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Abstract— **Non-invasive arterial pulse wave (PW) measurement provides valuable information on the vascular health. The aim of the study is to characterize the between-visit or day-to-day repeatability of combined finger and toe photoplethysmographic (PPG) signal analysis method called finger-toe plot (FT-plot) and compare it with the repeatability of other methods proposed for vascular characterization. Ten 22–36-year-old subjects were examined on 3 different days in order to find out the day-to-day repeatability of the results. The repeatability of the extracted parameters was analyzed by means of intra-class correlation coefficients (ICC) and free-marginal multirater κ agreement. ICCs varied widely from below 0.2 to almost 0.9, but κ coefficients higher than 0.7 were achieved for most of the results. Based on the presented results, the FT-plot analysis has at least sufficient day-to-day repeatability. However, further studies with real patients and different stages of cardiovascular diseases are required for confirming the findings.**

Keywords— **Atherosclerosis, Photoplethysmography**

I. Introduction

Aging and unhealthy lifestyle cause stiffening and thickening of the arterial walls. The stiffening due to the aging is classically known as arteriosclerosis and thickening, stenosis or occlusion of the arteries due to accumulation of cholesterol is known as atherosclerosis. The markers of these conditions are often concomitantly present and are considered as a continuum of degenerative changes and indicators of increased risk for severe cardiovascular events. Methods for estimating atherosclerotic changes include the angiograms and the measurement of carotid-femoral pulse wave (PW) velocity or the intima media thickness of the carotid artery by using ultrasonic transducers [1, 2], but they require either a skilled operator or expensive equipment. A standard method for screening the occlusive atherosclerosis is ankle-to-brachial pressure index (ABI), but its performance decreases when there are also type 2 diabetic changes present [3].

To detect especially subclinical atherosclerosis, there is a growing need for alternative methods for measuring the vascular system. Many arterial PW measurement based non-invasive methods have been proposed for characterizing the vascular status, as e.g. in [4, 5]. The propagation of the waves and their reflections and thus the shape of the observed PWs and parameters derived from them depends e.g. on arterial wall properties, fluidic properties of the blood, blood pressure and vascular resistance. Due to the complexity of the arterial tree, there are several theories about the origin of the wave reflections [5, 6, 7]. We understand that the peripheral PW consists of a heart beat induced percussion wave and its reflections from several impedance discontinuities of the arterial tree.

Earlier, a method called finger-toe plot analysis (FT-plot) was presented for classifying the subjects into healthy and atherosclerotic patients, and the average AUC (area under the receiver operating characteristic (ROC) curve) of 91.6% was found for the method [8]. The FT-plot utilizes the photoplethysmographic (PPG) signals recorded from the index finger and the second toe. In the present study, we aim to characterize the between-visit or day-to-day repeatability of the FT-plot analysis.

II. Materials and methods

A. Study subjects and measurement hardware

Ten volunteer test subjects without diagnosed cardiovascular diseases (see Table 1) were in supine position during the measurement conducted on three different days. The median difference between the first and last measurement was 5 days, having interquartile range of 3–9 days. Daily activities or nutrition of the test subjects were not restricted. The time of day when the recordings were made varied between 8 am to 5 pm. All the volunteer test subjects were legally competent, signed an informed consent, were informed on the purpose of the study, and accepted that the anonymized results based on the recorded signals can be reported. All the study subjects had a chance to ask for additional information and interrupt their participation at any point without disclosing the reason.

PPG signals were recorded from the left index finger and the second toe with transmissive PPG-probes connected to a wireless body sensor network (WBSN) having a sampling frequency of 500 Hz [9]. The device records only the dynamic component of the PPG (cut-off frequency 0.15 Hz). The excitation wavelength of the PPG probes was 905 nm. The duration of each recording was approximately 15 min.

B. Finger-toe plot analysis

A more detailed description behind the FT-plot analysis is presented in [8]. As a startpoint, a PPG signal from the second toe (Figs. 1a)–b) and 2a)–b)) is drawn as a function of

Table 1: Numbers and proportions of test subjects having different cardiovascular risk factors.

Subjects	10
Age: mean (std)	27.4 (3.9)
Males	7 (70%)
Diabetes	1 (10%)
Dyslipidemia	0 (0.0%)
Smoking	1 (10%)
Rheumatoid arthritis	1 (10%)
Hypertension	0 (0.0%)

the PPG signal recorded from the index finger and the features are extracted from the region that represents the falling parts of the PWs, i.e. the region from the peak value of the PW to the baseline of the PW. This corresponds in Figs. 1b) and 2b) to the curve from the right upper corner to the left lower corner and this region is extracted to Figs. 1c) and 2c). Before the features are extracted from the region shown in Figs. 1c) and 2c), it is rotated by -60° in order to enable curve fitting in cartesian coordinates. After the rotation, a 9^{th}-order polynomial p is fitted to the rotated curve by using least mean-square (LMS) algorithm. The 9^{th}-order polynomial follows sufficiently the original curve but does not suffer from overfitting. In addition to the polynomial, a line l is fitted to middle-region (i.e. to the region where $x_1 < x < x_2$, $x_1 = 0.15\Delta x$ and $x_2 = 0.85\Delta x$ where Δx is the width of rotated the FT-plot curve) of the rotated part of the FT-plot by using LMS algorithm. Eleven different features are extracted from the FT-plot as presented in [8], labeled as 1–11:

1. Maximum difference of the slopes in the middle-region, i.e. $\max(p') - \min(p')$.
2. Mean absolute slope of the middle-region, i.e. $\text{mean}(|p'|)$
3. Standard deviation of the slope of the middle-region, i.e. $\text{std}(p')$
4. Standard deviation of the absolute slope of the middle-region, i.e. $\text{std}(|p'|)$
5. Integral absolute error between the fitted line and polynomial fit in the middle-region, i.e. $\int_{x_1}^{x_2} |l(x) - p(x)| \mathrm{d}x$
6. Integral square error between the fitted line and polynomial fit in the middle-region, i.e. $\int_{x_1}^{x_2} (l(x) - p(x))^2 \mathrm{d}x$
7. The arc length of the middle-region normalized by the distance between its endpoints, i.e. $\frac{1}{\sqrt{(x_2-x_1)^2+(p(x_2)-p(x_1))^2}} \int_{x_1}^{x_2} \sqrt{1+[p'(x)]^2} \mathrm{d}x$
8. The arc length of the middle-region normalized by the distance between the endpoints of the rotated curve, i.e. $\frac{1}{\sqrt{(\Delta x)^2+(\Delta y)^2}} \int_{x_1}^{x_2} \sqrt{1+[p'(x)]^2} \mathrm{d}x$
9. The maximum absolute difference between the slope of the polynomial fit and the slope of the fitted line, i.e. $\max(|p' - l'|)$

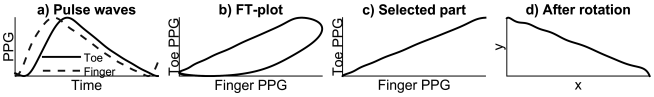

Figure 1: Finger and toe PPG PWs for an atherosclerotic patient (a). FT-plot, i.e. toe-PPG drawn as a function of finger-PPG (b). Region selected for the analysis (c). The selected region after the rotation (d).

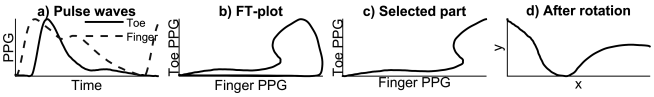

Figure 2: Finger and toe PPG PWs for a healthy subject (a). FT-plot, i.e. toe-PPG drawn as a function of finger-PPG (b). Region selected for the analysis (c). The selected region after the rotation (d).

10. The slope of the fitted line, l'.
11. Ratio of the areas under the finger and toe PPG, i.e. $\frac{A_{finger}}{A_{toe}}$.

In addition to these, 7 LDA-based (linear discriminant analysis) classifiers utilizing different combinations of features 1–11 were composed (Table 2 and [8]). In this study, the repeatability the features 1–11 and classifiers I–VII is evaluated.

C. Evaluation of the repeatability

In 1-way random effect model, observation Y_{ij} (j^{th} observation related to test subject i) is composed as

$$Y_{ij} = \mu_i + \varepsilon_{ij}, \tag{1}$$

in which μ_i subject-specific mean-observation and ε_{ij} is normally distributed zero-mean random error. Intra-class correlation coefficient (ICC) is used to estimate the repeatability of the series of measurements and it is defined as a ratio of between-subject variance and the sum of between- and within-subject variances. ICC based on one-way analysis of variance (ANOVA) is estimated for all the parameters as

$$\text{ICC} = (\text{MS}_{\text{bs}} - \text{MS}_{\text{ws}})/(\text{MS}_{\text{bs}} + (k-1)\text{MS}_{\text{ws}}) \tag{2}$$

in which MS_{bs} is between-subject mean squares, MS_{ws} is within-subject mean squares from 1-way ANOVA table and k is the number of observations per subject [10]. The ICCs are computed based on the averaged features (arithmetic mean over whole recording) extracted from each measurement.

The ICC assumes normally distributed data with equal population variances [10]. These requirements may be violated especially with the small number of datapoints per test subject when the pretests do not neccessarily reveal the viola-

Table 2: Features that different classifiers I-VII utilize.

Classifier	I	II	III	IV	V	VI	VII
Features	5,6,10,11	1,5,6,10, 11	2,3,5,6, 11	5,6,7,10, 11	5,6,9,10, 11	1,3,5,6, 10,11	4,5,6,7, 10,11

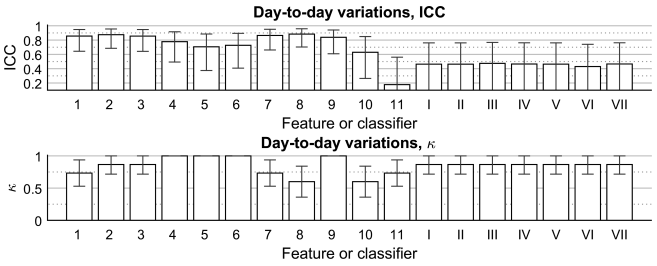

Figure 3: ICCs with 90% confidence limits and κ coefficients with 90% confidence limits for the measurements conducted on three different days.

tions [10]. For this reason, free-marginal multirater κ analysis was also implemented with the proportion of agreement expected by chance of $P_e = 1/(\text{number of categories}) = 1/2$ as

$$\kappa = (P_o - P_e)/(1 - P_e) \tag{3}$$

in which P_o is the proportion of overall observed agreement [11]. The free-marginal κ was selected instead of Fleiss' fixed-marginal κ because the value of the latter one depends strongly on the symmetry of the data [11]. The classification into two categories (healthy or atherosclerotic) for the κ analysis is based on the same data utilized in the ICC analysis: the test subjects are categorized based on the values of parameters derived from the FT-plots and the thresholds shown in [8].

III. Results

The ICCs and the κ coefficients for the averages of the measurements conducted on 3 different days are shown in Fig. 3. The confidence limits are 90% limits for ICC since the variations in the numerical values are wide and 90% for κ. The p-values are less than 0.01 for all ICCs shown in Fig. 3 except the FT-plot feature 11.

The numerical values of the analyzed parameters vary widely from day-to-day, causing wide confidence limits into Fig. 3. Still, the κ coefficients that are based on the classification results show at least substantial agreement: the differences in the κ values are caused by 0–4 differently classified instances for individual features 1–11 and one differently classified instance for LDA-classifiers I–VII. In this point of view, all the studied classifiers are practically exchangeable (Fig. 3) in terms of repeatability and classification performance reported in [8].

The test subjects were young and healthy, having probably relatively high heart rate variablity and vasoregulatory activity which may explain the high deviation in the numerical values of the analyzed parameters and thus lower ICC values. With respect to this, some of the individual FT-plot features 1–11 are more sensitive to the temporary changes of the cardiovascular system when deciding if the subject has atherosclerotic changes or not. On the other hand, the features 4–6 and 9 have $\kappa = 1$ (Fig. 3) as they produce negative diagnosis result for all the 30 measurements in our dataset.

Stress and short sleep are commonly known risk factors for cardiovascular diseases. Our results contain also indications that the deviations especially in the results of LDA classifiers may partially be explained by the changes in the activity of sympathetic nervous system: one test subject was stressed and had short sleep before two recordings, and the analysis results were close or below the threshold considered as a limit for atherosclerotic changes. Before third recording, the same test subject was doing physical exercise and the results were within our reference values reported in [8].

IV. Discussion

A. Comparison with ABI

Al-Qunaibet *et al.* have reported between-visit ICCs of 0.61 and 0.48 for left and right ABI, respectively [12]. A reliability coefficient defined as the ratio of the between-person variance to the total variance or ICC of 0.61 has been found in [13]. A better ICC of 0.87 has been reported in [14] for inter-week repeatability. Demir *et al.* have found that 12% of the participants displayed differences higher than 0.15 ABI points in three ABI measurements conducted within one week and ICCs of 0.808 single measurement and 0.927 averaged measurements [15]. As seen in Fig. 3, our day-to-day ICCs are 0.5–0.8 with most of the parameters.

B. Comparison with PW derived indices

Day-to-day repeatability of direct PW-derived indices, such as peripheral augmentation indices (pAIx), reflection indices, peak-to-peak times, and aging indices, has not been studied widely. Endes *et al.* report ICCs of 0.59 for the pAIx [16]. In our comparative study [17], direct PW-derived indices were extracted from the data recorded as PPG signals from index finger and second toe as well as dynamic pressure PWs from cubital fossa, wrist and ankles (posterior tibial artery) and the parameters having the best day-to-day repeatability provided the ICCs of 0.7–0.8. For the FT-plot derived features in this study, the ICCs based on the measurements conducted on different days vary mainly between 0.5–0.8 with wide confidence intervals (Fig. 3) and they are in the best cases at the same level as the best day-to-day ICCs found in [17] for direct PW derived features. Exceptions in the ICC values were observed with feature 11 (ICC below 0.2) and the LDA classifiers (ICCs around 0.45), but their κ values are at the same level with the features having higher ICCs. This indicates that the numerical values of the classifying variables

vary mainly in the healthy region of the possible values.

The repeatabilities of the FT-plot analysis and direct PW-derived parameters are roughly at the same level, but the FT-plot has better discrimination capability when dividing the subjects into healthy and atherosclerotic patients: AUCs of 0.8–0.97 were obtained in [8] for FT-plot derived features whereas AUCs in maximum of 0.88 were found for the direct PW-derived parameters [17].

C. Study limitations

The study population consisted of young adults having no diagnosed cardiovascular diseases or disorders, but the real status of their vasculature is unknown. The small size of the study population and the lack of real patients prevents the generalization of the results, so further repeatability studies with atherosclerotic patients and control subject of older age are needed.

V. Conclusions

This study concentrated on day-to-day or between-visit repeatablity of combined finger and toe PPG (FT-plot) analysis for finding atherosclerotic changes. Both ICCs and free-marginal multirater κ agreements were widely higher than 0.70, depending on the analyzed parameter. The reported results indicate that FT-plot has at least equal within-visit and between-visit repeatability compared with the ABI measurement and other PW based parameters. The results found in this and previous studies highlight the potential of the simple multichannel PPG based method. The method can be useful in the vascular screening in everyday use in health centers besides the ABI measurement and it could also facilitate preventive strategies against degenerative vascular diseases. However, the generalization of the results requires larger sample size and the measurements with real atherosclerotic patients.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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