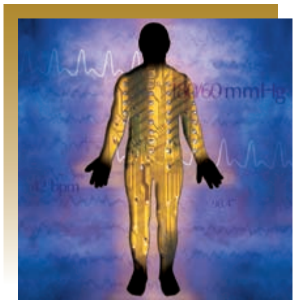

Mobile Monitoring with Wearable Photoplethysmographic Biosensors

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Technical and Clinical Aspects of a Ring Sensor for Ambulatory, Telemetric, Continuous Health Monitoring in the Field, in the Hospital, and in the Home

Wearable biosensors (WBS) will permit continuous cardiovascular (CV) monitoring in a number of novel settings. Benefits may be realized in the diagnosis and treatment of a number of major diseases. WBS, in conjunction with appropriate alarm algorithms, can increase surveillance capabilities for CV catastrophe for high-risk subjects. WBS could also play a role in the treatment of chronic diseases, by providing information that enables precise titration of therapy or detecting lapses in patient compliance.

WBS could play an important role in the wireless surveillance of people during hazardous operations (military, fire-fighting, etc.), or such sensors could be dispensed during a mass civilian casualty occurrence. Given that CV physiologic parameters make up the "vital signs" that are the most important information in emergency medical situations, WBS might enable a wireless monitoring system for large numbers of at-risk subjects. This same approach may also have utility in monitoring the waiting room of today's overcrowded emergency departments. For hospital inpatients who require CV monitoring, current biosensor technology typically tethers patients in a tangle of cables, whereas wearable CV sensors could increase inpatient comfort and may even reduce the risk of tripping and falling, a perennial problem for hospital patients who are ill, medicated, and in an unfamiliar setting.

On a daily basis, wearable CV sensors could detect a missed dose of medication by sensing untreated elevated blood pressure and could trigger an automated reminder for the patient to take the medication. Moreover, it is important for doctors to titrate the treatment of high blood pressure, since both insufficient therapy as well as excessive therapy (leading to abnormally low blood pressures) increase mortality. However, healthcare providers have only intermittent values of blood pressure on which to base therapy decisions; it is possible that continuous blood pressure monitoring would permit enhanced titration of therapy and reductions in mortality. Similarly, WBS would be able to log the physiologic signature of a patient's exercise efforts (manifested as changes in heart rate and blood pressure), permitting the patient and healthcare provider to assess compliance with a regimen proven to improve health outcomes. For patients with chronic cardiovascular disease, such as heart failure, home monitoring employing WBS may detect exacerbations in very early (and often easily treated) stages, long before the patient progresses to more dangerous levels that necessitate an emergency room visit and costly hospital admission.

In this article we will address both technical and clinical issues of WBS. First, design concepts of a WBS will be presented, with emphasis on the ring sensor developed by the author's group at MIT. The ring sensor is an ambulatory, telemetric, continuous health-monitoring device. This WBS combines miniaturized data acquisition features with advanced photoplethysmographic (PPG) techniques to acquire data related to the patient's cardiovascular state using a method that is far superior to existing fingertip PPG sensors [1]. In particular, the ring sensor is capable of reliably monitoring a patient's heart rate, oxygen saturation, and heart rate variability. Technical issues, including motion artifact, interference with blood circulation, and battery power issues, will be addressed, and effective engineering solutions to alleviate these problems will be presented. Second, based on the ring sensor technology the clinical potentials of WBS monitoring will be addressed.

WBS System Paradigm

For novel healthcare applications to employ WBS technology, several system criteria must be met. The WBS hardware solution must be adequate to make reliable physiologic measurements during activities of daily living or even more demanding circumstances such as fitness training or military battle. There must exist data processing and decision-making algorithms for the waveform data. These algorithms must prompt some action that improves health outcomes. Finally, the systems must be cost effective when compared with less expensive, lower technology alternatives.

WBS Design Paradigm

The monitoring environments for out-of-hospital, wearable devices demand a new paradigm in noninvasive sensor design. There are several design requirements central to such devices. Compactness, stability of signal, motion and other disturbance rejection, durability, data storage and transmission, and low power consumption comprise the major design considerations. Additionally, since WBS devices are to be worn without direct doctor supervision, it is imperative that they are simple to use and comfortable to wear for long periods of time. A challenge unique to wearable sensor design is the

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trade-off between patient comfort, or long-term wearability, and reliable sensor attachment. While it is nearly needless to say that WBS technology must be safe, it should be noted that there have been tragic reports of serious injury resulting from early home monitoring technology [2]. Evolving regulatory guidelines for hospital and home monitoring technology can be found in the *U.S. National Fire Protection Association Health Care Facilities Handbook.*

At the same time, the physiologic information generated by WBS technology must trigger some appropriate system action to improve health outcomes. Abnormal states must be efficiently recognized while false alarms are minimized. This requires carefully designed WBS devices, as well as innovative postprocessing and intelligent data interpretation. Postprocessing of sensor data can improve usability, as illustrated by recent improvements in pulse oximetry technology [3]-[5]. Data interpretation can occur in real time (as is necessary for detecting cardiovascular-related catastrophes) or offline (as is the standard-of-care for arrhythmia surveillance using Holter and related monitoring). Real-time alarm "algorithms" using simple thresholds for measured parameters, like heart rate and oxygen saturation, have demonstrated high rates of false alarms [6], [7]. Algorithms for off-line, retrospective data analysis are also in a developmental stage. Studies of novel automated "triage" software used to interpret hours of continuous noninvasive ECG data of monitored outpatients suggest that the software's diagnostic yield is not equal to a human's when it comes to arrhythmia detection [8], [9]. It will presumably require further improvements in WBS hardware, middleware, and software in order to fully exploit the promise of wearable ambulatory monitoring systems.

It is important to bear in mind the present limitations of the technology, such as reliability, system complexity, and cost, but there is a wide scope of exciting healthcare applications available for this technology, as will be discussed later in this article. WBS technology is a platform upon which a new paradigm of enhanced healthcare can be established. Considering that hardware solutions will inevitably become smaller, cheaper, and more reliable, and diagnostic software more sophisticated and effective, it seems more a matter of when cost effectiveness will be achieved for WBS solutions, not if.

Available WBS Monitoring Modalities

WBS solutions, in various stages of technologic maturity, exist for measuring established cardiopulmonary "vital signs": heart rate, arterial blood pressure, arterial oxygen saturation, respiratory rate, temperature, and even cardiac output. In addition, there are numerous WBS modalities that can offer physiologic measurements not conventional in contemporary medical monitoring applications, including acoustic sensors, electrochemical sensors, optical sensors, electromyography and electroencephalography, and other bioanalytic sensors (to be sure, some of these sensors have well-established medical utility, but not for automated surveillance). These less established WBS modalities are outside the scope of this review.

Wearable electrocardiogram systems represent the most mature WBS technology. Holter and related ambulatory electrophysiologic monitoring solutions have established utility in the diagnosis of cardiac arrhythmias. There has been substantial examination of this technology in the medical literature, with excellent reviews available [10]. Temperature is technically trivial to measure using WBS, but the continuous monitoring of body temperature is only a soft surrogate for perfusion, and it lacks established utility outside of traditional clinical settings [11], [12]. There is not a satisfactory ambulatory solution for cardiac output measurement; it has been shown that cardiac output can be extracted from thoracic bioimpedance measurements, although speaking and irregular breathing, as well as posture changes and ambulation, can corrupt this signal. In the future, bioimpedance is likely to prove a powerful WBS modality, since the signal carries information about pulsatile blood volumes, respiratory volumes, intracellular and extracellular fluid balances, and has been shown to enable tomographic imaging. Respiration can be measured using bioimpedance, chest wall geometry, and acoustic means. While the basic sensor technology exists for monitoring respiratory rate, it requires the conversion of a continuous waveform into an integer (breaths per unit time), or the imprecise conversion of the measured parameter into an estimated volumetric rate (liters of gas per unit time).

Ambulatory systems for arterial blood pressure measurement exist. The portapres, employing the volume clamp technique for measuring ABP, offers a continuous waveform. The technology encumbers a finger and the wrist of the subject, is somewhat uncomfortable, and requires some expertise to set up for a subject (for instance, the finger cuff size must be carefully matched to the finger). A more common WBS solution for 24-hour monitoring of ABP involves a portable version of the common oscillometric cuff that fits around the upper arm. This solution requires that the patient keep the monitored arm immobile while the cuff inflates for measurements. By report, this solution has been known to interfere with the sleep and other activities of monitored subjects (and has been reported to cause bruising of the arm at the cuff site) [13].

No fully satisfactory WBS solution exists for ABP monitoring. Because this physiologic parameter has been the cornerstone of many decades of clinical and physiology practice, it will be important to develop future WBS solutions for monitoring ABP. It is also worth investigating surrogate measures of ABP that prove easier to measure, such as pulse wave velocity (which correlates well with degree of hypertension [14], [15]) and the second-derivative of the photoplethysmograph. This article focuses on a wearable ring pulse-oximeter solution, which measures the PPG as well as the arterial oxygen saturation. The PPG contains information about the vascular pressure waveforms and compliances. Efforts to extract unique circulatory information, especially an ABP surrogate, from the PPG waveform are discussed later in this article. The PPG provides an effective heart rate (measuring heart beats that generate identifiable forward-flow), useful for circulatory considerations though less useful for strict electrophysiologic considerations. For instance, the PPG signal may reveal heart rate variability, provided ectopic heart beats, which corrupt the association with autonomic tone, can be excluded.

Development of a Wearable Biosensor—The Ring Sensor

Technical Issues of PPG Ring Sensors

Central to the ring sensor design is the importance of long-term wearability and reliable sensor attachment. Since continuous monitoring requires a device that must be noninvasive and worn at all times, a ring configuration for the sensor unit is a natural choice. Because of the low weight and small size, rings are generally worn without removal more often than watches. Additionally, recent studies have indicated that the finger is one of the best places for WBS sensor attachment [16]. The primary vasculature of the finger is located near the surface and therefore makes it optimal for monitoring arterial blood flow using noninvasive optoelectronic sensors. Thus, a ring is ideal for long-term measurements. As will be illustrated in the following sections, the development of the ring sensor has stressed first an understanding of and then the subsequent elimination of front-end signal artifacts. By implementing a mechanical design that is sensitive to the true causes of signal corruption, significant improvements in overall signal quality can be achieved and sensor effectiveness for various environments can be improved.

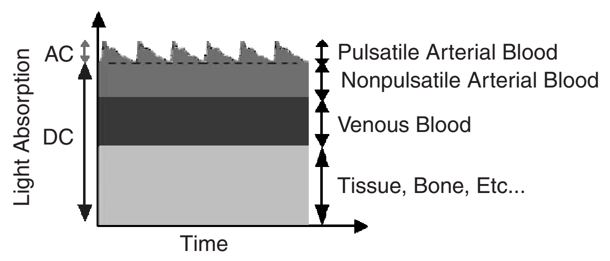

Fig. 1. Illustrative representation of the relative photon absorbance for various sections of the finger. The dc component is significantly larger than the ac component.

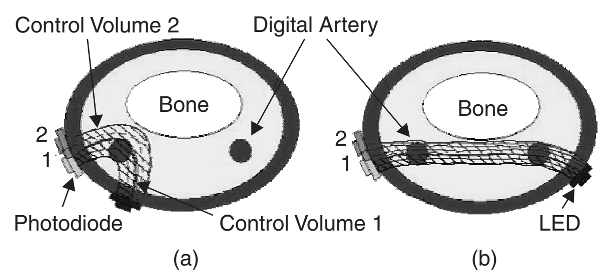

Fig. 2. (a) For the reflective illumination method, movement of the photodiode relative to the LED (position 1 to position 2) leads to a photon path that no longer contains the digital artery. (b) For the transmittal illumination method, movement of the photodetector relative to the LED still contains photon paths that pass through the digital artery.

Figure 1 shows the typical waveform of a photoplethysmograph signal obtained from a human subject *at rest*. The signal comprises a large segment of dc signal and a small-amplitude ac signal. The dc component of photon absorption results from light passing through various nonpulsatile media, including tissue, bones, venous blood, and nonpulsatile arterial blood. Assuming that these are kept constant, a bandpass filter can eliminate the dc component. However, wearable PPG sensors do not meet this premise since, as the wearer moves, the amount of absorption attributed to the nonpulsatile components fluctuates. Power spectrum analysis reveals that this motion artifact often overlaps with the true pulse signal at a frequency of approximately 1 Hz. Therefore, a simple noise filter based on frequency separation does not work for PPG ring sensors to eliminate motion artifact.

Furthermore, wearable PPG sensors are exposed to diverse ambient lighting conditions, ranging from direct sunlight to flickering room light. In addition, wearable PPG sensors must be designed for reduced power consumption. Carrying a large battery pack is not acceptable for long-term applications. The whole sensor system must run continually using a small battery. Several ways to cope with these difficulties are:

- ➤ secure the LEDs and the photodetector (PD for short) at a location along the finger skin such that the dc component may be influenced less by the finger motion
- ➤ modulate the LEDs to attenuate the influence of uncorrelated ambient light as well as to reduce power consumption
- ➤ increase the amplitude of the ac component so that the signal-to-noise ratio may increase
- ➤ measure the finger motion with another sensor or a second PD and use it as a noise reference for verifying the signal as well as for canceling the disturbance and noise.

In the following sections these methods will briefly be discussed, followed by specific sensor designs and performance tests. There are other techniques for reducing motion artifact for general-purpose PPG. These, however, are mostly signal processing techniques applicable to PPG intended for short-term use. The motion artifact problem we are facing in wearable PPG design is different in nature; the source signal quality must be improved before applying signal processing. Therefore, the focus must be placed on basic sensor design.

Techniques for Reduced Motion Artifact

Sensor Arrangement

The location of the LEDs and a PD relative to the finger is an important design issue determining signal quality and robustness against motion artifact. Figure 2 shows a cross-sectional view of the finger with the ring sensor. The LEDs and PD are placed on the flanks of the finger rather than the dorsal and palmar sides. These locations are desirable for two reasons:

➤ both flanks of fingers have a thin epidermal tissue layer through which photons can reach the target blood vessels with less attenuation
➤ the digital arteries are located near the skin surface parallel to the length of the finger.

It should be noted that an arterial pulsation is not only greater in magnitude than cutaneous pulsations but is also less susceptive to motion due to the naturally higher internal pressure. While the capillary collapses with a small external pressure on the order of 10~30 mmHg, the artery can sustain an external pressure up to 70~80 mmHg [17], [18]. Therefore, light static loads, such as contact with the environment, may not disturb the arterial pulsation.

For these reasons, at least one optical device, either the PD or the LED, should be placed on one lateral face of the finger near the digital artery. The question is where to place the other device. Figure 2 shows two distinct cases. One case places both the PD and the LED on the same side of the finger-base, and the other places them on opposite sides of the finger. Placing both the PD and the LED on the same side creates a type of reflective PPG, while placing each of them on opposite sides makes a type of transmittal PPG. In the figure the average pathway of photons is shown for the two sensor arrangements. Although the exact photon path is difficult to obtain, due to the heterogeneous nature of the finger tissue and blood, a banana-shaped arc connecting the LED and PD, as shown in the figure, can approximate its average path [19]. Although these two arrangements have no fundamental difference from the optics point of view, their practical properties and performance differ significantly with respect to motion artifact, signal-to-noise ratio, and power requirements [20]-[22].

Reflective PPG needs more secure attachments of the LED and PD to the skin surface, when compared to transmittal PPG. Once an air gap is created between the skin surface and the optical components due to some disturbance, a direct optical path from the LED to the PD may be created. This direct path exposes the PD directly to the light source and consequently leads to saturation. To avoid this short circuit, the LED light beam must be focused only in the normal direction, and the PD must also have a strong directional property (i.e., polarity), so that it is sensitive to only the incoming light normal to the device surface. Such strong directional properties, however, work adversely when a disturbance pressure acts on the sensor bodies, since it deflects the direction of the LED and PD leading to fluctuations in the output signal. As a result, reflective PPG configurations are more susceptive to disturbances.

In contrast, transmittal PPG configurations do not have the short circuit problems, since the LED and PD are placed on the opposite sides of the finger; no direct path through the air can be created. Additionally, this design allows us to use devices having a weak polarity, which is, in general, more robust against disturbances. Furthermore, transmittal PPG is less sensitive to local disturbances acting on the finger, since the LED irradiates a larger volume of the finger. In the transmittal PPG configuration, the percentage of the measured signal does not significantly change although some peripheral capillary beds are collapsed. The percentage change is greater for reflective PPG, since this volume is smaller.

Figure 3 shows an experimental comparison between transmittal and reflective PPGs. Two sets of PPG sensors, one reflective and one transmittal, were attached to the same finger. Both were at rest initially, and then shaken. The transmittal PPG was quite stable, while the reflective PPG was susceptive to the motion disturbances.

Lighting Modulation

As is the case with most other WBS technologies, on-board power is an extremely important design consideration and is often the limiting factor in design size, function, and flexibility.

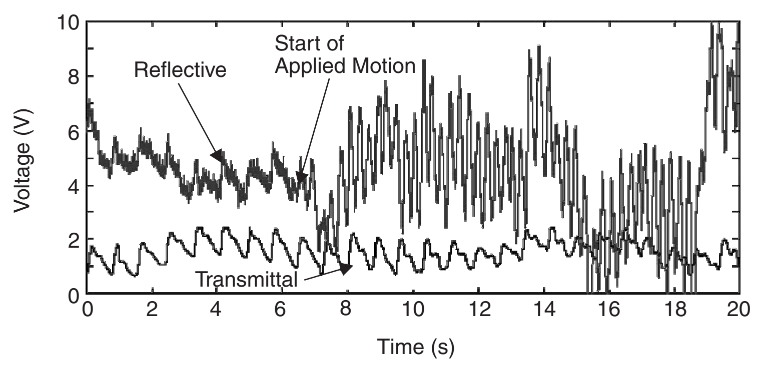

Fig. 3. Corruption of a continuous PPG waveform during the application of a simple chopping motion. Note that while the motion corrupts the reflective sensor signal, the transmittal sensor signal remains unaffected.

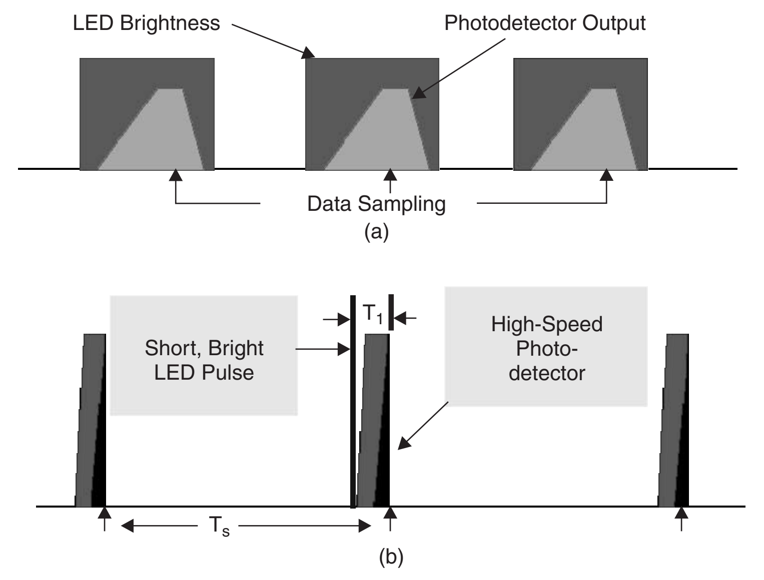

Fig. 4. (a) The slow response time of the photodetector meant that the LED had to be modulated at lower frequencies for data sampling. (b) A faster photodetector response time makes it possible to increase the modulation frequency of the LED.

To keep the overall unit small, the ring sensor design demands a power source that is no larger than the coin batteries used for wristwatches. Despite the superior stability and robustness, transmittal PPG consumes more power. According to the Lambert-Beer law, the brightness decreases exponentially as the distance from the light source increases. Transmittal PPG must have a powerful LED for transmitting light across the finger. This power consumption problem can be solved with a lighting modulation technique using high-speed devices. Instead of lighting the skin continually, the LED is turned on only for a short time, say 100 ~ 1000 ns, and the signal is sampled within this period. High-speed LEDs and PDs, which have become available at low cost in recent years, can be used for this purpose. Figure 4 shows a schematic of high-frequency, low-duty cycle modulation implemented to minimize LED power consumption. Utilizing fast rise-time optical detectors, it is possible to incorporate a modulation frequency of 1 kHz with a duty ratio of 0.1%, a theoretical power usage that is 1,000 times less than conventional full-cycle modulation methods [23].

Use of a strong light source needed for transmittal PPG may cause a skin-burning problem. As reported in [24], if the sensor is attached for a long time the heat created by a powerful LED may incur low-temperature skin burning. The aforementioned high-frequency, low-duty rate modulation described above is an effective method for preventing these types of injuries.

In addition to saving power, the modulation of LED lighting provides an effective means for reducing ambient light disturbances. Reading the PD output while the LED is turned off yields the baseline PPG level attributed to the ambient light alone. Subtracting this reading from the one acquired with the LED illuminated gives the net output correlated with the LED lighting. More sophisticated modulation schemes can be applied by controlling the LED brightness as a periodic time function. Computational power requirements often prohibit complex modulation, however. Design trade-offs must be considered to find the best modulation scheme.

Transmural Pressure

Increasing the detected amplitude of arterial pulsations (i.e., the ac component in Figure 1) improves the signal-to-noise ratio of PPG. It is well understood that the application of an external pressure on the tissue surrounding the artery will increase the pulsatile amplitude. Such a pressure reduces the transmural pressure; that is, the pressure difference between inside and outside of the blood vessel. The pulsatile amplitude becomes a maximum when the transmural pressure approaches zero, since the arterial compliance becomes maximal with zero transmural pressure [25], [26]. Applying a pressure, however, may interfere with tissue perfusion. Since the device is worn for long periods of time, the pressure must be kept such that it does not exceed levels that could damage other vasculature [27]. Thus, the mechanism for holding the LED and PD must be designed such that it provides a safe level of continuous pressure, well below the established clinical threshold.

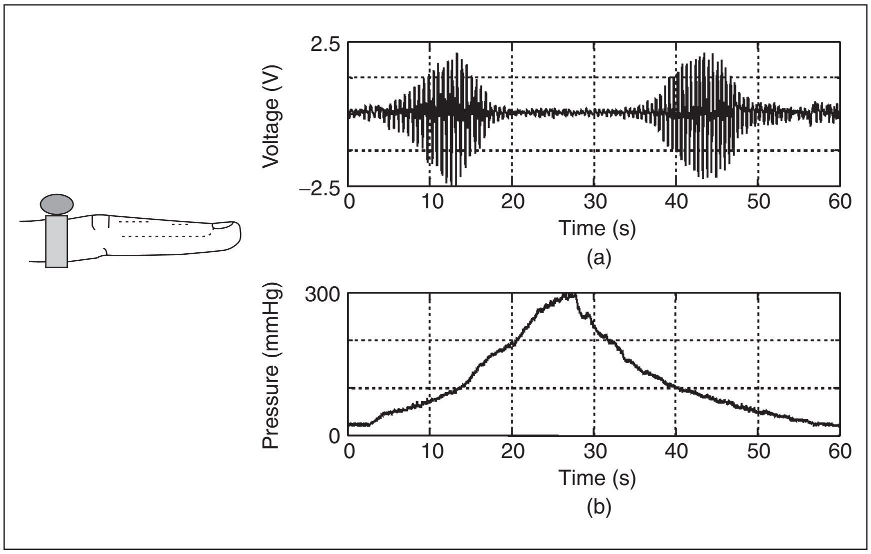

Fig. 5. (a) PPG signal amplitude. (b) Pressure at the photodetector.

Figure 5 shows the pulsatile amplitude of a finger base PPG for varied pressures generated by a finger cuff. As the cuff pressure increases, the PPG amplitude increases until it reaches a maximum. As the pressure keeps increasing further, the amplitude decreases due to occlusion of the blood vessels. The cuff pressure yielding the largest PPG amplitude, generally near the mean arterial pressure [28], is too high to apply for a long period of time. But, to prevent the capillary beds from being collapsed, the cuff pressure must be on the order of 10 mmHg, which is too low to obtain a sufficient PPG amplitude.

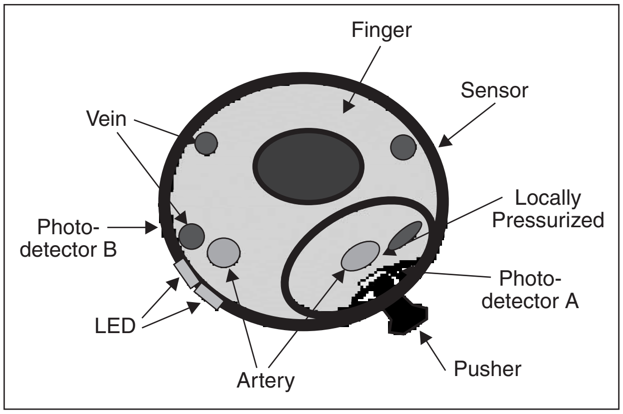

Fig. 6. The schematic of a locally pressurized sensor band.

A solution to this problem is to apply the pressure only at a local spot near the photodetector. When using a cuff or any of the devices that provide uniform surface pressure onto the finger or the arm, it constricts the blood vessels, thus limiting or significantly impeding the amount of blood supplied downstream. However, by providing a local, noncircumferential increase in pressure near the sensor's optical components, it is possible to amplify the plethysmograph waveform while avoiding the potentially dangerous situation of long-term flow obstruction. As shown in Figure 6, the tissue pressure in the vicinity of one of the arteries can be increased with use of a

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