The use of microcirculatory techniques in the assessment of pathophysiology, diagnosis and management of critical limb ischemia

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Citation for published version (APA):
de Graaff, J. C. (2003). The use of microcirculatory techniques in the assessment of pathophysiology, diagnosis and management of critical limb ischemia

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Chapter 2

The usefulness of laser Doppler in measuring toe blood pressures

Jurgen C. de Graaff, Dirk Th. Ubbink, Dink A. Legemate, Rob J. de Haan, Michael J.H.M. Jacobs


Abstract

Introduction To evaluate the clinical value and reproducibility of laser Doppler (LD) vs. Photoplethysmography (PPG) in the measurement of the systolic toe blood pressure.

Methods Toe blood pressure was measured in 60 patients in different stages of peripheral vascular disease by simultaneous digital sampling of PPG, and two LD signals, each with a different filter setting (3s: LD₃ and 0.03s: LD₀.₀₃), and cuff pressure. These measurements were repeated after one week. The signals were analyzed ignoring previous results. The agreement of the PPG- and LD-pressures, and reproducibility after one week was assessed by calculating the intraclass correlation coefficient (ICC). The agreement variation across the range of pressure values was visually explored by means of difference plots.

Results In 19 legs with a very low pressure only LD could adequately measure the pressure, while PPG did not. The ICCs between PPG and LD₃ and LD₀.₀₃ were ≥0.95. The ICCs of the one-week reproducibility of the PPG, LD₃, and LD₀.₀₃ pressures were 0.92, 0.88 and 0.86, respectively. The variation was equally distributed across the range of pressures in all three methods.

Conclusions LD is a reliable alternative to PPG to measure toe blood pressures. Furthermore LD is able to measure low pressures, which is relevant in the assessment of the presence of critical ischemia.
**Introduction**

Toe systolic blood pressure measurements play a prominent role in the diagnosis of critical leg ischemia, especially in diabetics, in whom the ankle pressure is not always reliable due to media sclerosis.\(^1\)\(^\text{2}\) The toe pressure is also important in patients with extensive wounds in whom the ankle cuffs or Doppler probes can not be applied. In patients with severe arterial insufficiency, toe pressure is correlated with the severity of the overall occlusive process,\(^4\)\(^\text{5}\) need for vascular intervention,\(^4\)\(^\text{5}\) healing potential of ulcers,\(^6\) and prediction of the need for amputation.\(^7\) The cut-off value used for the diagnosis of critical leg ischemia as defined in the European Consensus\(^8\) is low (30 mm Hg). Therefore the technique must be highly accurate when used in the low pressure range.

The principle of toe blood pressure is based on the method of arm blood pressure measurements as initially described by Riva-Rocci;\(^9\) a pneumatic cuff surrounding the limb is inflated to a pressure sufficient to stop blood flow.\(^10\) During slow deflation, the onset of resumption of blood flow distal to the cuff is defined as the systolic pressure. Nowadays, toe blood pressure is usually measured by either strain-gauge\(^11\) or photoplethysmography (PPG).\(^12\) Both methods can be used in the AC and DC mode. In the AC mode the resumption of blood is detected by the return of the pulsatile signal, which is reduced, or even absent, in patients with multiple occlusions as in patients with critical leg ischemia. In the absence of detectable pulsations, the plethysmograph can be DC coupled. The toe is exsanguinated with a tourniquet prior to inflation of the occluding cuff. Resumption of arterial inflow is then indicated by an upward shift from the baseline.\(^13\) However, both methods have their shortcomings. The strain-gauge is difficult to position at short digits and the element might exert some pressure on the toe, which influences measurement accuracy at low pressures,\(^14\) while the PPG in the DC mode is very sensitive to movement artefacts and not commonly used.

Many methods, such as clearance of radioisotopes,\(^15\) pink flush reappearance,\(^3\) audio PPG,\(^16\) pulse oximetry,\(^17\) and impedance sphygmography\(^18\) have been used for the measurement of toe pressures with varying success. More recently the laser Doppler (LD) technique has been suggested for this purpose.\(^14\)\(^\text{19}\) LD has also been used as an alternative technique for PPG in the measurement of skin pressure.

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**Figure 1.**

*Scheme of probe application on the big toe and signal analysis. All three signals are plotted in one graph for simplification, although signals were analyzed independently. The arrows represent the points at which the systolic pressures were read.*

![Scheme of probe application on the big toe and signal analysis.](image-url)
perfusion pressures.\textsuperscript{20,21} LD has theoretical advantages above PPG, since it is able to detect the minute microcirculatory blood perfusion in the skin. PPG is based on changes in the amount of reflected near infra-red light upon pulsatile changes in blood filling of the digit, whereas LD is based on the change in frequency shift of the reflected light caused by moving blood particles. Furthermore, LD is readily applied without compression, even to short digits. Andersson et al.\textsuperscript{14} compared LD with the strain gauge method and concluded that the LD technique is an alternative and complementary to the strain-gauge method in damaged or ulcerating toes and feet. Beinder et al.\textsuperscript{19} used LD in combination with a specially manufactured transparent plastic capsule for positioning the LD probe and cuff to the digit. The toe pressures thus obtained were in good agreement with data obtained by means of the strain gauge method measured in another group of patients. Furthermore, LD tended to be more sensitive than strain gauge at low pressures. However, the LD technique has not yet been compared to PPG, which is mostly used nowadays, in the same population.

In this study we compared two techniques (PPG and LD) for the measurement of toe blood pressure measurements as to its use, reliability and responsiveness in patients with different stages of peripheral vascular insufficiency. Additionally, we evaluated the one week intra-observer reproducibility to evaluate consistency of both methods.

Patients and methods

Patients
Sixty patients (37 men, 23 women, mean age: 66 \textpm 10 yr), referred to the vascular laboratory for the assessment of the ankle/brachial index, consented to participate in this study. Patient characteristics are listed in Table 1. In eight patients only one toe could be investigated, because in four patients the toe or foot was amputated, while in the remaining four patients it was not possible to measure the toe blood pressure with both techniques at the same time due to large wounds (n=3) or the shortness of the toe (n=1). The remaining 112 legs belonged to different stages of peripheral vascular disease; 20 legs without complaints, 54 with intermittent claudication, and 38 with rest pain, ulcers or gangrene. Patients were acclimatized in a temperature-controlled environment (23 \textpm 1 \textdegree C), during a resting period of at least 15 min.

Table 1. Patient characteristics (n=60)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>52%</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>36%</td>
</tr>
<tr>
<td>History of cerebrovascular accident or temporary ischemic attack</td>
<td>17%</td>
</tr>
<tr>
<td>History of cardiac failure</td>
<td>41%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>48%</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>41%</td>
</tr>
<tr>
<td>Presence of peripheral pulsations (dorsalis pedis or posterior tibial artery)</td>
<td>69% (of 112 legs)</td>
</tr>
</tbody>
</table>
Measurements
Measurements were performed in the supine position, which implies that, depending on the size and position of the foot, the toe was at or just above heart level during the measurement, which is the usual position for these measurements. The legs were covered with sheets or clothing to prevent cooling. Due to these preparations we refrained from local heating of the toe, which is sometimes advocated in PPG studies. The toe pressures were simultaneously measured with PPG and LD.

The PPG was AC coupled (filter settings: 0.4 to 2.3 Hz). A PPG consists of an infrared light-emitting diode and a photosensor, mounted adjacent to one another on a small probe. Blood, which is more opaque than surrounding tissue, attenuates light in proportion to its content in the tissue. The speed differences in the flow causing variations in amount of blood content in the digit result in a pulse contour, which is normally presented on a graph.

LD fluxmetry is a simple, non-invasive sensitive technique to assess cutaneous blood perfusion. In the LD instrument light with a wavelength of 780 nm is conducted through optical fibres to an area of the skin of about 0.5 mm² where it penetrates the skin to a depth of 1-1.5 mm and is reflected partly. This light, if backscattered by moving objects (principally erythrocytes), undergoes a frequency shift, which is proportional to the velocity, number and direction of moving objects (laser Doppler flux), and is expressed in Volts. Two filter settings of the output signal (time constants; tc) of the LD instrument were used; tc = 3 s (LD₃) for the detection of slow changes in blood flow (which can be compared with the DC mode), and tc = 0.03 s (LD₀₃), resulting in a signal that could trace heartbeats (which can be compared with the AC mode).

Blood pressure measurements
The ankle systolic pressures in the dorsal pedal and posterior tibial arteries at the level of the ankle were measured using a 8 Mhz Doppler probe and a cuff (12 cm) around the lower leg just above the ankle. The highest pressure was considered to represent the highest perfusion pressure. The ankle-to-brachial pressure index (ABPI) was calculated by dividing the ankle pressures by the highest of the left and right brachial blood pressure, measured by means of an automatic blood pressure monitor (Criticon, Dinamap™ Plus, Tampa, FL, USA), and expressed as a percentage.

For the toe blood pressure a cuff with a width depending on the diameter of the hallux (1.5, 2.5 or 3.3 cm disposable cuffs, Hokanson, Bellevue, WA), was wrapped around the base of the toe. The cuff width closest to 120% of the diameter of the hallux was chosen. The PPG and two standard LD probes (PF 408, Perimed, Sweden) connected to the LD instrument (Periflux 4001, Perimed, Sweden) were attached to the apex of the big toe (PPG at the centre and LD probes at both sites of the PPG) using double sided adhesion tape with a notch for the probe (Double-Stick Discs, 3M Health Care, Broken, Germany) and a probe holder (PF 104, Perimed, Sweden) for the LD probes (figure 1). The probe holder is a small (diameter: 15 mm) plastic holder in which the laser Doppler probe fits exactly and in which the tip of the probe is just (approx. 0.1 mm Hg) above the skin. By means of the probe holder and adhesive tape the exact distance from the skin is achieved without compressing the skin.

Our conventional instrument to measure peripheral pressures (PV-lab, Stöpler, EDI, Burbank, CA, USA) was modified so that the cuff pressure, PPG and LDF signals could be sampled on-line and analyzed off-line by means of a data
acquisition system (AcqKnowledge III and MP100WSW, Biopac System, Inc., Santa Barbara). The cuff was rapidly inflated up to a pressure at least 30 mm Hg higher than at which the pulsations in the PPG and LD<sub>0.03</sub> signal disappeared. Initially the LD showed an increase in flux after which the signal declined to the baseline (figure 1). After the LDF<sub>3</sub> signal had reached a stable baseline (after approximately 3 s.), the cuff was slowly deflated with a speed of approximately 3 mm Hg / s. The systolic pressure was defined as the pressure at which the (pulsatile) signal reappeared or rose gradually from the baseline (figure 1).

One single measurement of the toe blood pressure (with all three probes at the same time) was performed each session. In order to establish the one-week intra-observer reproducibility, the measurements were repeated after one week (t=1). All measurements and analyses were performed by one investigator (JdG), while ignoring previous results as much as possible.

### Statistical analysis

The differences between PPG vs. LD<sub>3</sub> and PPG vs. LD<sub>0.03</sub> pressures, respectively, were evaluated by the Student’s t-test for paired samples. Since we do not know the true pressure, the average of the LD<sub>3</sub> and PPG and the average of LD<sub>0.03</sub> and PPG were considered to be the best estimates of the true pressures. The differences between LD and PPG were also calculated with limits of agreement and intra-class correlation coefficients (ICC). The limits of agreement were defined as the mean difference ±2*SD of the difference, according to Bland and Altman. These limits reflect the interval in which 95% of the differences in pressures lie. A plot was made of the difference between the two measurements against their mean to check whether the measurement error was independent of the magnitude of pressure. The regression lines (with beta coefficient, indicating the direction of the deviation, and it’s p-value) indicate whether the variability in the pressures is independent of the magnitude of the pressures. The ICC (two-way random effects model) was calculated according to the method as described by Deyo et al. The ICC not only assesses the strength of linear correlation between two measurements, such as the Pearson correlation, but also detects systematic error. Thus, if one measurement is systematically higher or lower than the other, the ICC is correspondingly reduced. The same methods were used to assess the one-week intra-observer reproducibility and the comparison between LD<sub>3</sub> and LD<sub>0.03</sub>.

### Table 2. Mean blood pressures

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>toe pressure (SD) mm Hg</th>
<th>AP (SD) mm Hg</th>
<th>ABPI (SD) %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>PPG</td>
<td>LD&lt;sub&gt;3&lt;/sub&gt;</td>
<td>LD&lt;sub&gt;0.03&lt;/sub&gt;</td>
</tr>
<tr>
<td>Without complaints</td>
<td>20</td>
<td>100 (32)</td>
<td>101 (34)</td>
<td>98 (31)</td>
</tr>
<tr>
<td>Intermittent claudication</td>
<td>54</td>
<td>69 (28)</td>
<td>70 (26)</td>
<td>69 (27)</td>
</tr>
<tr>
<td>Rest pain, ulcers or gangrene</td>
<td>38</td>
<td>20 (21)</td>
<td>34 (14)</td>
<td>33 (15)</td>
</tr>
<tr>
<td>Overall</td>
<td>112</td>
<td>58 (40)</td>
<td>63 (34)</td>
<td>62 (34)</td>
</tr>
</tbody>
</table>

Mean toe blood pressure (measured with PPG, LD<sub>3</sub>, LD<sub>0.03</sub>), ankle pressure (AP) and ankle/brachial index (ABPI) in the legs measured at first measurement (t=0).
Results

The pressure could not be measured with PPG in 19 toes because no pulsatile signal could be detected (hence taken as 0 mm Hg), whereas all of these toe pressures could be measured with LD$_3$ (mean: 24 ± 14, range 8-64 mm Hg, number of pressures ≥ 30 mm Hg: 5), and 17 of these with LD$_{0.03}$ (mean: 21 ± 12, range: 0 - 48 mm Hg, number of pressures ≥ 30 mm Hg: 5). Of these patients one presented with intermittent claudication, 11 with rest pain, and 7 with ulcers or gangrene. The mean AP and ABPI were 64 (± 32, range 0 - 140) mm Hg and 41 (± 21, range: 0 -104) %, respectively. The incidence of diabetes mellitus among these patients did not differ significantly from the total patient group (39% vs. 36% resp.). Strikingly, in all but one limb no peripheral pulsations could be palpated. The pressure of 64 mm Hg, undetected by means of PPG, but detected by laser Doppler was found in a patient with CREST syndrome with severe microangiopathy without severe arterial occlusions.

Application to the toe of the LD probe using the probe holders was very simple. Except for one very short big toe, the two LD probes could be applied next to the PPG probe on the big toe in all patients investigated. The LD reading was quite stable and less influenced by movement artefacts than the PPG signal. The signal-to-noise ratio was found to be considerably lower with the LD than with the PPG signals. The blood pressures per patient subgroup are presented in table 2.

**PPG vs. laser Doppler**

Histograms depicting the differences between PPG an LD-pressures showed a normal distribution (graphs not shown). Table 3 presents the the mean difference, the SD of the differences, the limits of agreements and the ICC between PPG-pressure and LD-pressures. The mean differences were small and statistically not significant. The ICCs showed almost perfect agreement (≥ 0.95) between the PPG-pressure and LD-pressures (table 3).

In figure 2a and 2b the differences between PPG an LD-pressures are plotted against the mean of both measurements. The regression lines in both figures indicate the variability in the pressure scores show a small relation with only the magnitude of the LD$_{0.03}$ pressure values (beta coefficient figure 2a= 0.15, p= 0.14, and beta coefficient figure 2b= 0.28, p< 0.01).

There was no significant difference between LD$_3$ and LD$_{0.03}$ (table 3; beta coefficient figure 3= 0.05, p= 0.6).

**Table 3. Difference between PPG and LD pressures**

<table>
<thead>
<tr>
<th></th>
<th>n=</th>
<th>mean difference</th>
<th>SD of the difference</th>
<th>limits of agreement</th>
<th>p-value</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPG vs. LD$_3$</td>
<td>93</td>
<td>-0.8</td>
<td>9.5</td>
<td>-19.7 / 18.1</td>
<td>0.43</td>
<td>0.96</td>
</tr>
<tr>
<td>PPG vs. LD$_{0.03}$</td>
<td>91</td>
<td>-0.9</td>
<td>9.8</td>
<td>-20.4 / 18.6</td>
<td>0.36</td>
<td>0.95</td>
</tr>
<tr>
<td>LD$<em>3$ vs. LD$</em>{0.03}$</td>
<td>110</td>
<td>-0.6</td>
<td>8.6</td>
<td>-17.8 / 16.6</td>
<td>0.47</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Comparison between LD$_3$, LD$_{0.03}$ and PPG at t= 0, with mean difference and standard deviation of the differences and limits of agreement, p- value of the Student's t test for paired samples, and intraclass correlation coefficient (ICC). The limits of agreement reflect the interval within 95% of the differences in pressures lie, defined as the mean difference ± 2SD of the difference. Unmeasurable pressures were excluded.
Figure 2. Difference between pressure measured with PPG and with the LD setting that detects slow changes in the blood flow (LD$_3$, figure 2a) and the LD setting that could trace heart beats (LD$_{0.03}$, figure 2b) plotted against the mean pressure. The regression line of the differences (drawn line) and 95% limits of agreement (dotted lines) of the differences are presented as horizontal lines. The open squares represent the pressures which only be measured with LD.

Figure 3. Difference between LD$_3$-pressure and LD$_{0.03}$-pressure at t=0 plotted against the mean of both methods. The regression line of the differences (drawn line) and 95% limits of agreement (dotted lines) of the differences are presented as horizontal lines. The vertical dashed line represents the commonly accepted cut-off value for critical leg ischemia (< 30 mm Hg). The open squares represent the pressures which could only be measured with LD.
Chapter 2 - Toe blood pressure using Laser Doppler

Table 4. One week reproducibility

<table>
<thead>
<tr>
<th>n= 86 legs</th>
<th>mean t=0 (SD)</th>
<th>mean t=1 (SD)</th>
<th>Mean difference</th>
<th>SD of the difference</th>
<th>Limits of agreement</th>
<th>p</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP (mm Hg)</td>
<td>151 (23)</td>
<td>145 (19)</td>
<td>7.2</td>
<td>16.1</td>
<td>-25 / 39</td>
<td>&lt;0.01</td>
<td>0.72</td>
</tr>
<tr>
<td>AP (mmHg)</td>
<td>107 (38)</td>
<td>101(38)</td>
<td>5.9</td>
<td>20.4</td>
<td>-34 / 46</td>
<td>0.01</td>
<td>0.85</td>
</tr>
<tr>
<td>ABPI (%)</td>
<td>68 (23)</td>
<td>67 (25)</td>
<td>0.7</td>
<td>11.3</td>
<td>-22 / 23</td>
<td>0.57</td>
<td>0.89</td>
</tr>
<tr>
<td>PPG (mm Hg)</td>
<td>59 (39)</td>
<td>55 (37)</td>
<td>3.3</td>
<td>16.6</td>
<td>-29 / 36</td>
<td>0.04</td>
<td>0.92</td>
</tr>
<tr>
<td>LD₃ (mm Hg)</td>
<td>62 (34)</td>
<td>58 (31)</td>
<td>3.8</td>
<td>15.6</td>
<td>-27 / 34</td>
<td>0.03</td>
<td>0.88</td>
</tr>
<tr>
<td>LD₀.₀₅ (mm Hg)</td>
<td>62 (33)</td>
<td>57 (32)</td>
<td>4.9</td>
<td>14.7</td>
<td>-24 / 34</td>
<td>0.03</td>
<td>0.86</td>
</tr>
</tbody>
</table>

Mean brachial pressure (BP), ankle pressure (AP), ankle/brachial index (ABPI) and toe (PPG, LD₃, and LD₀.₀₅) pressure with standard deviation (SD), mean difference with standard deviation and limits of agreement, p-value of the Student's t test for paired samples, and intraclass correlation coefficient (ICC) of the one week reproducibility of each technique.

Reproducibility

For the analysis of the reproducibility only 86 legs were eligible, because the other patients were treated within that week. There was a small, but significantly lower brachial, toe and ankle pressure measured after one week, whereas the ankle brachial index remained stable during the one week time interval (table 4). The ICCs indicate a substantial reproducibility for all three methods (≥ 0.85). In figures 4a, 4b and 4c the differences between the first and the second PPG and LD pressures are plotted against the mean of the first and second measurement. The error of the measurement was found to be independent of the magnitude of the pressure values (beta coefficient figure 4a = 0.1, p = 0.42; beta coefficient figure 4b = 0.15, p = 0.12; beta coefficient figure 4a = 0.05, p = 0.67).

Discussion

This study shows that LD is a reliable and clinical useful technique for the measurement of systolic toe blood pressures. Moreover, LD is more responsive in detecting the reappearance of skin flow at very low perfusion pressures than PPG in the AC mode.

Andersson et al. already showed that LD seems to be more sensitive than the strain-gauge method in the low pressure range for measuring blood pressures. Although also critically reduced pressures could be measured with PPG (in our study as low as 15 mm Hg), this study showed that LD was able to measure toe blood pressures in 19 toes, which the PPG in the AC mode could not; these pressures varied between 6 and 64 mm Hg. This pressure range is important, since it is around the cut-off value for critical leg ischemia as proposed by the European Consensus (30 mm Hg). This means that the decision for invasive therapy could be influenced by the method used. A low value (e.g. 0 mm Hg) would suggest invasive treatment is required whereas a higher value would advocate initial conservative therapy.
Figure 4. Difference between the first and second measurement of PPG-pressure (figure 4a), LD$_{3}$ pressure (figure 4b) and LD$_{0.03}$ pressure (figure 4c) plotted against the mean of the first and second measurement. The regression line of the differences (drawn line) and 95% limits of agreement (dotted lines) of the differences are presented as horizontal lines.
The LD technique appears to most valuable in the absence of peripheral pulsations, and in patients with low ankle and toe blood pressures. On theoretical grounds, laser Doppler is probably more sensitive than PPG since LD is based upon the registration of a frequency shift (Doppler effect) of red light by the moving erythrocytes, whereas PPG is based upon a difference in the amount of reflected light by the absorption of near infrared light by the presence of erythrocytes in the underlying tissue. Hence, LD is able to detect very small blood displacements and is very sensitive in detecting the resumption of microcirculatory blood flow in the toe, as opposed to the more crude detection of blood filling by PPG. Therefore, we feel LD has an advantage over PPG in establishing CLI, since the absence of PPG pulsatility, which has even been suggested to predict to wound healing, does not have to be concomitant with a critically reduced perfusion pressure. On the other hand, LD has not been compared to the PPG in the DC-mode, which is the most accurate method of detecting toe blood pressure using PPG. But the DC mode appears to be commonly used less frequently, probably because this mode is very sensitive to movement artifacts and the toe has to be exsanguinated before inflation of the cuff. Moreover, LD has advantages over the PPG in DC mode, as the LD is hardly influenced by movement artefacts, and exsanguination of the toe is not required.

Another advantage of LD is that the LD probe can easily be applied to short digits, especially when much smaller probes (5 mm) or the transparent probe holder as described by Beinder et al. are used.19 Thus, in practice even digit II, III or IV might be used for toe blood pressure measurements, when the big toe is not available because of ulcerations or after amputation. Furthermore, toe pressures measured with LD are found to be as reproducible as pressures measured with PPG. The coefficients of repeatability are in agreement with other techniques such as strain gauge plethysmography.

On the other hand, the disadvantage of the LD method is that two extra devices (LD, cuff inflator, and data acquisition system) are needed instead of one, since the LD instrument is not routinely integrated in the peripheral vascular equipment, which increases the costs. A data acquisition system may not be required, but in our experience, often the first pulsations are missed during online determination with our conventional lab instrument (resulting in a lower pressure), whereas this will not occur when the analysis is performed offline.

The filter time for the LD signal did not seem to influence the results of the pressure measurement, although the longer time constant (LD₃) tends to be more sensitive. Both filter settings methods (LD₃ and LD₀.₀₉) yield comparative results as to PPG and the agreement between both methods and PPG is almost perfect (ICC > 0.95). The faster mode (LD₀.₀₉) is easier with pulsatile flux at higher pressures and the more DC (plethysmographic) mode (LD₃) is preferred to detect flux increase from baseline at lower pressures not showing any pulsatile flux. A further improvement of the LD and PPG technique might be the use of heated probes or the application of local heat, since the hyperemia increases the total skin perfusion, which pronounces reappearance of the skin perfusion.

Analysis of the reproducibility indicates that all three methods are comparable and reproducible (ICC > 0.85). Insight in the reproducibility of a technique, especially the limits of agreement, is important when interpreting the results of measurements of the same person within time, e.g. in the evaluation of therapy or progress of a disease. The limits of agreement of the ABPI are somewhat above 0.2, which is in agreement with the results of Fisher et al., but is more than the 0.15 which is generally reported. This somewhat larger variation is mainly
caused by the way of calculating the variability. The significantly lower ankle pressure is due to a lower systemic pressure after one week, probably due to reassurance of the patient during the second measurement, which is represented by a lower brachial pressure after one week.

In conclusion, LD is a responsive and reliable instrument to measure toe blood pressure as compared with routinely used techniques. We recommend to use LD in situations in which no signal can be detected with PPG and a decision is required as to the presence of critical leg ischemia.

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