Experimental paper

Detection of a spontaneous pulse in photoplethysmograms during automated cardiopulmonary resuscitation in a porcine model

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Abstract

Introduction: Reliable, non-invasive detection of return of spontaneous circulation (ROSC) with minimal interruptions to chest compressions would be valuable for high-quality cardiopulmonary resuscitation (CPR). We investigated the potential of photoplethysmography (PPG) to detect the presence of a spontaneous pulse during automated CPR in an animal study.

Methods: Twelve anesthetized pigs were instrumented to monitor circulatory and respiratory parameters. Here we present the simultaneously recorded PPG and arterial blood pressure (ABP) signals. Ventricular fibrillation was induced, followed by 20 min of automated CPR and subsequent defibrillation. After defibrillation, pediatric-guidelines-style life support was given in cycles of 2 min. PPG and ABP waveforms were recorded during all stages of the protocol. Raw PPG waveforms were acquired with a custom-built photoplethysmograph controlling a commercial reflectance pulse oximetry probe attached to the nose. ABP was measured in the aorta.

Results: In nine animals ROSC was achieved. Throughout the protocol, PPG and ABP frequency content showed strong resemblance. We demonstrate that (1) the PPG waveform allows for the detection of a spontaneous pulse during ventilation pauses, and that (2) frequency analysis of the PPG waveform allows for the detection of a spontaneous pulse and the determination of the pulse rate, even during ongoing chest compressions, if the pulse and compression rates are sufficiently distinct.

Conclusions: These results demonstrate the potential of PPG as a non-invasive means to detect pulse presence or absence, as well as pulse rate during CPR.

1. Introduction

High-quality cardiopulmonary resuscitation (CPR) requires minimizing interruptions to chest compressions. Pulse checks, even during potentially perfusing rhythms, may lead to prolonged interruptions which can negatively impact outcome. In particular, manual palpation can be time-consuming and is known to be unreliable even if performed by expert clinicians. Therefore, a rapid, objective method to detect the return of spontaneous circulation (ROSC) would be a valuable asset.

Monitoring of end-tidal CO₂, invasive blood pressure, or central venous oxygen saturation allows for a more objective assessment of ROSC, but requires a secured airway or placement of catheters. Trans-thoracic impedance (TTI) measurements and near-infrared spectroscopy (NIRS) are non-invasive, but TTI is strongly influenced by chest compressions and NIRS responds slowly upon ROSC. Despite the challenges, and even though...
determining whether an observed rhythm is life-supporting remains a clinical, situational assessment, such techniques can provide valuable support.

CPR guidelines mention the potential of photoplethysmography (PPG) to support ROSC detection. A PPG sensor, such as the well-known finger clip commonly used to monitor arterial oxygen saturation, measures transmission of light through tissue to detect cardiac-induced pulses in tissue blood volume. PPG is generally an easy-to-use and non-invasive technique to measure spontaneous pulse and other hemodynamic parameters, but using PPG to detect spontaneous pulse during CPR is not common clinical practice. Interpretation of the PPG signal can be compromised by low perfusion, temperature effects, delays by signal processing, and motion artifacts. It may also be difficult to determine if pulses in the PPG signal should be attributed to chest compressions or to spontaneous cardiac activity.

In this study, we investigated the potential of PPG to detect the presence and rate of a spontaneous pulse during CPR. We retrospectively analyzed PPG and arterial blood pressure (ABP) signals, simultaneously recorded in pigs undergoing automated CPR. PPG-based detection of a spontaneous pulse during CPR is a first step toward determining the potential use of PPG to support ROSC detection.

2. Methods

2.1. Study design

An automated-CPR animal study was conducted on 16 pathogen-free female Yorkshire pigs, with an average age of 10.7 weeks (range 7–12 weeks) and an average weight of 30 kg (range 25–36 kg). All animals received care in compliance with the Dutch Animal Experimentation Law and the Standard Operation Procedures of the Central Animal Laboratory of the Radboud University Nijmegen Medical Center, where the experiments were conducted. The Radboud University Animal Ethical Committee approved the protocol. The experiments were designed and executed using the Utstein-style guidelines. PPG-based detection of a spontaneous pulse during CPR was a secondary objective of the animal experiments, which were designed to study characteristics of automated-CPR and their relationship to ROSC. Only data pertinent to the PPG study are reported here.

2.2. Anesthesia and management

Animals received intramuscular (IM) premedication with ketamine (10 mg/kg), midazolam (1 mg/kg), and atropine (50 μg/kg). After intravenous (IV) access was gained, propofol (2–3 mg/kg) was administered, and the animals were orally intubated and moved to the operating table. Anesthesia was maintained with isoflurane (0.5–1% end-tidal) via a SmartVent 7900 Anesthesia Ventilator (Datex-Ohmeda, Finland), and by IV infusions of midazolam (0.6 mg/kg/h), sufentanil (5 μg/kg and 10 μg/kg/h), and vecuronium (0.2 mg/kg and 0.4 mg/kg/h). Amoxicillin (20 mg/kg) was administered IV.

Animals were ventilated through a bacteria-virus filter using an FiO2 of 0.4 and 6–7 cmH2O PEEP, with tidal volumes of 275–300 ml at a rate of about 20 min−1 to achieve end-tidal CO2 partial pressures of 30–40 mmHg. Five minutes before induction of cardiac arrest, FiO2 was increased to 1.0. Following cardiac arrest, ventilation was continued manually with an FiO2 of 1.0 via a pediatri- c 500 ml self-inflating bag, without isoflurane, and sufentanyl infusion was stopped.

During instrumentation, warm normal saline (0.9% NaCl) was administered to maintain a mean right-atrial pressure of 6–10 mmHg. Blood loss was compensated for by IV bolus of Voluven. Temperature was controlled with a water-filled mattress. Euthanasia was performed with 500 mg pentobarbital (IV bolus).

2.3. Instrumentation and monitoring

Instrumentation and monitoring was performed once the animal was installed on the operating table. End-tidal CO2 partial pressure, and airway pressure, flow and volume were monitored using spirometry (IntelliVue MP50 Patient Monitor, Philips, Andover, MA, USA). Via cutdown, a 20 G 16 cm cannula was placed in the left ilio-femoral artery for sampling purposes. Mikro-Tip® Pressure Catheters (Model SPC-360S, Millar Instruments, Houston, TX, USA) connected to a PCU-2000 Pressure Control Unit (Millar Instruments, Houston, TX, USA) were placed via the right femoral artery and vein, such that their tips lay just distal to the aortic arch (to measure arterial blood pressure, ABP) and in the inferior vena cava just proximal to the right atrium (to measure central venous pressure), respectively. Via cutdown to the right internal jugu- lar vein, a Swan-Ganz catheter (Edwards Lifesciences, Irvine, CA,
USA) was positioned in the pulmonary artery such that wedge was achieved. A flow sensor (Transonic® Animal Research Flowmeter T206, Transonic Systems Inc., Ithaca, NY, USA) was placed around the right common carotid artery. Catheter positions were confirmed by visual inspection at autopsy.

Raw red (660 nm) and near-infrared (900 nm) PPG signals were obtained using a forehead reflectance pulse oximetry probe (NellcorTM Oxisensor II RS-10, Covidien-NellcorTM, Dublin, Ireland), controlled by a custom-built photoplethysmograph. The probe was customized to enable placement by suturing between the nostrils (Fig. 1b), because it is a relatively stable measurement site in terms of motion, and it allows tight fixation of the probe to the skin.

PPG and ABP waveforms were recorded simultaneously using a 16 bit digital data acquisition card (DAQ) (NI USB-6259, National Instruments, Austin, TX, USA). A LabVIEW® (National Instruments, Austin, TX, USA) program controlled the DAQ.

### 2.4. Experimental protocol

The experimental protocol is outlined in Fig. 1c. After instrumentation, a 10 min baseline period, including blood gas analysis, documented the physiological condition of the animal. Subsequently, cardiac arrest was induced with a trans-thoracic electrical shock (90V, 50 Hz for 3 s, using a proprietary fibrillation device), followed by a 90 s hands-off period. CPR was then performed for 20 min, using a rhythm of thirty compressions and two ventilations (30:2 ratio). Chest compressions were delivered by a LUCAS™2 Chest Compression System® (Physio-Control Inc/Jolife AB, Lund, Sweden) or by a custom-built automated CPR device, which was randomly assigned. The compression rate was 100 min⁻¹, and the ventilation pause lasted 3.8 s. No vasoactive medication was given during this period. After 20 min of CPR, rhythm analysis was performed and defibrillation attempted at 4 J kg⁻¹ if appropriate, using the HeartStart MRx Monitor/Defibrillator (Phillips, Andover, MA, USA) with Adult Plus Multifunction Electrode Pads M3713A (Phillips, Andover, MA, USA). CPR was then immediately reinitiated for 2 min, after which the next rhythm analysis and pulse check were performed. If ROSC was diagnosed, CPR was stopped. If ROSC was not achieved, up to three additional 2-min cycles were performed. Starting after the first rhythm analysis, pediatric advanced life-support guidelines were used for medication, volume management, and critical care interventions.³⁴ Infusion of sufentanil was also restarted. Measurements were continued up to 20 min post-ROSC. After that, if or when ROSC was not achieved after four 2-min cycles, the experiment was ended, the animal was euthanized, and an autopsy was performed.

Blood gases were analyzed from samples drawn simultaneously from the left femoral artery and the right atrium. Blood samples were drawn after 5 min of baseline, at the beginning and end of CPR, 2 min after a second and fourth defibrillation attempt, and at the beginning and end of the post-ROSC period. Samples were analyzed on-site via two i-STAT® Blood Gas Analyzers (Abbott Point of Care Inc., Princeton, NJ, USA).

### 2.5. Data analysis

The PPG signal, reported in volts, is proportional to the detected light intensity, i.e., an increase in blood volume in the sampled tissue results in a decrease in the PPG signal. The PPG signal was limited in frequency to 11 Hz to reduce the influence of noise. Only the near-infrared PPG signal has been analyzed, because it had a better signal-to-noise ratio than the red PPG signal.³⁵

Both PPG and APB signals were analyzed retrospectively with special interest in the period before and after ROSC. The PPG time traces were analyzed to detect the presence of a spontaneous cardiac pulse. The observations were validated by comparing the PPG signal to the ABP signal. Furthermore, to gain more insight into the origin of the signals, spectrograms were plotted, which show which frequencies are present in the signals as a function of time. These spectrograms were obtained via Fourier transformation of consecutive segments of the time traces.

### 3. Results

We used PPG and ABP data from 12 out of 16 animals. PPG signals from the first four animals were excluded because of interference between the study probe and the clinical saturation probes. This was resolved by increasing the distance between the probes. Table 1 presents baseline and CPR data of the 12 animals included in our analysis, and the post-ROSC data of the nine animals with ROSC in this group.

### Table 1: Physiological variables of the 12 animals included in the study. Pulse rate, arterial blood pressure, and end-tidal CO2 were determined during the last 30s of baseline, 20 min CPR, and 20 min post-ROSC.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline (12 animals)</th>
<th>20 min CPR (12 animals)</th>
<th>20 min post-ROSC (9 animals)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Min</td>
<td>Max</td>
</tr>
<tr>
<td>Pulse rate [BPM]</td>
<td>93 (17)</td>
<td>64</td>
<td>124</td>
</tr>
<tr>
<td>Arterial blood pressure [mmHg]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>107 (10)</td>
<td>97</td>
<td>132</td>
</tr>
<tr>
<td>Systolic</td>
<td>122 (14)</td>
<td>109</td>
<td>157</td>
</tr>
<tr>
<td>Diastolic</td>
<td>94 (10)</td>
<td>80</td>
<td>114</td>
</tr>
<tr>
<td>Arterial blood</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaO2 [kPa]</td>
<td>60 (17)</td>
<td>27</td>
<td>77</td>
</tr>
<tr>
<td>pH</td>
<td>7.50 (0.04)</td>
<td>7.44</td>
<td>7.60</td>
</tr>
<tr>
<td>Lactate [mmol/L]</td>
<td>0.8 (0.4)</td>
<td>0.4</td>
<td>1.8</td>
</tr>
<tr>
<td>Hb [mmol/L]</td>
<td>4 (0.6)</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>SaO2 [%]</td>
<td>100 (0)</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Venous blood</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaCO2 [kPa]</td>
<td>6 (0.8)</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>pH</td>
<td>7.44 (0.03)</td>
<td>7.38</td>
<td>7.50</td>
</tr>
<tr>
<td>Lactate [mmol/L]</td>
<td>0.8 (0.4)</td>
<td>0.4</td>
<td>2</td>
</tr>
<tr>
<td>SvO2 [%]</td>
<td>91 (8)</td>
<td>72</td>
<td>100</td>
</tr>
<tr>
<td>End-tidal CO2 [mmHg]</td>
<td>38 (2)</td>
<td>35</td>
<td>43</td>
</tr>
</tbody>
</table>

BPM: beats per minute; CPR: cardiopulmonary resuscitation; Max: maximum; Min: minimum; ROSC: return of spontaneous circulation; SD: standard deviation. Arterial blood pressure was measured with a Millar catheter in the thoracic aorta. Units are indicated in square brackets.
Fig. 2. Distinct morphologies of the PPG and ABP waveforms during different stages of the experiment. (a) Baseline. PPG and ABP waveforms show a spontaneous pulse rate of approximately 110 beats per minute. Continuous ventilation causes slow variations in both PPG and ABP waveforms. (b) CPR during cardiac arrest (ventricular fibrillation). (c) CPR after defibrillation. Traces start 16 s after the shock. As early as the first ventilation pause following successful defibrillation, spontaneous cardiac output can be seen in both PPG and ABP waveforms. This is the same animal (#R1) as in Figs. 3 and 4d.

3.1. Spontaneous pulse during ventilation pauses

Fig. 2 illustrates the different morphologies of the PPG and ABP signals during the CPR protocol. During baseline, cardiac pulses were visible in the PPG and ABP waveforms (Fig. 2a). After induction of cardiac arrest, automated chest compressions caused oscillations in PPG and ABP signals (Fig. 2b), and no spontaneous pulsations could be observed consistent with persisting cardiac arrest. Following successful defibrillation, subsequent ventilation pauses showed pulses at an increasing rate (Fig. 2c).

3.2. Spontaneous pulse during chest compressions

After successful defibrillation, increasing irregularity could be observed in the PPG waveform resulting from the influence of both chest compressions and spontaneous cardiac output (Fig. 2c). Spectrograms of the PPG and ABP signals show the chest compressions at a rate of 100 min⁻¹ before and after defibrillation (Fig. 3). In addition, after defibrillation, a disorganized spectral activity appeared, filling the frequency band from 0 to 200 min⁻¹. About 1 min after the shock, a distinct spectral component appeared at
about 125 min⁻¹, increasing to about 140 min⁻¹, and continuing when compressions were stopped. In this controlled setting, this component could only be a spontaneous pulse.

For all 12 animals, the PPG and ABP frequency spectra showed strong resemblance (Fig. 4). For animals without return of spontaneous pulse, the spectra only contained components due to the automated chest compressions (Fig. 4a–c). For animals with ROSC, the spontaneous pulse resulted in one or more additional components in the spectra (Fig. 4d–l). The pulse rate could be readily identified in the frequency spectra in eight out of nine cases. In Fig. 4f, the pulse rate was close to the compression rate and was only observable as a small broadening in the right flanks of the chest compression components.

3.3. Trend of relative PPG amplitude

In a case of transient ROSC (Fig. 5), CPR was stopped when ROSC was diagnosed, and restarted when the circulation was considered inadequate. During the period without compressions, the spectrograms of the PPG and ABP signals (Fig. 5a and b) showed a spontaneous pulse. The pulse amplitude in the PPG time trace decreased in this period and had almost disappeared when compressions were restarted (Fig. 5c).

4. Discussion

The aim of the present study was to investigate whether PPG signals can be used to detect the presence or absence of spontaneous cardiac-induced pulsations during CPR. This could be a first step toward objectifying and shortening ROSC determination. Raw PPG data acquired with a custom-built photoplethysmograph were
Fig. 5. Decreasing pulse amplitude observable in PPG signal during transient ROSC. The defibrillation shock was applied at 31:40 (dashed line). CPR was stopped at 33:41, and restarted at 35:08. (a) Spectrogram of the PPG signal. (b) Spectrogram of the ABP signal. (c) Time traces of the PPG and ABP signals. The insets show two close-ups of the PPG and ABP waveforms. The spectrograms were obtained by partitioning the 0.1-Hz high-pass filtered signals in segments of 10 s with 90% overlap and applying a Hamming window. For convenient time referencing, the time axis corresponds to the center of each segment. The spectrograms have been normalized by the magnitude of the spectral compression component in the signal at the beginning of the trace shown. This is the same animal (#N1) as in Fig. 4a. ABP: arterial blood pressure; CC: chest compressions; PPG: photoplethysmography; ROSC: return of spontaneous circulation.

analyzed retrospectively in both time and frequency domains, using the ABP as a reference.

Although PPG and ABP waveforms have comparable morphology, it is important to note that ABP represents the blood pressure in the macrovasculature, while PPG reflects the blood volume pulse in the microvasculature. As such, besides ABP, also arteriolar vasomotor tone and microvascular shunting affect the PPG waveform. Therefore, during CPR, decreased ABP and increased vasomotor tone might significantly reduce the pulsatility in the PPG waveform while ABP pulsatility remains. Nevertheless, the data show that presence and rate of a spontaneous cardiac pulse could be determined from a PPG signal during CPR. A PPG time trace could be used to detect spontaneous pulses during ventilation pauses, as illustrated in Fig. 2c. However, Fig. 2c also illustrates that it can be challenging to directly identify the spontaneous pulses in the PPG time trace during compressions. To resolve this, a spectral analysis was performed, which facilitates the identification of a spontaneous pulse and its rate during chest compressions, as shown in Figs. 3 and 4d, e, f.

During CPR, a PPG measurement performed at a stable site has the advantage of being less sensitive to motion artifacts than a TTI measurement, which is performed at the chest. Furthermore, PPG shows pulse presence faster than NIRS. However, the frequency spectra also show that real-time identification of a spontaneous cardiac pulse in the PPG signal during automated CPR may not be straightforward in all cases. Three complicating situations can occur, the first two being specifically related to ongoing chest compressions. First, the presence of spectral components in addition to the pulse and compression rates (and their harmonics) can complicate the identification of the spontaneous pulse component...
(Fig. 4d,e, and h–l). As these additional spectral components seem to arise at rates equal to the sum and difference of the compression and pulse rates, they may indicate an interaction between the chest compressions and the spontaneous cardiac activity. Second, when the pulse rate is close to the compression rate, the spontaneous pulse is difficult to identify in the spectrum (Figs. 4f, 5a, and 5b). And third, in general it can be technically challenging to identify a rapidly varying pulse rate in the spectrum, because variations in the rate result in a less well-defined, broadened peak in the spectrum (Fig. 4i and k). Furthermore, in case of manual CPR where the compression rate may fluctuate, an independent measurement of the manual compression rate can potentially be used to identify the chest compression rate in the spectrum and distinguish it from a spontaneous pulse rate.

In addition to using PPG signals to obtain feedback on manual chest compression rates as described by Xu et al. and Spittal, our data show that PPG signals can offer information about the presence or absence of a spontaneous cardiac pulse during CPR, making it potentially useful to support ROSC detection. Via PPG-based screening for pulse during ongoing compressions, absence of spontaneous cardiac activity can be noted which may prevent unnecessary or lengthy pauses in chest compressions for examination of ROSC. Furthermore, detection of return of spontaneous pulse during ongoing compressions may guide administration of vasopressors, as vasopressors may have detrimental effects when administered following a shock that has resulted in a perfusing rhythm. The broad spectral activity in the PPG during CPR following the defibrillation shock (Figs. 3 and 5) may provide an early indication of start-up of spontaneous cardiac output, or other muscular activity. Reinstitution of CPR may be guided by fading of a spontaneous pulse in the PPG, which may indicate lack of a perfusing rhythm (Fig. 5c). These observations warrant further research on the potential of PPG as a ROSC indicator.

This study, however, has some limitations. First, an animal model is never fully representative of clinical scenarios, but it allowed comparison between PPG signals and invasively measured ABP in a controlled environment. Second, suturing the PPG sensor to the nose to limit excessive motion artifacts is not representative of good clinical practice. However, the goal of this study was determining the feasibility of identifying a spontaneous pulse in a PPG signal during CPR, and not dealing with the technical solution for corrupting motion. Finally, to be able to detect a spontaneous pulse in humans during CPR in clinical practice, a central-site PPG measurement (e.g., from the facial region) may be preferred over a peripheral site, as centralization and the associated vasconstriction can severely compromise peripheral pulsatile blood flow.

5. Conclusions

After ROSC, cardiac pulses could be observed in the nasal PPG waveform during ventilation pauses. During chest compressions the contribution of spontaneous cardiac activity could be identified by analyzing the PPG frequency spectrum, when the pulse and compression rates were sufficiently distinct. We conclude that PPG has potential to support detection of ROSC during CPR.

Conflicts of interest

None of the authors have monetary or other interests which may have influenced this paper. Ralph Wijshoff was supported by a grant from NL Agency, IOP Photonic Devices, IPD083359 HIP – Hemo- dynamics by Interferometric Photonics. Gerrit J. Noordergraaf is a consultant for Philips Research.

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