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ORIGINAL ARTICLE

Roadmap of Photoplethysmography Technology in Advanced Cardiovascular Assessment

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Abstract: *This review explores the trajectory of photoplethysmography (PPG) technology from its inception in 1934 to its integration into smart devices in 2013. While PPG has proven effective in estimating left ventricular ejection time (LVET) and distinguishing between hypertensive and normotensive patients, challenges persist. The need for a robust mathematical model to explain physiological behaviors, address calibration protocols, and handle waveform variability is emphasized. Despite limitations, PPG is on the cusp of achieving clinical-grade confidence, particularly in estimating blood pressure and tracking vasomotor states. Integration into wearable devices is a prominent trend, with major companies exploring applications for improved health monitoring. Open-source databases and the availability of physiological data aim to enhance understanding, paving the way for universally accepted protocols. As PPG advances, it holds promise for personalized healthcare, revolutionizing treatment evaluations and preventive measures. However, potential disagreements over protocols may impede progress. Nevertheless, the technology's potential to remotely monitor cardiovascular markers could reduce physicians' workload for routine tasks. PPG stands as a beacon for the future of noninvasive cardiovascular assessment.*

Keywords: *photoplethysmography roadmap; cardiovascular assessment; cardiovascular disorders; left ventricular ejection time; blood pressure estimation*

INTRODUCTION

Cardiovascular diseases are, according to WHO, the most common cause of death globally. There are made continuous efforts to reduce the incidence, morbidity, and mortality of these conditions. All over the world, the physicians involved in preventing, detecting, and treating cardiovascular diseases are insufficient and subjected to an overwhelming workload: theoretically, after a certain age, virtually all individuals have a certain risk of developing cardiovascular conditions and these patients, after diagnosis, need periodical evaluation for monitoring, assessment of treatment efficacy and, also, management of complications. Therefore, in the context of nowadays technology capabilities, it has raised the question if there could be developed some methods to monitor these patients over a distance, using suitable medical technologies to non-invasively measure some biomarkers.

At present, it is available to remotely measure, using various wearable devices, pulse, SpO_2 and to record an ECG. However, in detecting or monitoring the risk of adverse events, it would be useful to be able to remotely monitor arterial blood pressure, hypertension being the most prevalent cardiovascular risk factor, or, more advanced, to monitor various parameters of heart performance.

Photoplethysmography (PPG) technology has already demonstrated promising efficiency in distinguishing between normotensive and hypertensive patients or in estimating left ventricular ejection time. In our opinion, with more research in this field and with better mathematical models that can explain all physiological behaviors, PPG could help healthcare professionals offer personalized care regarding the prevention, treatment, and follow-up of cardiovascular diseases.

PHOTOPLETHYSMOGRAPHY APPLICATIONS

Short History

The founding concept of the PPG technique is older than a

century when German physicist M.R. Bonnsman invented a photocell device in 1934 intended for peripheral blood volume evaluation [1]. This novel method was taken over by Alrick Hertzman [2,3] for further investigations in the physiological domain. Based on numerous experimental investigations, but limited by the technology capabilities at that time, he proposed blood volume variation as the origin of the PPG signal. No new progress in this technique has been made in the next years since the associated sensor was more of a tool in circulation research.

A valuable clinical application emerged in the form of blood oxygen saturation ratio (SpO_2) [4], pioneered by Takuo Aoyagi in the 1970s [5]. The device, now known as a pulse oximeter, was introduced into U.S. clinical monitoring a few years later, confirming its utility. Following this significant advancement, there was no immediate surge in research within the PPG technology domain; instead, efforts were concentrated on enhancing the accuracy of SpO_2 measurements. The pulse oximeter device became commercially accessible in the 2000s, owing to technological advancements and its availability in the open market [6].

Technology nowadays

The subsequent period that drew attention to PPG was marked by the integration of this technology into the first smartwatches in 2013 [7]. This significant development raised awareness among both academic and industry researchers regarding the potential for cardiovascular monitoring through wearable devices. While the well-established SpO_2 measurement and heart rate determination are valuable for assessing heart performance during resting periods or intense activity [8,9], they do not constitute a comprehensive tool for physicians to remotely monitor a patient in terms of cardiovascular disease (CVD) prevention or tracking.

Therefore, intense research has commenced in the PPG domain over the last decade, exploring various capabilities as depicted in Figure 1. One sought-after application is noninvasive arterial blood pressure (ABP) monitoring, considered a crucial hemodynamic marker in the evaluation of cardiovascular diseases (CVD) [10,11]. By incorporating this targeted assessment into smart devices such as watches, bracelets, and rings, personalized healthcare becomes accessible for end-users. The confidence in this feature has prompted major companies like Samsung [12] to integrate it into their devices. Start-ups such as Valencell [13] and Aktiia [14] assert their ability to provide this measurement using Machine Learning (ML) techniques. Additionally, numerous individual research entities report significant progress in this direction, leveraging artificial intelligence (AI) networks [15].

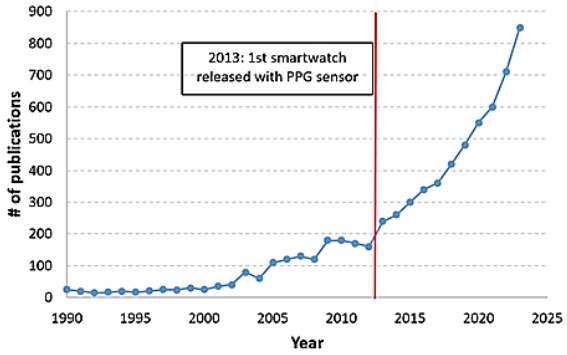

Figure 1: A timeline of PPG-related publications every year from 1990 to 2023. Data obtained from Google Academic, last accessed on 15th December 2023

The key factors contributing to the popularity of PPG encompass the mitigation of motion artifacts, the precision of SpO_2 readings and heart rate measurements, initiatives for extracting arterial compliance, and the estimation of blood pressure. Furthermore, a novel approach, remote photoplethysmography (rPPG) [16], has emerged in recent years, focusing on extracting hemodynamic information through facial recognition. The advancement of information technology, notably the internet and easy access to information, has played a significant role in augmenting the popularity of PPG.

However, as depicted in Figure 1, the upward trend in the number of publications does not align with the maturity of the technology. Regrettably, numerous topics are repetitive, merely contributing to the validation of specific assessments rather than yielding outstanding discoveries or breakthrough research. As will be presented in the next section, a strategy focused solely on PPG signal interpretation is not sustainable. Reflective sensors are commonly employed for wearable applications, as illustrated in Figure 2, in contrast to the transmissive ones more prevalent in clinical settings.

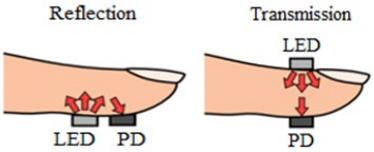

Figure 2: Two types of PPG modes: reflective and transmissive. In wearable devices, the first mode is prevalent, while in clinical settings the second one is present.

Eligible models must be developed to comprehensively explain all observed physiological behavior, and the correlation or causation with arterial blood pressure needs to be elucidated. Without such a focused direction, the repetition of topics will persist without yielding new and significant discoveries.

PPG as a standalone biomarker

As a standalone biomarker, information extracted from PPG waveform contour analysis becomes crucial. Following this approach, significant features such as the tidal wave (TDW) [17] and the dicrotic wave (DCW) [18] can be associated with the vasomotor state. The latter waveform component proves to have a strong correlation in estimating vasomotor tone, as observed in Figure 3, where the dicrotic notch sharpens proportionately with the level of vasodilation [19]. When combined with other waveform markers, such as the ratio between systolic upstroke and downstroke, and aided by Machine Learning (ML) models, the hypertensive state can be reliably detected [20].

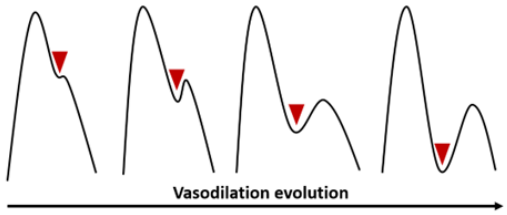

Figure 3: Evolution of PPG waveform during vasodilation progress, by highlighting incisura or DCW feature. Reconstructed after the findings on [19]

Another application involves the myocardial performance index (MPI or TEI) [21], as the PPG waveform encompasses information about isovolumetric contraction time (IVCT) [22], isovolumetric relaxation time (IVRT), and left ventricular ejection time (LVET) [23]. Despite the potential for overestimation and underestimation of measurements due to the hemodynamic state, these values closely align with the golden standard method of Doppler echography.

PPG in sensor fusion

One popular technology in this category is represented by the pulse pressure transit time (PTT) method [24], developed for arterial compliance and blood pressure assessment. The current literature protocol [25] guides the measurement of this marker from the electrocardiogram (ECG) R peak to the PPG systolic point, as depicted in Figure 4.

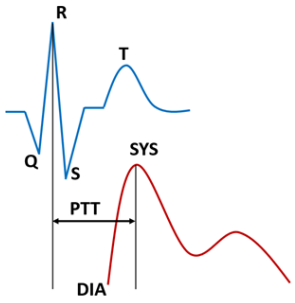

Figure 4: PTT protocol based on guidelines [25]

Based on the physical equation developed by Moens–Korteweg [26], which describes the traveling behavior of mechanical pulse pressure, blood pressure estimation can be extracted. Thus, a stiffer system will promote rapid traveling of the pulse wave, resulting in a shorter PPT time. Conversely, an elastic system, due to its ability to absorb mechanical energy, will slow down the traveling mode, leading to a longer measured time.

Another application that combines PPG capabilities involves fusion with a medical cuff. During cuff inflation, PPG acts as a monitor of blood supply at the targeted site. After a certain point, the externally induced pressure will trigger blood vessel occlusion, which is reflected by a missing PPG waveform. This measurement approach was embedded in the Omron smartwatch [27] to enhance the accuracy of blood pressure assessment.

A recent application involves remote photoplethysmography [16], which targets face recognition in combination with pulsatile detection of facial skin. By selecting two separate regions of interest (ROI), such as the chin and forehead, equivalent approaches to the PPT technique are employed to compute and estimate blood pressure, as depicted in Figure 5.

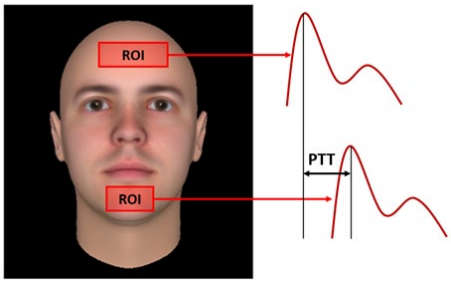

Figure 5: Principle of rPPG. Two locations of skin pulsation generate PPG waveform but with a time delay in between. This delay is exploited by a similar to the PPT method to extract blood pressure estimation

PHOTOPLETHYSMOGRAPHY LIMITATIONS

Physiological model

Despite the important and useful applications of the PPG technique, either standalone or in conjunction with other methods, the technology has demonstrated some limitations.

The first significant limitation pertains to the proper understanding of PPG origin, particularly in relation to pulse formation. While Alrick Hertzman proposed blood volume variation as a working model in the 1930s, recent investigations have revealed some drawbacks. One common limitation arises during reduced SpO_2 readings [28], which actually represent the ratio between oxygenated and deoxygenated blood volume. Additionally, the hand position

concerning the heart level [29] modulates the PPG waveform amplitude according to specific rules, contrary to the initially proposed volume variation model. Therefore, significant progress in the hemodynamic domain cannot be achieved without a suitable PPG model that can explain and predict different physiological states. At this juncture, two mathematical models are required: one to elucidate the optical nature of the recorded signal and another to describe the mechanical nature that provides a specific waveform morphology. Training Machine Learning (ML) or Artificial Intelligence (AI) systems with a large set of hemodynamic data will not unveil the true relationship between these two physical quantities. Instead, it serves as an interim step to understand which waveform components are predominant in blood pressure assessment.

A recently developed model proposes the red blood cell deformation effect as the origin of PPG formation [30]. The mere presence of erythrocytes in the measurement area modulates the direct component or baseline of the recorded waveform. Interestingly, as cells move under a defined velocity field, they deform in the capillary regime. Thus, targeting red blood cells with light results in the absorption of radiant flux proportional to the deformation level. Given that many publications attempt to correlate arterial blood pressure (ABP) waveform with PPG, it is observable that the physiological stimuli contributing to PPG formation are the blood flow velocity at the capillary level, ranging from 50 µm/s to 2000 µm/s [31]. As a result, as depicted in Figure 6, the PPG waveform is exclusively modulated by the velocity values through the capillary network, reflected in the final waveform by red blood cell deformation.

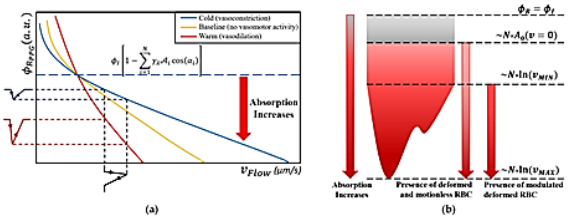

Figure 6: RBCM MODEL. Reused from [30]

It is important to note that both the mechanical blood pressure pulse and red blood cell deformation—precursors for PPG—are driven by blood flow velocity. Therefore, this physical quantity serves as the same input stimulus, the causal factor, for both associated waveforms. In this context, a correlation rather than direct causation exists between arterial blood pressure (ABP) and PPG information. From this standpoint, estimations of hemodynamic markers can be extracted with the aid of wearable technologies. However, due to the logarithmic nature of PPG origin, as depicted in Figure 6, the hemodynamic information will undergo modifications that could lead to wrongly interpreted results.

Finally, without a proper optical model, the improvement of pulse oximeter sensors becomes challenging. The most critical design considerations are related to mechanical features, such as the frequency of the LED used, initial light flux power, and the arrangement of the photodiode. In terms of signal processing, important design inputs include signal amplification, sampling frequency, and filtering stages.

Measurement protocols

All the aforementioned PPG measurement capabilities require a universally agreed-upon protocol to ensure that different devices provide consistent results for the same user or patient. This requirement is crucial for accurate measurements to be eligible for clinical applications. Moreover, regardless of the device's manufacturer, doctors need to rely on the measured data to provide correct treatment or formulate an observational plan.

While the PPT method has demonstrated high-confidence results in estimating blood pressure with the defined protocol, there is still an applicability problem on the user end. Measuring PPT involves two sensor readings simultaneously: EKG and PPG, as discussed earlier. Even though the latter doesn't require user intervention, the former necessitates the user to close the electrical circuit of their body to perform an EKG. Consequently, the measurement cannot be performed frequently without user intervention, for example, during sleep or physical exercise. In essence, it shares the same measurement limitations as a traditional oscillometric blood pressure device [32].

For assessments that involve standalone PPG sensors, a major limitation is the calibration protocol process. Given the optical nature of the recorded quantity, the readings need to be calibrated with a mechanical reference, especially for applications intended for blood pressure estimation. In the assessment of vasomotor state, where absolute values aren't critical, a protocol should outline which PPG waveform components, besides DCW, need to be evaluated for high-confidence results. This is necessary due to the various waveform morphologies that appear in the real world, apart from the idealized perfect shape.

The same approach is necessary for measurements involving time values, such as left ventricular ejection time (LVET) determination. While the association with the TDW feature yields good results, a common agreement on the onset and ending points is essential. Given that the TDW component comprises a finite disturbance event in combination with different morphologies, a protocol is also required for

consistency in interpretation.

Finally, from a numerical standpoint, all the measured hemodynamic markers should be evaluated by a specialist within the proper context. The obtained data must be assessed to determine if the measurements were intended for prevention, treatment evaluation, or cardiovascular disease monitoring.

PHOTOPLETHYSMOGRAPHY FUTURE

An important stride in pulse oximeter technology has already been taken by integrating it into wearable devices. The increased computational power per integrated circuit in these devices holds the potential to enhance the signal processing part of the technology.

The availability of open-source databases containing hemodynamic and physiological data intended for researchers [33,34] will contribute to a proper understanding of PPG technology. In the final analysis, having such resources will help reduce, mitigate, or avoid the discussed drawbacks with a supportive tool.

The existing technological capabilities are poised to elevate PPG technology to clinical grade, enabling it to provide high-confidence measurements. Consequently, cardiovascular markers such as LVET and MPI can be remotely monitored, reducing the need for unnecessary physician office visits. This advancement holds potential benefits for both patients and doctors.

The capability to monitor patients' markers with a higher frequency rate would enhance the evaluation of the efficiency of the treatment plan. Additionally, cardiovascular diseases (CVDs) could be prevented or tracked more effectively, enabling better control and management.

An important assumption pertains to future protocols. The competition to embed hemodynamic markers into wearable devices will likely lead the first entity with proven and credible tracking capabilities to establish standalone protocols. Consequently, the community researching in the respective domain will likely follow the defined rules. However, a potential drawback is that this could trigger disagreements over a common, acceptable protocol, which may delay the accessibility of personalized healthcare [35].

CONCLUSIONS

The age-old noninvasive method, photoplethysmography, holds immense potential for enhancing cardiovascular assessment. However, realizing this potential requires the development of a proper mathematical model that can link and explain all physiological behaviors.

While the interest in PPG surged with the advent of the first smart devices in 2013, no disruptive progress has been achieved since then. Instead, some recurrent topics have been validated rather than proposing novel waveform markers for association with clinical applications. Blood pressure estimation and vasomotor state tracking are currently receiving the most attention, with popular companies piloting projects to integrate them into wearable devices.

Despite current limitations, PPG has shown validity, especially in estimating LVET and in binary detection between hypertensive and normotensive patients. Given the current context of technological advancement, there is optimism that this technology will achieve clinical-grade confidence. Consequently, it is anticipated to become an integral part of human lives by providing easy accessibility to personalized healthcare. This, in turn, will unlock improved health monitoring and contribute to a reduced workload for physicians in handling less critical tasks.

Conflicts of interest and sources of funding

The authors declare no conflict of interest.

Authors' contribution

For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, L.E. and L.D; methodology, L.E.; software, L.E.; validation, L.E., A.F and L.D.; formal analysis, L.E; investigation, L.E.; re-sources, L.D.; data curation, A.F.; writing—original draft preparation, L.E.; writing—review and editing, A.F; visualization, L.E.; supervision, A.F.; project administration, L.D.; All authors have read and agreed to the published version of the manuscript." Please turn to the CRediT taxonomy for the term explanation. Authorship must be limited to those who have contributed substantially to the work reported.

Ethics approval and consent to participate

Not applicable.

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