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Photoplethysmography

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The photoplethysmographic (PPG) waveform, also known as the pulse oximeter waveform, is one of the most commonly displayed clinical waveforms. First described in the 1930s, the technology behind the waveform is simple. The waveform, as displayed on the modern pulse oximeter, is an amplified and highly filtered measurement of light absorption by the local tissue over time. It is optimized by medical device manufacturers to accentuate its pulsatile components. Physiologically, it is the result of a complex, and not well understood, interaction between the cardiovascular, respiratory, and autonomic systems. All modern pulse oximeters extract and display the heart rate and oxygen saturation derived from the PPG measurements at multiple wavelengths. "As is," the PPG is an excellent monitor for cardiac arrhythmia, particularly when used in conjunction with the electrocardiogram (ECG). With slight modifications in the display of the PPG (either to a strip chart recorder or slowed down on the monitor screen), the PPG can be used to measure the ventilator-induced modulations which have been associated with hypovolemia. Research efforts are under way to analyze the PPG using improved digital signal processing methods to develop new physiologic parameters. It is hoped that when these new physiologic parameters are combined with a more modern understanding of cardiovascular physiology (functional hemodynamics) the potential utility of the PPG will be expanded. The clinical researcher's objective is the use of the PPG to guide early goal-directed therapeutic interventions (fluid, vasopressors, and inotropes), in effect to extract from the simple PPG the information and therapeutic guidance that was previously only obtainable from an arterial pressure line and the pulmonary artery catheter.

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Introduction

The photoplethysmographic (PPG) waveform is the core technology of the pulse oximeter. This wave is displayed on monitors throughout the critical care areas of the hospital (operating room (OR), emergency room (ER), postanesthesia care unit (PACU), intensive care unit (ICU), etc.). Unlike the electrocardiogram (ECG), it is rarely recorded or analyzed. This chapter endeavors to make the PPG waveform more useful to the practicing clinician. In addition, it explores some of the exciting research presently being carried out to expand its clinical usefulness.

At its heart, the PPG technology is remarkably simple consisting of a light source on one side of the tissue bed and a light detector on the other. Holding one hand in front of a bright light and looking at the red glow creates a PPG in its simplest and most accessible form. If your eyes were a bit more sensitive, you would see the subtle darkening of your hand with each heartbeat.

History

The PPG is not a new discovery [1,2]. It was first described by Alrick Hertzman in 1937 [3]. This ultimately led to a remarkable series of papers by Hertzman [4–7] examining the physiology and potential uses of this waveform (Fig. 1). It was Hertzman who named it the photoelectric plethysmograph based upon his belief and early observations that its creation was linked to blood volume changes. He chose the term “plethysmos,” which is derived from the Greek word for fullness. This expressed his belief that he was measuring the fullness of the tissue when he measured the amount of light absorption. Subsequent research has demonstrated he was not far off on his assumption with a close correlation ($r = 0.9$) between the PPG and the more traditional strain gauge plethysmograph [8].

It is important to note that Hertzman was working from the simplistic model of light that was prevalent at the time. This was before the quantum complexities and scattering characteristics of light were generally appreciated [9]. His theories were derived from Beer–Lambert’s law of light, whose primary assumptions were that light absorption is directly proportional to the path length, concentration of substances, and the light absorption by each of those substances [10]. The modern day theory of light/tissue interaction is more complex and well laid out by Paul Mannheimer [11]. There are two major take-home messages to the practicing clinician: (1) there is more to the pulse oximeter waveform than a simple representation of the cardiac pulse (e.g., not just a “poor man's

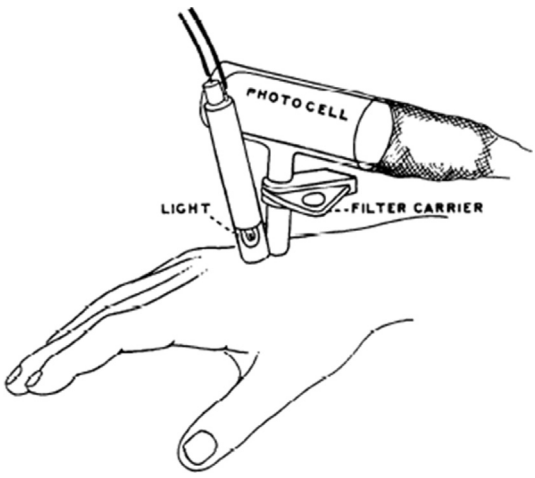

Fig. 1. The photoelectric plethysmograph in position over the skin of the hand. From 1938 showing Hertzman's original setup for measuring the PPG (Used with permission from The American Physiology Society via Rightslink) [4].

arterial line") [12] and (2) there is more to the PPG waveform than a simple display of tissue blood volume change [13] (although this is not a bad place to start when considering this waveform).

At this point, it is important to talk about some of the nomenclature used when describing the PPG particularly in the research literature. In the same way, Hertzman was influenced by his belief that he was measuring the "fullness" of the tissue when he called his device a photoplethysmograph. Subsequent investigators also made some basic assumptions. One of those assumptions was that the only blood that caused modulation of the PPG was arterial. This component of the PPG was termed AC (after alternating current found in electrical circuits). This was the core assumption that allowed Takuo Aoyagi to develop the pulse oximeter in the 1970s [14]. The unchanging background absorption was labeled DC (for direct current). This simple definition has been a source of unending confusion. For example, how exactly is the DC measured? In the scientific literature, it has been measured at the troughs of the PPG, at the peaks (because of its normally inverted display), and at the mean of the PPG pulses. Subsequent research has demonstrated that venous blood also moves and modulates at the cardiac, respiratory, and autonomic frequencies [12,15,16]. This has unfortunately led to confusing nomenclature in the literature such as referring to the ratio of slow-modulating DC signals to cardiac modulations as DC% or the respiratory-induced intensity variations of the PPG as RIIV (Fig. 2). As our understanding of the fundamental physiology the PPG improves, hopefully so will our nomenclature.

Physiology

It should be stated up front that the unfiltered PPG waveform is complex. It appears to be the end result of arterial and venous blood interaction with the cardiac, respiratory, and autonomic systems. The level of the vasculature that creates the signal is still an active area of research and debate [17]. The general consensus is that the cardiac component of the waveform comes from the site of maximum pulsation within the arteriolar vessels, where pulsatile energy is converted to smooth flow just before the level of the capillaries [18]. To this day, there is no known method of calibration of the PPG. This means one cannot directly compare the absolute numbers of one person's PPG to another's (e.g., people have different thicknesses of fingers, color of their skin, and amount of fat and muscle in their tissue). As the existence of the pulse oximeter demonstrates

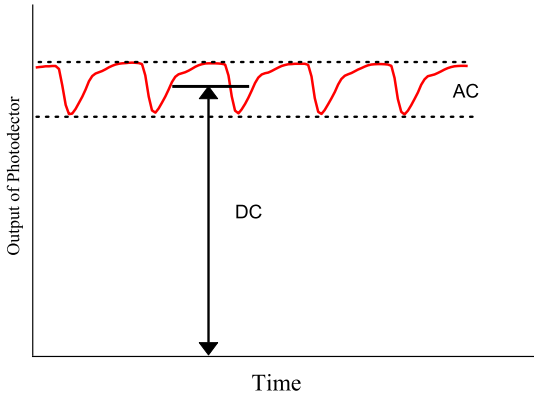

Fig. 2. The components of a raw PPG waveform. The infrared waveform (~940 nm) is always displayed because of its stability. When this waveform is displayed on a clinical monitor, it is always inverted so that it goes in the same direction as the arterial pressure waveform. AC (as in alternating current) is the term given to the component that modulates at the cardiac frequency. The DC (as in direct current) refers to the steady-state light absorption of the tissue (i.e., bone, fat, and muscle). There is tremendous confusion regarding where exactly the DC should be measured from. Most people use the mean as illustrated here but it would be equally valid to use the top of the waveform (which actually corresponds to the diastole!). Note this diagram does not take into account the movement of venous blood or the effects of ventilation. This has led to a bewildering variety of nomenclature when discussing these types of phenomenon.

though, all is not lost; one can measure how the light absorption changes over time and the impact of various physiologic systems (cardiac, respiratory, and autonomic). One can also study these changes at different wavelengths to allow for the measurement of the ratio between substances (oxy vs. deoxyhemoglobin and plasma vs. total hemoglobin).

PPG display on modern clinical monitors

This naturally brings us to the question: what exactly is the clinician looking at on their clinical monitors when it comes to the PPG/Pleth/pulse oximeter waveform? First, the displayed waveform actually has little to do with the patient's oxygen saturation. The most frequent use of the PPG waveform is the examination of its regularity and pulsatile quality to detect artifacts potentially causing a low displayed oxygen saturation. As was explained to me by a senior professor during my anesthesia residency, the PPG waveform "tells you if your pulse oximeter is working".

Given the degree of filtering that medical device manufacturers have elected to impose on this waveform, this should come as no surprise. Biomedical engineers, influenced by their marketing departments, have for the most part concluded that physicians are fairly simpleminded. It would appear they do not want to worry us with "messy details" and are striving to give us "smiley" versus "frowny" face displays to guide our therapeutic interventions. Unfortunately, part of their motivation might also be the protection of proprietary technology, not unlike William Morton in 1846 adding red dye and perfume to diethyl ether to create "Letheon" [19]. In the end, whatever the motivation, the result is the same; the clinician is presented with a simplified version of the patient's physiology.

Pulling back the curtain a bit, the PPG as displayed is the inverted infrared waveform (~940 nm), which has two major filters on it. First, there is a band-pass filter, eliminating slow gradual changes, as well as the fast spiky changes. In other words, the waveform is continually being smoothed and "auto-centered." Next, the waveform is having its size (amplitude) constantly being adjusted (e.g., "auto-gain"). This is accomplished by two means, a modification of its amplification by the electronics and an adjustment of the light intensity of the light source (light-emitting diodes (LEDs)). If you have ever witnessed the pulse oximeter probe getting brighter and dimmer on a patient's finger, this is a manifestation of the device attempting to determine the optimum light brightness of its LEDs.

Let us explore that a bit. It is important to understand what we are looking at and why. It is inverted so that the PPG looks like an arterial pressure waveform. In reality, with each heartbeat during systole, the amount of light that actually gets to the detector is less than during diastole. The clinician is shown the infrared waveform (as opposed to the red (~660 nm) waveform) precisely because it is influenced less by oxygen saturation. The infrared waveform can be thought of as the "calibrating" wavelength for the oxygen saturation calculation. It is filtered so that it does not drift off the screen, and so that the cardiac pulse is still clearly visible over a wide range of clinical conditions (vasodilated vs. vasoconstricted and weak pulse vs. a bounding one). Even in its standard, highly filtered presentation, it can still be quite useful for clinical care.

Cardiac arrhythmia, heart rate variability, and pulse transit time measurement

The PPG, on the standard clinical monitor, is an outstanding detector of cardiac arrhythmia [20]. In particular, it is very sensitive to any irregularity of the pulse. This is especially apparent if the patient is having premature ventricular or atrial beats (Fig. 3). It will allow for the rapid detection and diagnosis of atrial fibrillation, which is often difficult to diagnose directly from the ECG. Its sensitivity and specificity significantly improve with the concurrent display of the ECG. To the practicing clinician's advantage, the source of artifacts for devices (PPG and ECG) is very different. As an example, the ECG is sensitive to electrocautery, while the unshielded PPG can be influenced by infrared heating lamps. It is a rare situation that could simultaneously, and in a coordinated fashion, corrupt both waveforms.

Given the PPG sensitivity to heart irregularity, it has been observed that the PPG can be used to measure heart rate variability (HRV) and has a high degree of correlation with the ECG-derived HRV [21,22]. HRV, in turn, has been proposed as a monitor of the autonomic system and could potentially be

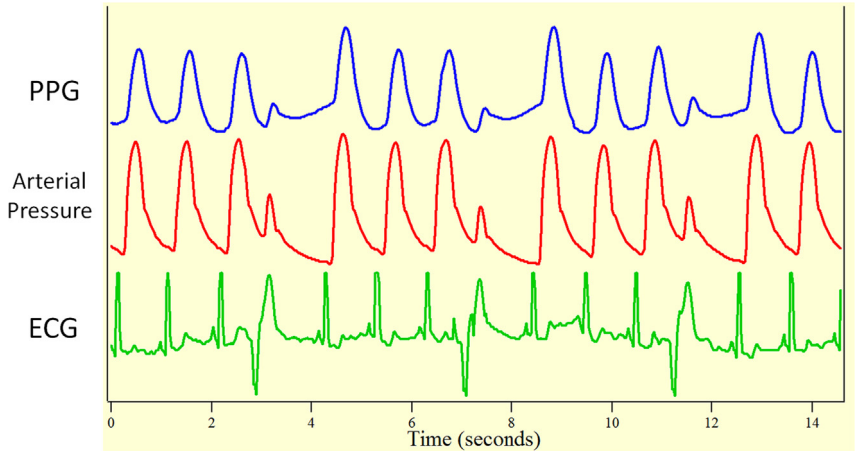

Fig. 3. The effect of cardiac arrhythmia (PVCs) on the PPG.

used for the early detection of shock [23]. Research efforts using the PPG as a source of measurement of HRV are still early, and they do not yet meet the standards of measurement suggested by cardiology societies [24].

Another intriguing use of the PPG, when combined with the ECG, is the measurement of pulse velocity through the body [25]. Called the pulse transit time (PTT), it is obtained by measuring how long it takes the PPG to arrive at a distal portion of the body (i.e., finger or toe). It is calculated by using the QRS of the ECG as the start time and the upward deflection of the PPG marking the arrival of the pulse. Short PTTs have been associated with high blood pressure, aging, arterial sclerosis, and diabetes [26], the basic observation being that the stiffer the vessel, the more rapidly the pulse will travel through it [27]. PTT has been proposed as a method of following rapidly changing blood pressure noninvasively during anesthesia induction [28] or spinal anesthesia [29]. As a continuous monitor of noninvasive blood pressure, the results from PPG analysis alone have been disappointing and would appear to require frequent calibration [30,31]. Given the complexity of the underlying physiology, we would be surprised if a new method of analysis were developed that would allow for continuous blood pressure measurement.

PPG pulse amplitude

One of the prominent features of the PPG is the size of the pulse beat. It is sometimes referred to as pulse amplitude or pulse height. Unfortunately, given the tendencies of medical device manufacturers to filter the PPG, and specifically use “auto-gain” or “auto-amplification,” this limits its usability by the practicing clinician. Early pulse oximeters, such as the Oxipleth by Novametrix, had the ability to have the user turn off or lock the degree of amplification. Masimo, in its pulse oximeters, has introduced the measurement of a “perfusion index” (PI) that can be used, in a limited manner, as a substitute for an amplitude measurement. Physiologically, the PPG amplitude is as a result of a complex interaction of stroke volume, vascular compliance, and tissue congestion effects. Table 1 summarizes the conditions that tend to affect PPG pulse amplitude. Importantly, the PPG has been shown to be sensitive to even small amounts of pulsatile blood flow (as small as 4% of the baseline as determined by laser Doppler) [32,33]. One should never confuse a large PPG pulse with a high arterial pressure. It is not unusual for the PPG amplitude to decrease during significant increases in blood pressure that are due to increased sympathetic tone. In addition, while clearly being related to cardiac stroke volume especially at the extremes, there appear to be too many confounding factors to allow for the creation of a direct linear relationship between the PPG pulse and cardiac output [34–37].

The above limitations do not preclude one from using the PPG to estimate the systolic blood pressure. This is done by using the ability of the PPG to detect a peripheral pulse. Using a manually

Table 1
Factors affecting PPG pulse amplitude.

- Decreased amplitude (smaller pulses)
  - Vasoconstriction
    - Pharmacological: phenylephrine, ephedrine
    - Physiological: cold, surgical-induced stress
  - Increased tissue congestion (venous)
    - Hand position lower than the heart (when measured at the finger)
    - Trendelenburg position (when measured at the ear)
    - Abdominal Laparoscopy
    - Valsalva maneuver
  - Low stroke volume (when critically reduced)
- Increased amplitude (larger pulses)
  - Vasodilation
    - Pharmacological: nitroprusside
    - Physiologic: warming, sedation, sepsis
    - Anesthetic: regional blocks
  - Decreased tissue congestion (venous)
    - Hand position held above the heart (when measured at the finger)

controlled blood pressure cuff with the PPG finger probe on the same side, one inflates the cuff until all signs of cardiac pulsations are absent from the PPG. The blood pressure cuff is then slowly deflated until the pulse is once again detected. This pressure has a high correlation to the systolic blood pressure ($r = 0.9$) [38,39]. This technique has been found to be helpful both in noisy environments and with neonates because of the difficulty of using stethoscopes [40].

PPG morphology

Within the PPG pulse morphology, there are a number of interesting features. Like the arterial line, pressure in the dicrotic notch (incisura) can often be identified. The review paper on the PPG, by Murray [41], has an excellent discussion on the interpretation of the presence and location of this feature. He relates the dicrotic notch position to vascular tone. Supported by the analysis of arterial pressure waveforms by the physiologist O'Rourke [42,43], he reports that a high arterial vascular tone (low compliance) is associated with the notch occurring early and high up on the downward diastolic curve. On rare occasions, one can even find hyperresonate notches that occur in both the arterial pressure waveform and the PPG. They are located just before, or just after, the systolic peak and have also been associated with high vascular tone. Some investigators have even gone so far as to analyze the speed of change in the PPG (as measured by the second derivative) to detect the impact of aging and hypertension, as well as to monitor drug effects [44,45].

In contrast to the arterial pressure waveform, the PPG can also display venous pressure waveform characteristics. These are often first detected by the presence of large peaks during diastole [12]. In the presence of hypervolemia, high abdominal pressure (laparoscopic surgery), and heads-down position (Trendelenburg), the PPG can take on CVP waveform (a–c–v) characteristics that interfere with the function of the pulse oximeter [46].

Assuming one is capable of measuring the PPG amplitude, which has been minimally filtered, the next consideration is the region of the body where it is being measured. In the finger, where the walls of the cutaneous vessels are richly innervated by α-adrenoceptors, the sensitivity to changes in the sympathetic system are greater than when compared to other areas of the body such as the earlobe [47]. Once a baseline measurement has been established, the pulse oximeter amplitude can be followed as a monitor of vascular sympathetic tone [48,49]. An intriguing potential use of the plethysmograph may be as an indicator of minimum alveolar concentration-blockade adrenergic

response (MAC-BAR) [50], the dose of anesthetic required to block adrenergic response in 50% of individuals who have a surgical skin incision. The degree of sympathetic responsiveness a patient retains during anesthesia might have important clinical implications. Another, and related, use of the PPG is the detection of the success and duration of spinal, epidural, and regional anesthetics [51–54].

PPG & functional hemodynamics

One of the most promising avenues of investigation is the exploration of the interaction between the PPG waveform and the respiratory system. Based upon the principles of functional hemodynamics [55], it is hoped that early goal-directed therapy will allow for improved patient outcomes [56,57]. The PPG efforts are based upon the success of using the arterial line pressure waveform to determine the patient's fluid responsiveness (answering the fundamental question of whether the cardiac output will go up if the patient is given intravenous fluid?) [58,59]. Early research in this direction has been quite promising [60–63] (Fig. 4). With further investigations, it has become apparent that the PPG, while providing a good predictive power regarding fluid responsiveness under stable and controlled conditions ("on the rifle range"), tends to become unstable and susceptible to artifacts in the dynamic situations found in a typical OR or ICU ("in the jungle") [64–68].

The authors of this chapter have spent a number of years examining this specific use of the PPG (using respiratory-induced modulation to predict the requirement for additional intravenous fluid).

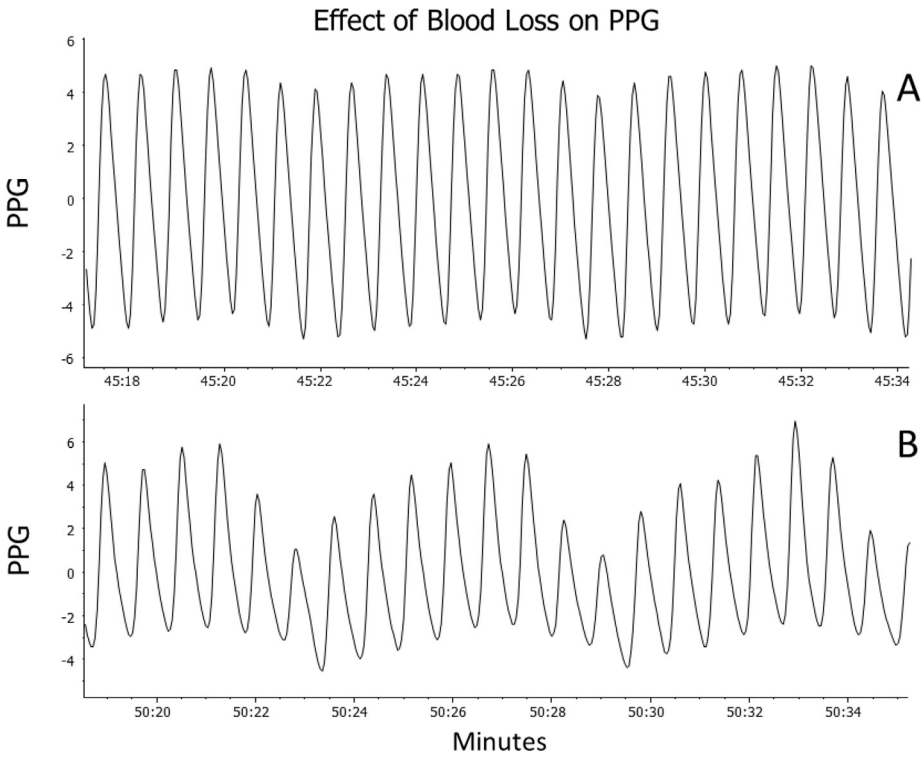

Fig. 4. The effects of acute hypovolemia (i.e., bleeding) on the PPG. It is from a patient who suffered a sudden blood loss (~500 cc) during a surgical procedure. It demonstrates a shift from a simple baseline venous modulation (A) to a combined arterial and venous modulation (B).

We have come to the conclusion that three parallel investigations are needed. First, there needs to be an improved understanding of the physiology behind the modulation of the PPG waveform. This specifically needs to be focused on what components of the modulation are associated with the peripheral movement of venous and arterial blood (during both spontaneous and mechanical ventilation) and how these modulations interact with the autonomic system (awake vs. anesthetized patients) [69]. Second, there is a need for an improved understanding of how the airway pressure and tidal volumes interact with both the pulmonary and systemic cardiovascular systems [55,58]. Third, improved electronics and digital signal processing techniques are needed to isolate these respiratory-induced changes in these challenging real-world environments [70].

This naturally leads to the question: is there a way for the practicing anesthesiologist to use these insights regarding PPG ventilator-induced modulations in today's OR? The key to answering this question is understanding the source of sensitivity (false negatives) and specificity (false positives) of this measurement. Regarding the sensitivity, it is clear that the patient needs to undergo mechanical ventilation [71], using a controlled volume mode [72] with adequate tidal volume breaths (>8 cc/kg) [73]. Once these conditions are met, one can decide/measure if a significant degree of modulation is occurring. The clinical cutoff appears to be approximately 15% [74,75]. Interestingly, there is a fair amount of debate whether or not a clinician can just “eyeball” the screen for a measurement of waveform modulation [76,77]. Our recommendation would be to either slow the scroll speed (<12.5 cm/s) of the screen or print out the PPG, using a strip chart recorder (once again using a slower printing speed). The key observation here is that if there is little or no modulation, despite adequate ventilation, one can be confident that the patient is not hypovolemic. In other words, there are very few causes (none as far as we know) for a “false negative”. On the other hand, if the wave is modulating (rocking up and down), hypovolemia is among the leading causes for this but not the only cause. One also has to consider the potential for other causes such as cardiac tamponade, asthma, high airway pressures, and tension pneumothorax [78].

Research considerations

For research purposes, there are two basic methods of analysis that can used to analyze the PPG waveform, namely time domain and frequency domain [79,80]. In the time domain analysis, the key features of the PPG waveforms that are measured include amplitude (related to pulse pressure/SV/vascular compliance), area, width (at either the base or 50% height), as well as maximum slope (related to dP/dT) and minimum slope (related to the speed of vessel relaxation and blood run). With frequency domain analysis, for example, using Fourier transformation, the PPG waveforms can be described as the sum of simpler underlying harmonics (sine and cosine waves). The advantage of this approach is the powerful assumption that the PPG waveform is due to two physiologic metronomes, the heart and the lungs (especially during mechanical ventilation) [81].

There is the intriguing possibility of using PPG to measure vascular compliance in both arteries and veins by combining its volumetric information with pressure measurements taken directly from the vessel or from a blood pressure cuff [82]. The venous/arterial compliance ratio can be calculated by assuming that the baseline modulation (DC) of the PPG at the respiratory frequency (0.1–0.4 Hz) is due to changes in venous blood volume while cardiac modulations (AC) of the PPG (0.8–2.5 Hz) are due to changes in arterial blood volume. This information is then combined with the pressure information from a peripheral venous pressure waveform and a blood pressure cuff to calculate the compliance ratio [83].

Another active line of investigation includes relating the preload information from venous modulation (DC/respiratory modulation) to stroke volume variation present in the cardiac portion of the PPG (AC/SV modulation). From this work, it is hoped that information regarding cardiac function and the Starling curve might be obtained noninvasively [83].

One of the most exciting avenues of research at the moment is the development of the pulse oximeter camera [84–87]. These are noncontact systems that would allow for the detection of the PPG at a distance, using either ambient light or infrared spotlights. The potential for such systems is remarkable, particularly in the field of public health. Consider the potential for monitoring, noninvasively and nonintrusively, the waiting room of a crowded ER or passengers on a long-distance airplane flight. This technology has a strong “Star Trek” medical tricorder feel to it.

Practice points

- While the PPG is often thought of as a substitute for an arterial line pressure measurement, in reality it is a volumetric signal, measuring how big the finger or ear blood vessels (arterial and venous) become with each heartbeat and breath.
- With the modern pulse oximeter, the PPG is a highly filtered waveform with both auto-centering and auto-gain adjustments being made continuously.
- The PPG is exquisitely sensitive to any change in cardiac rhythm. It is an excellent detector of irregular heartbeats such as PVCs, PACs, and A-fib especially when used in conjunction with the electrocardiogram.
- On some clinical monitors, the PPG can be examined for modulations during routine positive pressure ventilation; if absent, it is unlikely the patient is hypovolemic.
- The size (height or amplitude) of the PPG pulse reflects the interaction of the cardiac stroke volume and local vascular compliance.
- The medical device manufacturers have to be convinced that practicing clinicians should have access to more display options (filter settings, scroll speed, wavelength selection, and AC and DC values) when it comes to the PPG waveform.

Research agenda

- As remarkable as it might sound, the physiologic source of the PPG waveform is still unknown. The determination of the true physiologic source of the PPG waveform is a high priority.
- We lack the ability to calibrate the PPG. This leaves us with only the capability to monitor changes over time such as those caused by the cardiac pulse or pulmonary ventilation. Using multiple wavelengths, we can determine the ratios of substances but not their absolute measurements. The development of the capacity to calibrate the PPG waveform would unlock the true potential of this signal.
- Further research efforts are needed regarding the potential use of the PPG in early goal-directed interventions based upon the principles of functional hemodynamics.
- The three most promising avenues of investigation (in order of their present maturity) include optimization of the patients' (1) blood volume, (2) vascular tone, and (3) cardiac function.
- Pulse oximeter cameras (noncontact systems), while still in their infancy, appear to hold tremendous promise for the future of this waveform. Personally, we are convinced that Dr. McCoy's medical tricorder from Star Trek is, in actuality, a photoplethysmographic device.

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