DIAGNOSTICS OF PERIPHERAL ARTERIAL OCCLUSIVE DISEASE USING DIFFERENT CLASSIFICATION STRATEGIES IN ASSOCIATION WITH IMPEDANCE PLETHYSMOGRAPHICAL FEATURES

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Abstract: Peripheral arterial occlusive disease (PAOD) leads to a decrease of blood supply in the lower extremities. Consequences of this diminished blood circulation reach from restriction of mobility and endurance of walking to surgical removal of the affected limb. The early detection of PAOD can avoid the mentioned consequences by paving the way for conservative therapy. In clinical practice, PAOD is diagnosed by determination of ankle-brachial-index (ABI) and angiographical methods. The objective of the work presented here is the comparison of different classification strategies diagnosing PAOD by means of impedance plethysmography. The study included 44 control subjects and 29 patients suffering from PAOD. The diagnostics of PAOD is achieved by fuzzy-inference-systems (FIS), k-nearest-neighbor method, Bayes classifier, decision trees and neural nets. The comparison of these five classification methods for selected parameter set reveals that the highest values for sensitivity and specificity are achieved by application of FIS in association with the parameter set selected by a decision tree. Sensitivity is 100% and specificity is 93%. In conclusion, the early diagnostics of PAOD with impedance plethysmogram can be realised.

Introduction

Peripheral arterial occlusive disease (PAOD) leads to a decrease of blood supply in the lower extremities. Consequences of this diminished blood circulation reach from restriction of mobility and endurance of walking to surgical removal of the affected limb. The early detection of PAOD can avoid the mentioned consequences by paving the way for conservative therapy, e.g. movement training to stimulate the development of collateral vessels. In clinical practice, PAOD is diagnosed by determination of ankle-brachial-index (ABI) by means of Doppler ultrasound and angiographical methods. So far, the diagnostic information obtained from plethysmographical methods is based on single parameters describing magnitude and other features of the impedance plethysmogram (IPG) [1,2]. The objective of the work presented here is the comparison of different classification strategies using several parameters in order to diagnose PAOD by means of impedance plethysmography. So far, this has never been examined.

The advantage of this early diagnosis in comparison to the clinical accepted method of ABI determination would be that impedance plethysmography is not restricted to non-diabetes patients. Diabetes may be followed by media sclerosis that leads to false ABI values resulting in wrong diagnosis.

Materials and Methods

The study included 44 control subjects (11 women, 33 men; 49±19 years) and 29 patients (2 w., 27 m., 62±8 years) suffering from PAOD diagnosed by means of digital subtraction angiography. The extent of the disease is described by the classification after Fontaine as follows: 7 patients suffer from PAOD with the stage IIa, 20 are classified as IIb, 1 as III and 1 as IV. Patients were included without any restrictions except the appropriate electrode application was not achievable, e.g. in the case of necrosis or amputation.The IPGs were acquired by the 2 channel monitoring system multiscreen© (medis GmbH, Germany) using ECG spot electrodes for both legs. The measurement electrodes were placed 4cm below tuberositas tibiae and 4cm above malleoli medialis in the area of tibial artery posterior. The current electrodes (1mA, 100kHz) were placed at the upper thighs (above superficial femoral

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artery) and on both feet above dorsal artery of pedis (Figure 1).

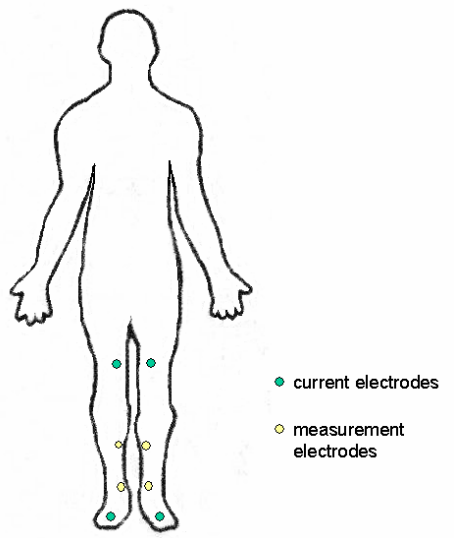

Figure 1: Electrode positions

The signals were acquired with a sampling frequency of 200Hz. The impedance signals and the electrocardiogram (ECG) were obtained simultaneously in supine position after 20min of acclimatisation at a room temperature of 25°C. The legs were raised for enhanced signal-to-noise-ratio. The measured signals were averaged over at least 100 heart cycles. The IPGs are described by different kinds of parameters. Figure 2 gives an overview of ordinary parameter definitions of the peripheral impedance plethysmogram.

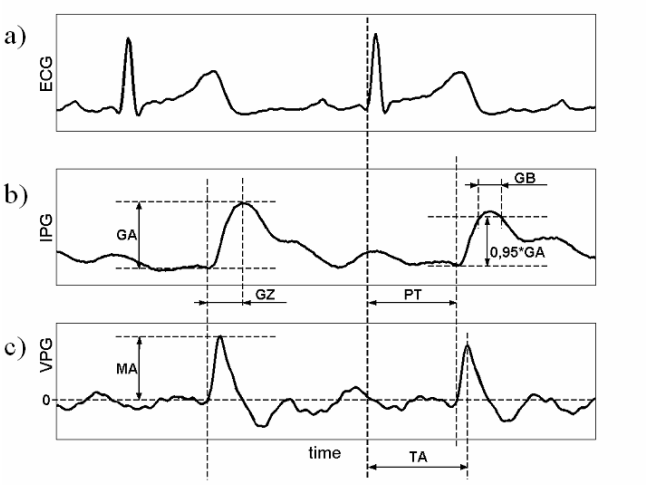

Figure 2: Parameter definitions of the peripheral impedance plethysmogram: a) ECG, b) impedance plethysmogram (IPG), c) velocity plethysmogram (VPG). The VPG is the first derivation of the IPG.

The following parameters are shown [2]: the amplitude (*GA*) of the peak, the width (*GB*) of the peak, the time (*GZ*) of reaching the peak, the propagation time (*PT*), the maximal slope (*MA*) of the anacrotic part of IPG (which is the maximum of the first derivation of IPG, called velocity plethysmogram (VPG)), the time (*TA*) between Q wave of ECG and *MA*. Moreover, the ratio (*IQ*) of *GA* and baseline electrical impedance (*Z0*) and the ratio (*AQ*) of *MA* and *Z0* are computed.

Moreover, methods of differential geometry are also used analysing the IPG [3]. Various parameters quantifying the curvature of the catacrotic part of the IPG are computed by means of the curvature function κ that is defined for a function y by:

$$\kappa = \frac{y''}{\sqrt{\left(1+y'^2\right)^3}} \qquad (1)$$

These parameters are amplitudes, time points and areas of κ waves. Adequate normalisation has been undertaken for all parameters entering the classification process.

Another possibility characterising the catacrotic part is the falling straight line which is drawn from the top of the IPG to the following zero crossing of the IPG [4].

Figure 3 illustrates the falling straight line at a control subject.

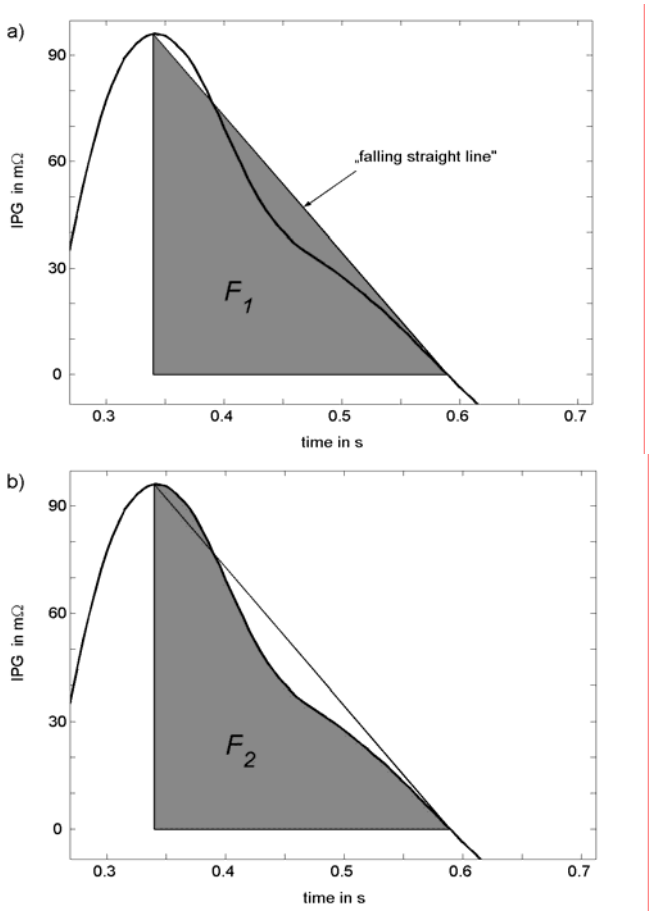

Figure 3: IPG of a control subject with the falling straight line. a) area F_1 below the falling straight line in the catacrotic part of the IPG; b) area F_2 below the IPG

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The areas F_1 and F_2 are used to quantify the curvature of the catacrotic IPG part by computation of the ratio FV of these areas.

$$FV = \frac{F_2}{F_1} \qquad (2)$$

Moreover, the time-frequency-distributions obtained by applying continuous wavelet transform (116 wavelets) and different transforms of Cohen´s class (Wigner, exponential and conus kernel) are analysed. Coefficients normalised by means of the maximum coefficient values are extracted out of anacrotic and catacrotic parts of the IPG. In summary, 150 parameters are computed out of the IPG to diagnose PAOD.

For parameter selection, two steps are applied. First of all, the U-test of Wilcoxon, Mann and Whitney is used to determine the significant parameters ($p<0.01$) that are adequate to distinguish between control subjects and patients suffering from PAOD. This test is used because no information on the distributions have to be known. For further selection of parameters, principal component analysis (PCA) and a decision tree are employed deriving different feature sets.

The diagnostics of PAOD is achieved by three kinds of fuzzy-inference-systems (FIS), k-nearest-neighbor method, Bayes classifier, decision trees and neural nets (MLP – multi layer perceptron). Different kinds of FIS means that one FIS is based only on expert knowledge (Expert), another FIS is also based on this knowledge whereas parameters of the membership functions are optimised using a backpropagation algorithm (Anfis – adaptive neuro FIS). The last FIS is completely built up by means of cluster analysis (Genfis – generated FIS). The implementation is done within Matlab© (The MathWorks, Inc.)

The comparison of the classification strategies is achieved by determination of sensitivity (Se) and specificity (Sp). Cross validation is performed.

Results

The test by Wilcoxon, Mann and Whitney revealed 13 out of 150 parameters that show significant differences between control subjects and patients suffering from PAOD:

- Number of extreme values in catacrotic IPG: *AnzEx*
- Number of extreme values in catacrotic VPG: *AnzWp*
- Area ratio: *FV*
- Amplitudes of the first, third and fifth maximum of the curvature function κ; normalised by *GA*: χ_1, χ_3, χ_5
- Ratio of *GA* and *Z0*: *IQ*
- Ratio of *MA* and *Z0*: AQ
- Area below κ; normalised by heart rate: A_{norm}
- Arc length of catacrotic IPG, normalised by *RR* interval in ECG: S_{norm}
- Percentage of time points of extreme values of κ in catacrotic IPG in relation to the *RR* interval in: $t\chi_1$, $t\chi_2$, $t\chi_3$

The parameter selection by PCA and decision tree reveals different feature sets. The first principal component describes 94% of the variance which is inherent in all significant parameters. The first principal component is almost identical to A_{norm}. A decision tree selects three parameters to be best adequate entering the classification process: *FV*, *IQ*, χ_1.

Five classification procedures are applied using the different parameters sets selected by PCA and decision tree. The following tables show the corresponding classification results.

Table 1: Classification results diagnosing PAOD using the parameter set selected by PCA

Classifier	Sort	Se	Sp	Efficiency
FIS	Expert	90%	84%	86%
	Anfis	90%	86%	88%
	Genfis	76%	89%	84%
decision tree		87%	89%	88%
Bayes-classifier		90%	84%	86%
k nearest-neighbour	k=1	79%	91%	86%
neural net	MLP	90%	86%	88%

Table 2: Classification results diagnosing PAOD using the parameter set selected by a decision tree

Classifier	Sort	Se	Sp	Efficiency
FIS	Expert	1000%	91%	95%
	Anfis	100%	93%	96%
	Genfis	93%	91%	92%
decision tree		79%	84%	82%
Bayes-classifier		93%	93%	93%
k nearest-neighbour	k=1	97%	89%	93%
neural net	MLP	97%	89%	92%

The results reveal that the Anfis-classifier in combination with the parameter set selected by a decision tree is most adequate for PAOD diagnosis with IPG. Table 3 depicts the rules established by a human expert whereas the structure of this Anfis is summarised by table 4.

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Table 3: Rules of Anfis in combination with the parameter set selected by a decision tree. The rules have the same weight for PAOD diagnosis.

Rules
1. **If** (*FV* is low) **or** (*IQ* is high) **or** (χ_1 is high) **then** (Result is healthy) (Factor: 1)
2. **If** (*FV* is high) **or** (*IQ* is low) **or** (χ_1 is low) **then** (Result is PAOD) (Factor: 1)

Table 4: Structure of Anfis in combination with the parameter set selected by a decision tree

Structure	
Name	= paod_finalAnfis_mod_OR
Type	= sugeno
NumInputs	= 3
InLabels	= *FV* *IQ* χ_1
NumOutputs	= 1
OutLabels	= Result
NumRules	= 2
AndMethod	= min
OrMethod	= max
ImpMethod	= min
AggMethod	= max
DefuzzMethod	= wtaver

The graphical representation of this structure is given in Figure 4. On the left hand side the membership functions of input parameters are shown. On the right hand side the output parameters can be seen whereas 0.5 is implemented as the threshold discriminating between control subjects and patients with PAOD. If the output is smaller than 0.5 the diagnosis is set to "healthy", otherwise to "PAOD".

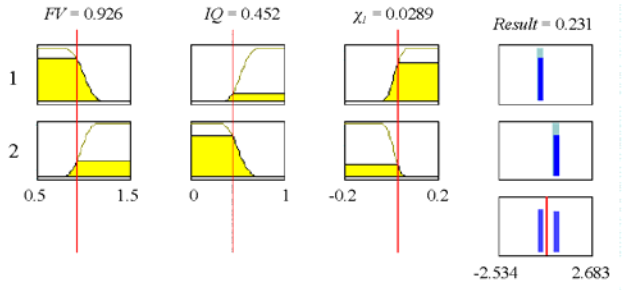

Figure 4: Graphical representation of the Anfis classifier that leads to the highest diagnostic efficiency (in combination with the decision tree parameter set).

As an example, figure 4 shows *FV* = 0.928, *IQ* = 0.452 and χ_1 = 0.0289 which lead to the *Result* of 0.0289.

Discussion

Parameters revealing significant differences between control subjects and patients suffering from PAOD are extracted out of anacrotic and catacrotic IPG. This result is in accordance to [1,2,3,4,5]. Besides conventional features like *IQ* it is also shown that features computed by means of differential geometry lead to an enlargement of significant parameter vector.

The examinations in the time-frequency domain turn out in no significant parameters which is against our expectations.

The features that are most adequate for diagnostics quantify the curvature of the catacrotic part of the IPG whereas different parameter sets are chosen by the selection methods. Moreover, the normalised amplitude IQ is also seen suitable for classification.

The comparison of five classification methods for each parameter set reveals that the highest values for sensitivity and specificity are achieved by application of Anfis in association with the parameter set selected by a decision tree. Sensitivity is 100% and specificity is 93% (efficiency: 96%). In opposition to that, the decision tree leads to the following classification results: sensitivity of 79% and a specificity of 84% (efficiency: 82%). Three control subjects are wrongly diagnosed having PAOD whereas the output values of Anfis are 0.72, 0.56 and 0.54 suggesting further clinical evaluation due to this unclear outcome.

PCA is less suitable for parameter selection than decision trees that take the discrimination properties of features into account, not only the contributing variance to the parameter set. The advantage of using knowledge of human experts in combination with optimised fuzzy membership functions is seen as the main reason for the good performance of Anfis related to other classification methods.

Earlier classification results regarding PAOD diagnosis by means of IPG led to maximal values of sensitivity = 91% and specificity = 90% [1,6]. The improvement reported by this paper is mainly due to the introduction of differential geometry for feature extraction. The inclusion of the knowledge of human experts has already been mentioned.

Thus, the early diagnosis of PAOD can be accomplished by using IPG. This leads to more reliable information on peripheral circulation at patients suffering from diabetes (media sclerosis).

Conclusion

The application of various methods regarding parameter selection and classification lead to different values of sensitivity and specificity. Highest values are achieved by means of the FIS (Anfis) in association with parameters selected by a decision tree. Thus, the early diagnostics of PAOD with IPG can be realised.

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