrectly diagnosed<sup>21</sup> leading to unnecessary hospital admission.

Furthermore, false-positives occur in 30% of patients studied<sup>22</sup>. On the basis of this it would appear sensible to consider the benefits of PPG to screen for DVT, since claims have been made that this technology has a high negative predictive value. Prior to introducing this technology as an assessment tool to identify the presence of venous insufficiency and screen for DVT, it is important to review the supporting evidence. Therefore, a literature search was conducted and is reviewed in this paper. The review of the literature is divided into two sections: firstly looking at venous insufficiency, and secondly reviewing evidence to support its use in screening for DVT. PPG and LRR are used interchangeably throughout this paper. Fig 3.

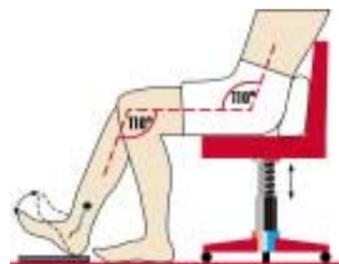


Figure 3  
Typical patient position

### PART 1 - Identifying venous disease using PPG

In 1979 Abramowitz et al<sup>6</sup> conducted a piece of research to compare PPG with the 'gold standard' of AVP to assess its ability to identify the presence of chronic venous insufficiency. This laboratory study used a sample of 25 patients with post-phlebitic syndrome, 14 with simple varicose veins and a control group of healthy volunteers. Sampling was purposive to reflect the disease being studied, however there was no information regarding informed consent or how ethical issues were addressed, which is important considering the

invasiveness of AVP. The results of the correlational analysis indicated a close relationship between PPG and AVP in determining normal and impaired venous functions of the legs. However, the small sample size and study setting would limit generalisation of the results. Similar studies followed where PPG was compared to AVP<sup>2,7,23,24,25</sup> but these also failed to include a large enough sample size. Furthermore, although evidence exists that venous reflux is more pronounced with age and that concomitant arterial disease may affect the venous refill time<sup>26</sup> only two studies appear to consider age as an important variable<sup>2,25</sup>. Even so in both these studies the age of the control group is below 60 years, this is the age at which it has been suggested that natural changes to the venous system may occur<sup>27</sup>. In spite of the limitations, in each of the studies the researchers suggested a close correlation between the two techniques could be demonstrated. As a result PPG became widely adopted within vascular and surgical departments as part of the routine assessment for lower leg venous function. Having established the value of PPG as an aid to diagnosis, or an alternative to AVP in determining the presence of venous insufficiency, further research concentrated on comparing the diagnostic accuracy of PPG to other techniques of investigation, or how well it correlated with the clinical grading of the severity of venous disease.

### Diagnostic accuracy of PPG

In other studies PPG was compared to different methods of investigation, which included Air Plethysmography (APG), Strain Gauge Plethysmography (SGP) and Duplex Ultrasonography to consider how well it diagnosed venous insufficiency and if it was possible to measure the severity of the disease<sup>28,29,30,4,31,32,33</sup>. To assess the ability of PPG to do this accurately, a study in Japan by Hirai et al<sup>28</sup>

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compared SPG with PPG. The researchers acknowledged that the small purposive sample recruited of 12 volunteers and 17 patients were too small to obtain criteria for prediction. However, the findings indicated that PPG appeared more able than SPG to assess the circulatory haemodynamics of the skin but that perhaps SPG had greater diagnostic accuracy for deep venous disease. The researchers conclude that perhaps it would be appropriate to use both methods of investigation to enable better accuracy of the assessment. Van Bemmelen et al<sup>30</sup> agreed that PPG provided some indication of venous insufficiency but questioned its value when this can be identified by inspection of the skin if trophic skin changes are visible. However, Bays et al<sup>32</sup> reported a high incidence of false negatives and suggested that PPG was only accurate when visible skin changes were present.

Hubner's<sup>34</sup> work reports on a review of patient attendance's to a phlebology department over a four-year period to identify the benefits of using PPG by light reflection (LRR) as part of a routine screening for venous disease. The study is described as a 'statistical survey', where the results of assessment using LRR on 1852 patients seen within the department are evaluated. It is difficult to identify from the report how the use of LRR was established and there is some confusion over the analysis of the data. However, this could have resulted from problems due to translation of the paper. It would appear that following LRR on these patients, 169 were suspected of having a deep venous insufficiency and subsequently went on to have phlebography. The results demonstrated agreement with LRR in 127 patients. These figures were then used to claim an accurate diagnostic rate of 97.7%. However, the rationale for the calculation was not provided which led the reader to

believe there may be some error in the calculation.

A report by McEnroe et al<sup>35</sup> describes a study in a similar setting, which aims to identify the number of patients with deep venous insufficiency and the percentage with deep valvular incompetence as opposed to those with deep vein obstruction. This study also examines how deep venous insufficiency affects clinical grading. Support for the study and its methodology is provided by a comprehensive literature review. A large sample of 386 consecutive patients referred to vascular service over the previous 48 months was used. The researchers acknowledge bias in their sample due to the high proportion of patients seen within their department who had deep venous insufficiency. Data obtained for analysis was from a review of the patient's records. This retrospective approach provided detailed information and description of the investigations. However, no reference was made on how the data was extracted from the records and how it was interpreted or assessed for interrater reliability. This is important in order to assess the accuracy of the data. These researchers claimed a close correlation of clinical symptoms with venous refill time, demonstrated by a frequency diagram. However, this was not easy to interpret.

Ifrati et al<sup>33</sup> report on a laboratory study, which investigates whether or not haemodynamic differences exist between classified stages of venous disease and if non-invasive assessment techniques are able to identify them. Techniques assessed were PPG, APG and duplex ultrasonography. In this study, participants were initially examined by a consultant surgeon to grade clinical severity of disease, and then underwent the panel of tests with their clinical grading blinded from the operators, thus avoiding expectancy

bias. This is in contrast to another study<sup>36</sup> of a similar design where the same investigator conducted all measurements. The statistical analysis used by Ifrati et al was described using t-tests, which was misleading, as there were more than two variables being analysed. Although these results may be questionable they dispute previous claims of a close correlation of clinical symptoms with venous refill time.

Rutgers et al<sup>31</sup> also attempted to dispute the claim that PPG can be used to accurately identify the clinical severity of disease, but raised controversy with their suggestion that some traces were 'uninterpretable', which does not appear within other papers. In response, Kurgan et al<sup>37</sup> suggest that use of only a 50% refilling time in the study by Rutgers et al is responsible for these findings, which raises issues about the need to standardise the technique.

A more recent paper reported on a comparison of LRR and duplex scanning in the diagnosis of chronic venous insufficiency<sup>38</sup>. This was published under the heading of original research however, any claims of this being a piece of research should be questioned as this paper describes a retrospective data collection from patients notes. It included 42 patients who had been investigated for venous insufficiency using LRR and had then gone on to have duplex scanning. The results identified shortened refill times using LRR and venous reflux was confirmed by duplex ultrasonography in 41 patients demonstrating a 97.6% accuracy of LRR. However, considering that the time lapse between the LRR and the duplex ranged from 2 months to 8 years this claim should be treated with caution.

Although PPG can identify the presence of venous insufficiency debate does exist regarding the accuracy of PPG to differentiate

between the clinical grading and severity of venous insufficiency. As all papers appear to have used different grading systems to describe the severity of venous insufficiency it would call for a standardisation of approach in reporting the clinical grading as previously documented<sup>39</sup>. As a result it is important to evaluate the evidence regarding the reliability of PPG to differentiate between deep and superficial vein incompetence.

### Deep versus superficial vein incompetence

PPG can be used to distinguish between deep and superficial vein incompetence by using a tourniquet applied above the knee at a pressure of approximately 50mmHg, which is sufficient to restrict flow in the superficial venous system, **Fig 4**.

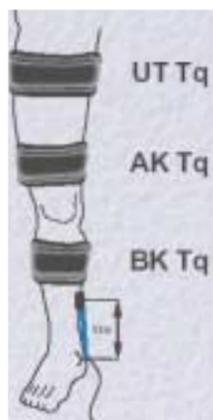


Figure 4  
Tourniquet positions

If a previous abnormal venous refill time reverts to normal, then the venous insufficiency has been restricted to the superficial system<sup>1</sup>. It would appear from the literature there is agreement with this<sup>24,28,29,31,35,40</sup>. Most of the studies reviewed assessed venous function using PPG in patients both with and without tourniquets being applied to the limb. Pearce et al<sup>40</sup> recorded venous filling time by PPG in 89 patients, 47 had post-phlebotic syndrome, 29 had primary varicose veins and 13 following an episode of acute deep

vein thrombosis. Assessment was also carried out on asymptomatic limbs within this group of patients; all of these had a significantly longer refill time than those with symptoms of venous disease. Postoperatively, after long saphenous vein stripping, 30 of 34 limbs reverted to normal venous refill time when measured by PPG. This suggests that PPG can be used to determine the effectiveness of surgical intervention. The researchers acknowledge that the small numbers of patients would limit the study's conclusions.

Two other studies<sup>24,29</sup> also considered the use of PPG to distinguish between deep and superficial venous insufficiency. Hirai et al<sup>29</sup> demonstrated a significantly shorter refill time in the group with chronic venous insufficiency compared to those in the control group and those with simple varicosities. However, when the tourniquet was applied, the refill time in both those with chronic venous insufficiency and those with simple varicosities improved and the significance of the difference between the groups disappeared. This suggests that the presence of symptoms of chronic venous insufficiency does not necessarily indicate a disturbance of venous flow within the deep venous system.

In contrast Nicolaides and Miles<sup>24</sup> analysed their simultaneous measurements of AVP and PPG, with and without tourniquets, using correlation. This demonstrated a linear relationship between the two techniques although this relationship did not exist if a mean of the AVP measurements was used. This strengthens the evidence that PPG is not able to distinguish the severity of venous insufficiency but with the use of tourniquets, can distinguish between deep and superficial venous insufficiency. This is accepted by other researchers<sup>30</sup> but they also suggest that as PPG cannot locate the actual site of venous insufficiency it should not be used in isolation to

aid surgical decision-making. However, the benefits of using PPG in identifying venous disease are apparent and perhaps could aid in the nursing assessment of patients with leg ulceration and identify the 'at risk' who could subsequently be offered preventative treatment. Further evidence evaluated was on the benefits of using PPG to screen for DVT.

### PART 2 – Using Photoplethysmography to screen for Deep Vein Thrombosis

Deep vein thrombosis is a serious condition since the thrombus may migrate to the lung, producing a Pulmonary Embolism (PE). This is often a fatal complication of lower limb DVT, which may totally occlude the perfusion of part or all of one or both of the lungs and may cause collapse and sudden death in some patients. Therefore, a DVT may constitute a medical emergency. However up to 20% of patients with a suspected DVT may have other diagnoses such as a ruptured Baker's cyst, superficial thrombophlebitis, calf muscle haematoma or ruptured plantaris tendon<sup>45</sup>. This makes the clinical diagnosis difficult and often inaccurate and the PPG offers a reliable way to screen for the presence of a DVT using non-invasive technology.

In 1991 two studies were identified where the researchers had evaluated the use of LRR as a non-invasive technique for screening patients with DVT<sup>41,42</sup>. Thomas et al describes a prospective study over a 5-month period where 131 legs of 119 patients were assessed. The findings identified a negative predictive value (NPV) of 92% and therefore provided a sensitivity of 92%. The researchers also reported a high specificity of 84%, which suggests that the majority of those with a positive result did in fact have this condition. This high sensitivity was also found in a

further study but these researchers reported a lower specificity<sup>20</sup>. In this study 103 limbs of 100 patients referred to the x-ray department with suspected DVT were assessed, each of the patients had ascending contrast venography (ACV) and colour flow duplex imaging (CFDI). In addition to these investigations Digital PPG (D-PPG) was performed. Of the 103 limbs 37 were found to have a DVT. All the patients with a venous refill time of greater than 20 seconds had normal ACV and CFDI demonstrating 100% sensitivity. Therefore, the D-PPG provided a negative predictive value of 100% validating it as a screening tool in the diagnosis of DVT. Of the patients identified as positive i.e. those with a venous refill time of less than 20 seconds only 51% went on to have a DVT confirmed by ACV and CFDI thereby gave a positive predictive value and specificity of 51%. The researchers concluded by stating that a negative D-PPG effectively excludes a DVT and a positive test requires further confirmation. Fig 5.

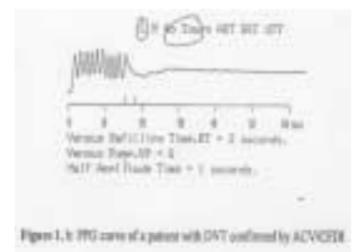
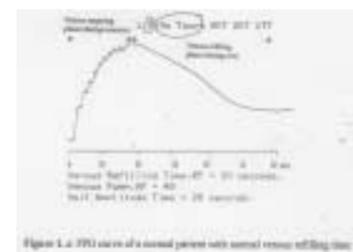


Figure 5  
Normal and abnormal PPG curve

Further work located described local audits and implementation of protocols in the management of patients with suspected DVT's<sup>43,44</sup>. Tovey<sup>43</sup> demonstrated a cost effective

service could be provided, which saved over 1000 bed days per year when patients with suspected DVT were seen by a special 'DVT team' and screened for further investigations using PPG and D-Dimer test without the need for admission. Williams et al<sup>44</sup> also claimed a cost-effective service was developed using similar screening programmes.

Patel<sup>45</sup> undertook a prospective comparison of PPG against duplex ultrasound on 143 consecutive patients undergoing investigations for a possible DVT and also a control group of 20 normal subjects. The PPG was performed prior to the Duplex but the results were not available till the end of the study to avoid any bias. In total 186 legs were assessed and the results again demonstrated a sensitivity of 100% with a specificity of 71%. However, this researcher was able to increase the specificity to 89% when the limbs were assessed using an above knee tourniquet and 100% using a below knee tourniquet.

### Discussion

It would appear that PPG is able to identify the presence of venous insufficiency and may be valuable towards differentiating between a deep and superficial incompetence and as a non-invasive technique offers obvious advantages over investigations such as AVP. Furthermore, it has proved effective in the screening for the presence of a DVT, where the negative predictive value has been reported as high as 100% therefore, producing a high sensitivity. However, the specificity is lower as a number of false positives have been reported. It is important to identify reasons why a false positive may occur, which could include; the age of the patient and being unable to perform the test, leg oedema, which reduces reflectivity, inability to dorsiflex the foot possibly due to arthritis or a reduced reflectivity in patients with arterial disease<sup>41</sup>.

### Conclusions

This paper describes the technique of photoplethysmography (PPG) and reviews the literature regarding the accuracy of the investigation to support its use in the assessment of patients both with venous ulceration and to screen for those at risk of ulceration. As leg ulcer management is now mainly the responsibility of the nurse it is important that appropriate techniques of investigation are implemented. Current assessment techniques to determine the ankle brachial pressure index using Doppler ultrasound to screen for arterial disease fail to establish whether or not an individual's leg ulceration is the result of venous insufficiency. Objective confirmation of venous insufficiency as the cause of leg ulceration using this form of investigation means that nurses no longer need to rely primarily on the elimination of arterial disease to treat venous ulcers appropriately with compression therapy. However, the use of PPG could play a major role in screening individuals with known risk factors for the presence of venous insufficiency and the review of this literature provides some evidence that PPG may be of value if considering a leg ulcer prevention programme.

It has been demonstrated that PPG provides a high negative predictive value when screening for DVT and as such would be beneficial as a diagnostic aid. This may subsequently reduce the amount of unnecessary referrals and admissions to secondary care.

It would appear from the evidence presented in this paper that PPG, which is easy to perform, can be used in diagnostic centres in primary care and is without risk to the patient and would therefore enhance both assessment techniques and screening programmes for venous insufficiency and the presence of a DVT.

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