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Detection of hemodynamic adaptations during impending syncope: Implementation of a robust Algorithm based on Pulse Arrival Time Measurements only

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Abstract—**Syncopes are a major public health concern since they can cause severe injuries e.g. by associated falls. We previously demonstrated the feasibility of syncope prediction based on the pulse arrival time (PAT) analysis. Importantly, algorithms for early detection of impending syncope need to be robust against measurement noise, in particular photo-plethysmography (PPG) artifacts, causing false detection.**

We introduce in this work an algorithm concept to deal with artifacts as well as to detect the onset of syncope based on tracking of relative PAT changes only. Our method has been shown useful to improve detection performance for measurements during impending syncope in patients undergoing head-up tilt table testing which might improve syncope prediction.

I. Introduction

Syncope is a transient, self-limited loss of consciousness, usually leading to falling [1,2]. The onset of syncope is relatively rapid and the subsequent recovery is spontaneous, complete and usually prompt. The underlying mechanism is a transient global cerebral hypoperfusion. Syncopal episodes are typically brief. Complete loss of consciousness in vasovagal syncope is usually no longer than 20s in duration. In some forms of syncope there may be a pre-monitory period in which various prodromal symptoms, (e.g. light-headedness, nausea, sweating, weakness and visual disturbances) offer warning signs for an impending syncope. However, patients often neglect these indications. The common prodromes or warning symptoms suggestive of vasovagal syncope are less frequent in elderly [3].

Based on the Framingham study [4], the incidence of a first report of syncope was 6.2 per 1000 person-year, which means a 42% prevalence of syncope during the life of a person living 70 years (assuming constant incidence rate over time). The incidence increases with age starting at the age of 70 (23% prevalence during a 10-year period in the population older than 70). Other studies reported the prevalence of syncope during the life of a person being rather around 20% [2].

Head-up tilt table test (HUTT) is the standard diagnostic method, in which there is an attempt to induce syncope during a passive standing exercise of about 30 min. Different types of syncope are diagnosed based on a combined analysis of the heart rate (HR) and systolic blood pressure (SBP) responses during the test [1]. Sporadic events are diagnosed typically via continuous measurements with implants monitoring electrocardiogram (ECG). Isometric counter-pressure maneuvers can help to prevent blood pressure (BP) decrease, which allow the patient to avoid or delay consciousness loss. Tilt training is also an established technique used to improve patient's life quality.

Warning devices could help a patient to apply these counter-maneuvers earlier e.g. by making a patient aware of an impending event. An approach monitoring BP continuously showed good results to predict syncope [5]. However, with existing BP measurements such as the vascular clamp method, this approach cannot be realized in ambulatory scenarios. Therefore, research has been done on BP surrogates, with promising results emerging for PAT [6-12]. PAT increases consistently and significantly during a critical BP decrease [11-13].

This paper discusses an algorithm strategy to infer the onset of a syncope using the PAT approach robustly (section III). Based on clinical data acquired during HUTT (section II), it presents the results (section IV) on the phase of syncope onset, the challenge and solution of optimized artifact removal and finally the detection performance based on optimized parameters to detect syncope onset. Section (V) and (VI) discuss and conclude based on our results.

II. Data Acquisition and Experimental Methods

A. *Clinical Study and Database Description*

Data of 55 patients with a history of unexplained faints have been acquired during HUTT (ClinicalTrials.gov Identifier: NCT01262508). The study was approved by the local ethical committee. All patients gave written informed consent to participate.

HUTT consisted of 3 phases: 1.) at least 15 min resting period in supine position, 2) passive standing of the patient at 70° and 3.) a resting period in supine during which the patient recovered from the test. If syncope occurred during phase 2, patients were immediately tilted back to the horizontal position. If syncope did not develop during the initial 20 minutes after tilt, 400 µg of glycerol trinitrate (GTN) were administered sublingually while the upright position was maintained for additional 15 min. The patient's posture and symptoms, such as dizziness, sweat, tremor, etc., were recorded during the procedure. The test was considered positive (po) if the patients experienced syncope in the presence of bradycardia, hypotension or both as defined by the European Society of Cardiology [1].

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Data of 44 patients could be finally included with their characteristics shown in Table I. Exclusion of data sets refer to BP decreases not associated with neurally mediated syncope (NMS) or problems with data acquisition, such as the absence of the reference BP or low signal quality in BP and ECG signals.

TABLE I
PATIENT CHARACTERISTICS

	Tilt positive (#21)	Tilt negative (#23)
Age [y]	55±19	61±20
Weight [kg]	85±16	73±13
BMI [kg/m2]	26.9±4.6	25.5±4.8
Male/female	13/8	14/9
GTN yes/no	19/2	17/6

B. *Experimental Setup*

As previously described in [12], SBP and other hemodynamic parameters were monitored with the "Taskforce Monitor" [18], which measures two ECG leads (@ 500 Hz), an Impedance Cardiography (ICG) signal (@50 Hz) as well as continuous non-invasive blood pressure BP (@50Hz). ECG-II lead (@ 500 Hz) and a PPG signal (@126 Hz, Standard SpO2 – sensor at the index finger) to extract PAT were measured by a Philips MP50. Data from both systems were synchronized in time via detected R-peaks in one of each ECG signals from the Taskforce and MP50 with an accuracy of less than 1ms.

III. ALGORITHM APPROACH

A. *Algorithm Overview*

Figure 1 depicts the block-diagram of the implemented signal processing scheme to detect an impending syncope. There are essentially three steps consisting of 1.) the detection of characteristic features from the ECG and PPG to extract HR and several PAT measures, 2.) an efficient scheme to remove automatically outliers of HR and PATs followed by a smoothing scheme and finally 3.) an algorithm to infer a significant relative change in PAT.

For patients with test positive, the detection result was considered true positive (TP), if an alarm was generated after the start of the BP decrease before syncope, whereas false positive (FP) was assigned when an alarm is generated outside of this time window. For patients with test negative, true negative (TN) events were assigned if no alarm was generated during standing position, whereas false negative (FN) events were assigned when alarms are generated.

B. *Pulse Detection and Feature Extraction*

In the very first step of the algorithm consecutive pulses within the PPG and ECG signal are identified. ECG-R-peaks were detected by a Pan-Tompkins algorithm [14]. Pulses in the PPG signal were located with a slightly adapted algorithm [15]. PPG-pulse onset was defined as the lowest minimum before the PPG-peak or the upslope. Since PPG peaks and pulse onsets are sensitive to artifacts, the relative heights at 20%, 50% and 80% of the PPG pulse amplitude were also determined. Therefore, five different PATs were extracted from both signals defined as time interval between the R-peak of the ECG and the characteristic points in the PPG systolic waves: PATfoot, PAT20, PAT50, PAT80 and PATmax. HR was inferred from consecutive detected R-peaks in the ECG.

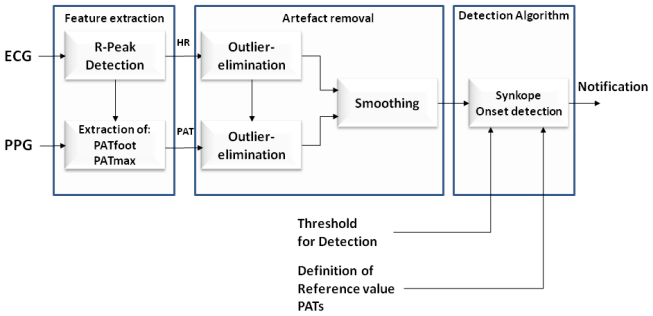

Figure 1: Signal processing steps to detect an impending syncope consisting of: 1) feature extraction, 2) Artifact removal and 3) Syncope onset detection

C. *Artifact Removal*

It is well-known that the PPG signal is prone to artifacts mainly caused by movements, in particular with a probe at the finger. Therefore, special emphasis was given to an efficient algorithm concept to automatically and robustly detect noisy segments in the PPG and ECG features. Different approaches in artifact handling have obviously a crucial impact on the overall detection performance. The implemented concept is described in [16], which offers a sensitivity of 77.84% and a specificity of 75.88% for artifact detection. Artifact periods were typically much less than 30 s in duration, which is well below the typical characteristic times for syncope onset (> 1 minute, Table II).

D. *Interpolation and smoothing*

After removal of periods with artifacts, a linear interpolation scheme was implemented. The minimal sampling frequency was determined by an analysis of a PCA-filtered characterization of all syncope onsets (section III, A) giving a minimal sampling frequency of 0.022 Hz. Finally, we used an interpolation at the frequency of 2 Hz, well above the required minimal sampling frequency.

High frequency noise of the PAT was reduced in a consecutive step with the help of two different types of low pass filters: 1) a 10 seconds window moving average filter or 2) a Butterworth low pass filter with a 0.05Hz cutoff frequency.

E. *Syncope Onset Detection Algorithm*

The syncope onset detection algorithm is based on tracking of relative PAT changes only (no HR included) during the HUTT standing exercise. We used the normalized measure of PAT (nPAT):

$$nPAT = PAT/PATref \quad (1)$$

with PATref as one-minute PAT average in the second minute after the patient was tilted up. The feasibility of the basic concept was shown in [9], where syncope onset was detected in case nPAT crosses a threshold (SR) of 1.1. The described sequence is visualized in Figure 2 for an example case, where the upper diagram shows SBP (blue) and nPATfoot (black). PATfoot reference is determined in the time window marked by a black bar, the threshold SR by a red line at 1.1. If nPATfoot crosses SR=1.1, this moment is interpreted as "syncope onset is detected".

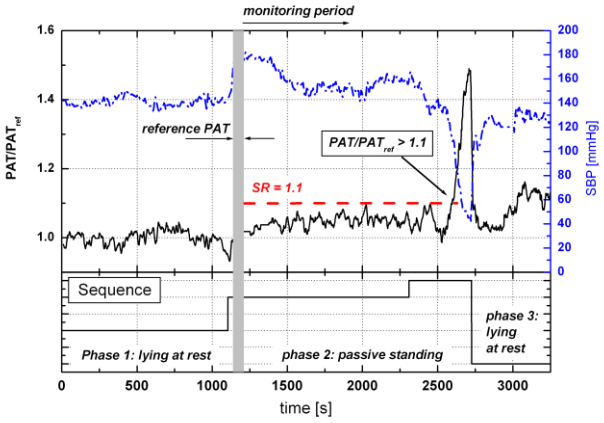

Figure 2: upper diagram: nPATfoot (black) and SBP (blue) during HUTT. The reference PATfoot was determined as 1 min average (black bar) of PATfoot during a period 1 min after tilt. Lower diagram: phases of HUTT in our experiments.

IV. Results

A. *Characterization of PAT responses during Syncope onset*

Typical responses of syncope onset were characterized using data of patients with syncope episodes by investigating PATs segments of 150 seconds before tilted back. The extracted segments were cleaned from noise by a PCA – filtering procedure removing high frequency components related to short-term PAT changes. For that purpose, PAT signal segments were re-sampled at 8 Hz and concatenated in a matrix to apply a Principal Component Analysis (PCA). The first 3 PCA components contained more than 80 % of variance for all segments and were used to construct filtered PAT-responses. Based on a 3dB criterion in the power spectra the typical response times have been determined. They range from 90 s to 117 s corresponding to a highest frequency of 0.011 Hz (Table II). This frequency response translates into a minimum sampling frequency needed e.g. for interpolation of 0.022 Hz. The PAT-responses of all patients show the behavior of an integrator as defined in system theory.

TABLE II
MAXIMUM 3DB FREQUENCIES OF THE POSITIVE HUTT RECORDS FOR EACH PAT.

	PAT max	PAT 80	PAT 50	PAT 20	PAT Foot
Max f [Hz]	0.0085	0.0105	0.0096	0.011	0.011
Period [s]	117.8	95.6	104.4	90.5	91.3
Power ratio [%]	1.22	1.33	1.27	1.34	1.32

B. *PAT-HR-responses tilt positive vs. tilt negative*

Figure 3 shows the HR-PATfoot-response of two patients during passive standing. The plot at the left refers to a patient with tilt positive (PATfoot reference of 221 ms and HR reference of 76 min^{-1}), where a significant increase accompanied with passing of the 10% increased PATfoot threshold is obvious. The diagram on the right shows the result for a patient with tilt negative (PATfoot reference of 253 ms and HR reference of 73 min^{-1}), where during the complete phase PATfoot remains well below the critical PATfoot of 279 ms. In both cases, a state change is visible with the increase in HR triggered by GTN administration.

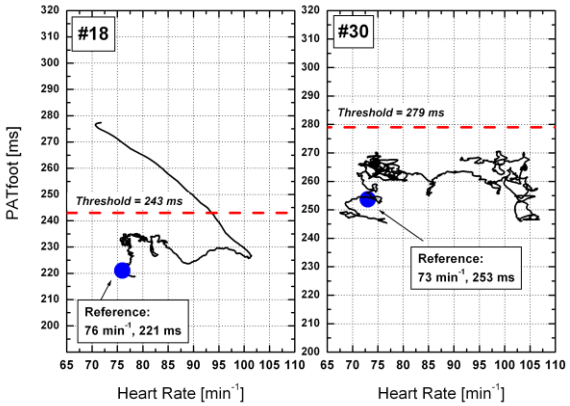

Figure 3 HR-PATfoot-responses of two patients during passive standing, PATfoot threshold was calculated as 10% above PATfoot reference; left picture: patient with tilt positive; right picture: patient with tilt negative

C. *Detection performance using different smoothing algorithm and optimized thresholds*

In [11], we found as optimal detection threshold SR=1.1. However, in the current work a different experimental setup and a different location of the PPG sensor was used. Additionally, we included several PAT measures possibly having different optimal detection thresholds as well. Therefore, we determined optimal SR via analysis of the receiver operating characteristics (ROC) for each PAT measure separately. Besides analyzing raw PAT signals we also investigated two noise removal strategies, i.e., an average filter and a Butterworth filter. The detection performance is shown in Table III.

For the raw signals, different optimal thresholds for the different PATs have been found ranging from 1.13 to 1.19. The best detection results were obtained for PAT50 with sensitivity (SE) of 90.5% and specificity (SP) of 83%. The average prediction time was 82±78 s.

Optimal thresholds using a moving average filter increased from 1.17 to 1.24 again with the highest value for PATfoot. An improvement of SE was observed, with particular emphasis to PATfoot where SE increased from 62% to 81% and SP remained almost unchanged. The detection times decreased significantly to (66 to 74) s except for PATfoot and PATmax.

SR decreased even further using a Butterworth filter to 1.11 – 1.13. Best result here is for PAT20 with a SE of 95% and SP of 79% and a prediction time of 74±70.5 s.

Obviously, the detection performance is in general better for PATs not at the extremes, i.e., PATfoot and PATmax. The best result in terms of prediction time was 109s using a Butterworth filter for PATfoot, however, compromised by a SE of 85% and SE of 75%. The use of the filters improved the SE performance in particular for the PATfoot where a significant increase from 62% to 85% was observed. This effect has not been found for PATmax and only marginally for PAT20, PAT50 and PAT80.

TABLE III
IMPACT OF DIFFERENT SMOOTHING STRATEGIES ON ALGORITHM PERFORMANCE

		PATfoot	PAT20	PAT50	PAT80	PATmax
Filter Raw	Threshold	1.19	1.14	1.13	1.14	1.13
	SE (%)	61.90	85.71	90.48	80.95	61.90
	SP (%)	78.26	75.00	83.33	82.61	64.00
	PPV (%)	72.22	75.00	82.61	80.95	59.09
	Prediction time (s)	85.53	78.72	81.94	81.94	82.00
	STD (s)	78.24	72.26	77.66	77.66	99.11
Moving Average	Threshold	1.24	1.17	1.17	1.17	1.18
	SE (%)	80.95	95.24	90.48	85.71	57.14
	SP (%)	79.17	79.17	83.33	79.17	79.17
	PPV (%)	77.27	80.00	82.61	78.26	70.59
	Prediction time (s)	83.82	74.24	66.39	66.46	80.03
	STD (s)	78.35	70.22	56.70	59.53	94.31
Butterworth	Threshold	1.13	1.11	1.11	1.11	1.12
	SE (%)	85.71	95.24	90.48	90.48	61.90
	SP (%)	75.00	79.17	83.33	79.17	75.00
	PPV (%)	75.00	80.00	82.61	79.17	68.42
	Prediction time (s)	109.97	74.52	77.71	65.70	80.99
	STD (s)	90.12	70.45	71.78	60.01	91.05

V. DISCUSSION

In the present study we found that the characteristic times of syncope onset are in the order 1.5 to 2 min. before syncope, giving often a relatively long time window to warn a patient when a critical PAT increase is detected. The observed PAT responses follow a system response similar to an integrator.

Previous results on typical HR-PAT-responses discussed in [17] could be confirmed in this larger study, where PAT increases significantly and consistently for tilt positive patients. Different areas in the HR-PAT plot are assigned to different risk – levels [17], where a detection based on PAT only seemed feasible.

This has been investigated using a simple algorithm that tracks the relative changes of PAT measures only, taking into account different PAT measures extracted from the PPG systolic signal segment. PATfoot and PATmax measures performed worse in terms of detection performance when compared to PAT20, PAT50 and PAT80. This might be related to a higher robustness in the extraction of these features. The exact detection of PPG onset is sometimes difficult in particular during low blood pressure. The compromised performance of PATmax might be due to the typically broad PPG maximum giving a less well defined characteristic feature accompanied with a higher variance of PATmax.

Smoothing strategies helped to improve the detection performance with a reasonably high SE and SP. Using only the PAT measure, we found syncope onset detection times in a range of 66 to 85 s however, associated with very high variances. The results are comparable with those found previously in [11]. This refers to prediction times of more than 2 minutes or only few seconds.

VI. CONCLUSION

Our results confirm that PAT might be an easy-to-measure parameter, which allows a reliable prediction of impending syncope. Our findings suggest that automatic robust artifact removal and implementation of a linear interpolation scheme are useful techniques in the improvement of signal quality and "surrogate blood pressure" monitoring during impending syncope in patients undergoing head-up tilt table testing. Therefore, herein we present a robust algorithm based on pulse arrival time measurements which might improve syncope prediction. This could be implemented in applications such as safeguard devices protecting patients at risk from recurring syncope.

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