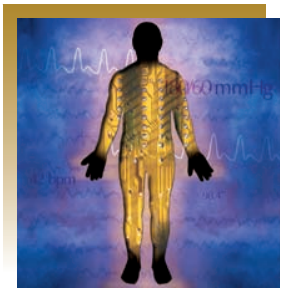

Mobile Monitoring with Wearable Photoplethysmographic Biosensors

H. HARRY ASADA,
PHILLIP SHALTIS,
ANDREW REISNER,
SOKWOO RHEE, AND
REGINALD C. HUTCHINSON

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

 0739-5175/03/$17.00©2003IEEE

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.

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.

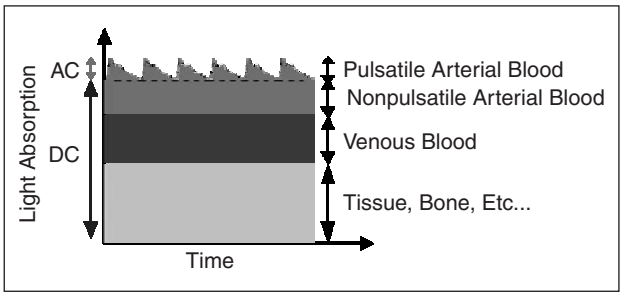

Fig. 1. Illustrative representation of the relative photon absorbance for various sections of the finger. The dc component is significantly larger than the ac component.

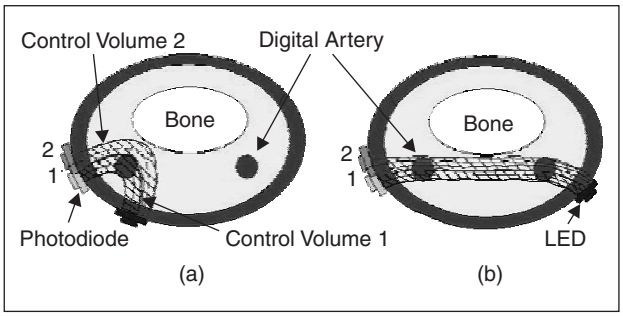

Fig. 2. (a) For the reflective illumination method, movement of the photodiode relative to the LED (position 1 to position 2) leads to a photon path that no longer contains the digital artery. (b) For the transmittal illumination method, movement of the photodetector relative to the LED still contains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

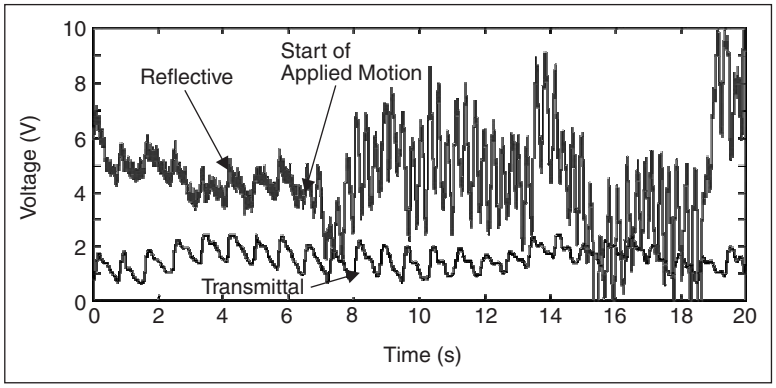

Fig. 3. Corruption of a continuous PPG waveform during the application of a simple chopping motion. Note that while the motion corrupts the reflective sensor signal, the transmittal sensor signal remains unaffected.

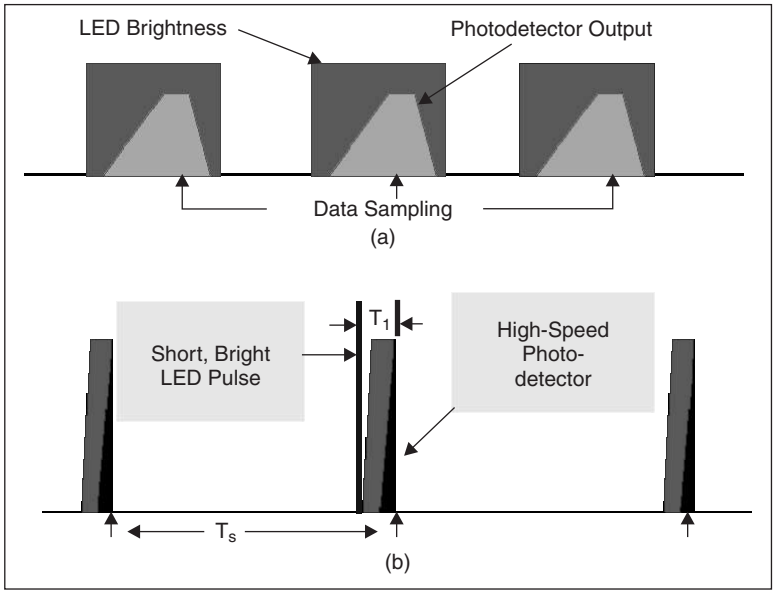

Fig. 4. (a) The slow response time of the photodetector meant that the LED had to be modulated at lower frequencies for data sampling. (b) A faster photodetector response time makes it possible to increase the modulation frequency of the LED.

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.

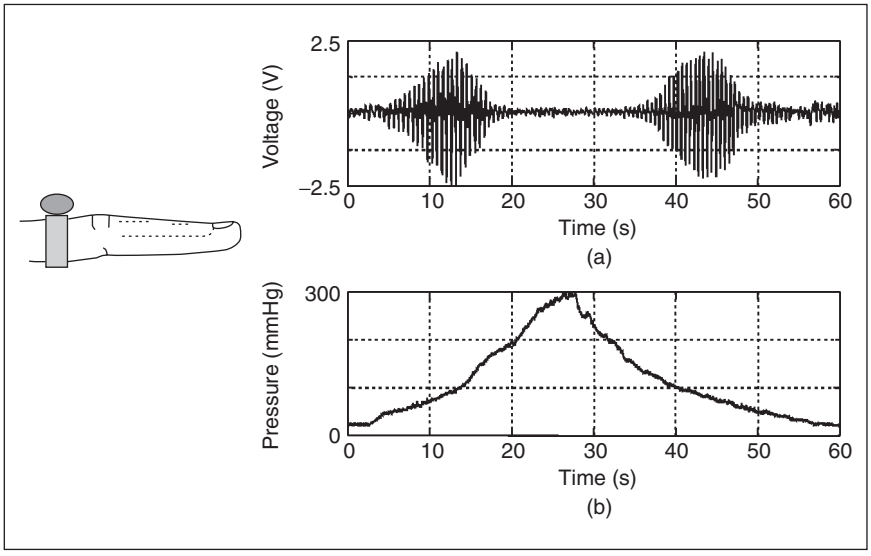

Fig. 5. (a) PPG signal amplitude. (b) Pressure at the photodetector.

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.

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

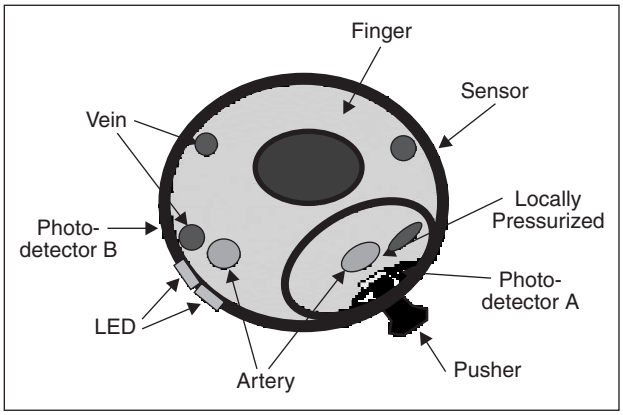

Fig. 6. The schematic of a locally pressurized sensor band.

special mechanism pushing Photodetector A toward the skin. This mechanism, which is attached to the sensor band, would change the pressure distribution such that the transmural pressure of one of the arteries could be high enough to obtain a large pulsatile signal while keeping the pressure low elsewhere to allow for sufficient blood perfusion. As long as the pressurized area is small enough to perfuse it from the surrounding tissue, the local pressurization causes no major complication although the pressure is applied for many days.

Noise Reference

Wearable sensors are to be used with no supervision by medical professionals, as mentioned previously. It is therefore important to monitor whether signals have been obtained under proper conditions. Although the techniques described above are effective for reducing motion artifact, it is still necessary to verify the signal before sending it out for clinical diagnosis. Questionable data can be rejected if the wearable sensor has a means to monitor the hand motion and other sources of disturbances. In the following section, a novel method for detecting finger motion for the verification of signal reliability as well as for recovering the correct signal from a distorted signal will be described.

The motion of the finger can be measured with an accelerometer attached to the body of the ring. MEMS accelerometers are now available at low cost, but they are still too bulky and/or consume too much power to use for the ring sensor. There is no commercially available product satisfying both the power limit and form factor requirements. Instead of using a standard sensor dedicated for motion measurement, the PPG optical sensor can be used as a motion sensor. The fact that PPG is susceptive to motion disturbances implies that the sensor has the potential to be an effective detector of motion. With minor modifications to the original PPG design, the PPG motion detector would have a high sensitivity to detect the nonpulsatile dc component shown in Figure 1. The techniques developed for reducing motion artifact are to be reversed in order to increase the motion sensitivity. First, the reflective PPG arrangement should be used, so the distance between the LED and PD must be shortened. The pressure should be kept low so that less pulsatile signals may be observed. The location of the PD should be away from the arteries and close to a vein instead. In addition, the wavelength of the LED should be selected such that it is more sensitive to the reduced hemoglobin (i.e., approximately 660 nm), since the nonpulsatile vein is filled mostly with the reduced hemoglobin. Figure 6 shows a desirable location for the photodetector detecting the finger motion. Photodetector B in the figure is placed close to the LED as well as to a vein on the low-pressure side. Figure 7 shows an experimental result of the reflective PPG exposed to hand motion. It is clear that the PPG signal has a strong correlation with the acceleration of the hand.

The motion detector can be used not only for monitoring the presence of motion but also for canceling noise. By using PD-B as a noise reference, a noise cancellation filter can be built to eliminate the noise of PD-A that correlates with the noise reference signal. Assuming that the hemodynamic process observed by PPG is stationary and that the noise is additive, adaptive noise canceling methods, such as the classical Widrow method [29], can be applied in order to recover the true pulsation signal from corrupted waveforms. As shown in Figure 8, the noise-canceling filter combines two sensor signals; one is the main signal captured by PD-A and the other is the noise reference obtained by PD-B. The main signal mostly consists of the true pulsatile signal, but it does contain some noise. If we know the proportion of the noise contained in the main signal, we can generate the noise of the same magnitude by attenuating the noise reference signal and then subtract the noise from the main signal to recover the true pulsatile signal. If the noise magnitude is not known a priori, it must be determined adaptively during the measurement. Various algorithms for adaptive filtering can be applied to tune the filter in real time. Some can determine optimal filter gains and parameters based on the evaluation of the recovered signal, as shown in Figure 8 by the feedback from the output to the

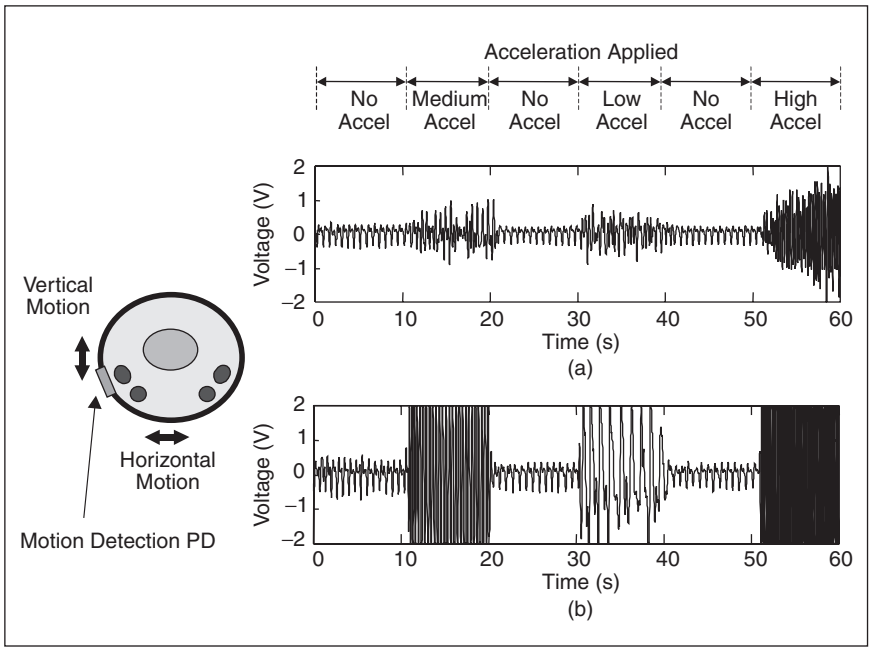

Fig. 7. Reflective PPG used as a motion detector: PPG output has a strong correlation with the vertical and horizontal acceleration of the finger. (a) Photoplethysmogram with vertical acceleration. (b) Photoplethysmogram with horizontal acceleration.

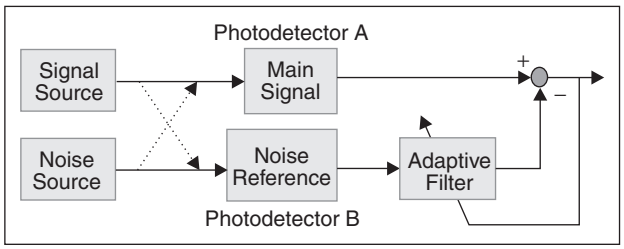

Fig. 8. Block diagram of adaptive noise cancellation using second PPG sensor as noise reference.

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.

adaptive filter block. Details of this adaptive filtering method are beyond the scope of this article. The dual photodetector design shown in Figure 6 provides both main signal and noise reference that are distinct. This allows us to implement noise-canceling filters effectively despite complex motion artifact.

Prototyping and Results

Based on the methodologies for reducing motion artifact, several prototypes of the ring sensor have been designed, built, and tested. In implementing these methods, design trade-offs among accuracy, sampling rate, power consumption, size, and weight have been made.

Prototype A

Figure 9 shows the first ring sensor prototype that contains an optical sensor unit, analog and digital processing units, and an RF transmitter, all of which are encapsulated in a compact body and powered by a tiny cell battery used for wristwatches. The ring has a PIC microcomputer performing all the device controls and low-level signal processing, including LED modulation, data acquisition, filtering, and bi-directional RF communication. The acquired waveforms, sampled at 100 Hz, are transmitted to a PDA or a cellular phone carried by the patient through an RF link of 105 kbps at a carrier frequency of 915 MHz. The cellular phone then accesses a Web site for data storage and clinical diagnosis.

An obvious source of signal corruption results from the direct interaction of the sensor unit with the wearer's surrounding environment; e.g., holding objects, touching surfaces, etc. Thus, the body of the ring must separate the sensor unit in order to decouple the sensor unit from these interactions. To this end, a double ring configuration was designed and implemented, as shown in Figure 10. The disturbance force is born by the outer ring and is not transmitted to the inner ring holding the sensor unit. Moreover the outer ring serves as an optical shield for protecting the sensor unit from the ambient light.

In this early development, the power consumption of the LEDs and the imbedded CPU clock were a major bottleneck limiting the design. The distance between the LEDs and PDs had to be shortened for power saving considerations, and the CPU clock was minimized in order to extend the battery life to a few weeks. See [30] for power budget and design details. To evaluate the overall performance of motion artifact resistance, data were continually taken from a wearer performing daily office work (e.g., typing and writing) and the acquired data were examined to see how often the waveforms were corrupted and how many of them were usable. The result was that 35% of the data in a two-hour session was not corrupted and usable.

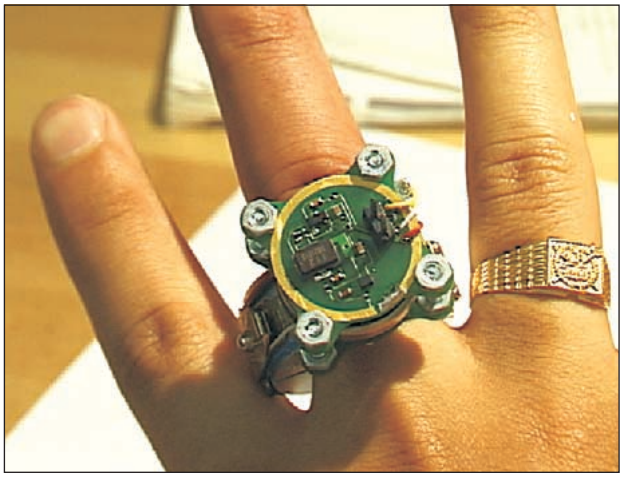

Fig. 9. First prototype ring sensor with RF transmitter powered by a coin-size cell battery.

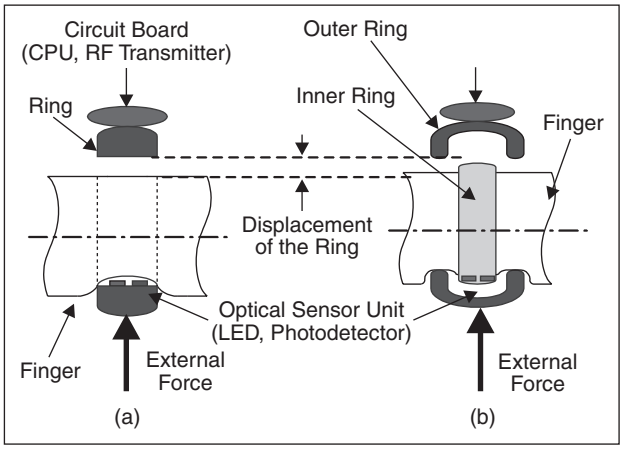

Fig. 10. Dislocation of ring sensors due to external load. (a) Traditional single-body design under external force. (b) New isolating double ring sensor under external force [31].

Continuous monitoring also enables caregivers to gather accurate data about patients' home physiologic states, since patients measuring their own blood pressure may leave out unsatisfactory numbers.

Prototype B

To improve motion artifact resistance and accuracy, a transmittal PPG ring sensor, Prototype B, has been built and field-tested. Prototype B has high-speed optical devices enabling the lowering of the LED duty rate to 1/1,000. The LED used is 6.7 times brighter than that of Prototype A, while the resultant power consumption is 173 times smaller than before. The sensor band was redesigned with the use of bio-compatible elastic materials to better hold the LED's and PD's, maintain a proper level of pressure, optically shield the sensor unit, and secure the contact with the skin consistently in the face of finger motion (see Figure 11). As a result, the waveform of this transmittal PPG was quite stable. Figure 3 presented earlier is the experiment of Prototype B. Note that the transmittal PPG (Prototype B) signal did not collapse even when the hand was shaken. Additionally, the analog filtering circuit was optimized for quality of signal. These modifications greatly improved the ability of the device to measure traditionally difficult variables such as heart rate variability (Table 1, Figure 12).

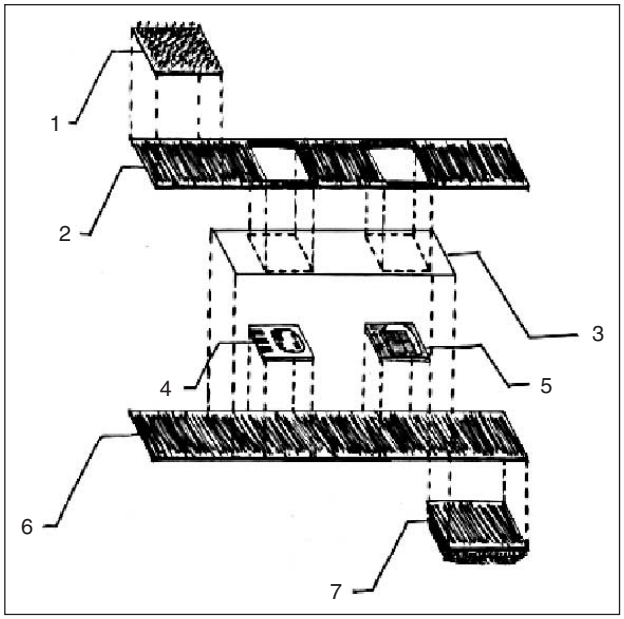

Fig. 11. Redesigned sensor band that protects optical components from direct contact with skin and hides wires from outside environment.

This Prototype B ring sensor was recently given IRB approval for patient testing in the Pulmonary Function Testing Laboratory at the Massachusetts General Hospital. Due to hospital regulations a tethered version of Prototype B was benchmarked with a Nellcor –395 fingertip pulse oximeter for motion artifact resistance and oxygen saturation measurements during patient motion (defined to be motion while riding a stationary bicycle). Each patient voluntarily participated in the study and was given the opportunity to end the testing at any point, if desired. Plethysmographs from both devices were sampled and recorded using a National Instruments DAQ Card-6024E for PCMCIA data acquisition board at a sampling frequency of 1000 Hz, for a time of approximately 30 minutes. Oxygen saturation measurements were addition-

TABLE 1. RMS error (beats/min) of the pulse rates from the ring sensor B compared with those from EKG and Nellcor PPG devices. Significant improvements have been made when comparing the ring sensor/EKG error to the EKG/Nellcor error.

EKG and Ring Sensor B	Nellcor PPG and Ring Sensor B	EKG and Nellcor PPG
1.43	3.15	2.88

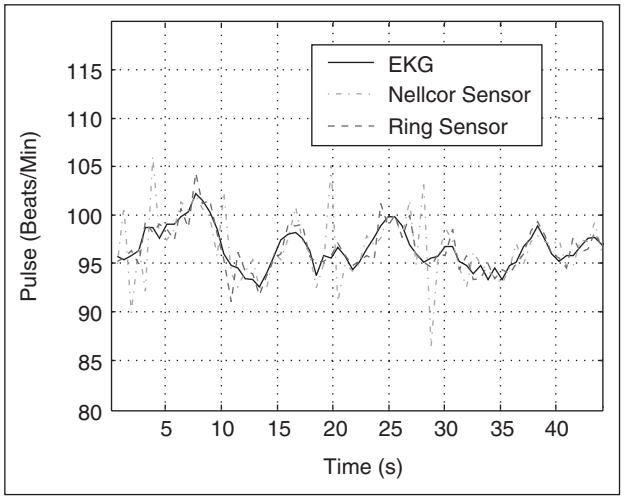

Fig. 12. Beat-to-beat pulse rate of Prototype B ring sensor benchmarked with EKG and FDA-approved fingertip PPG by Nellcor.

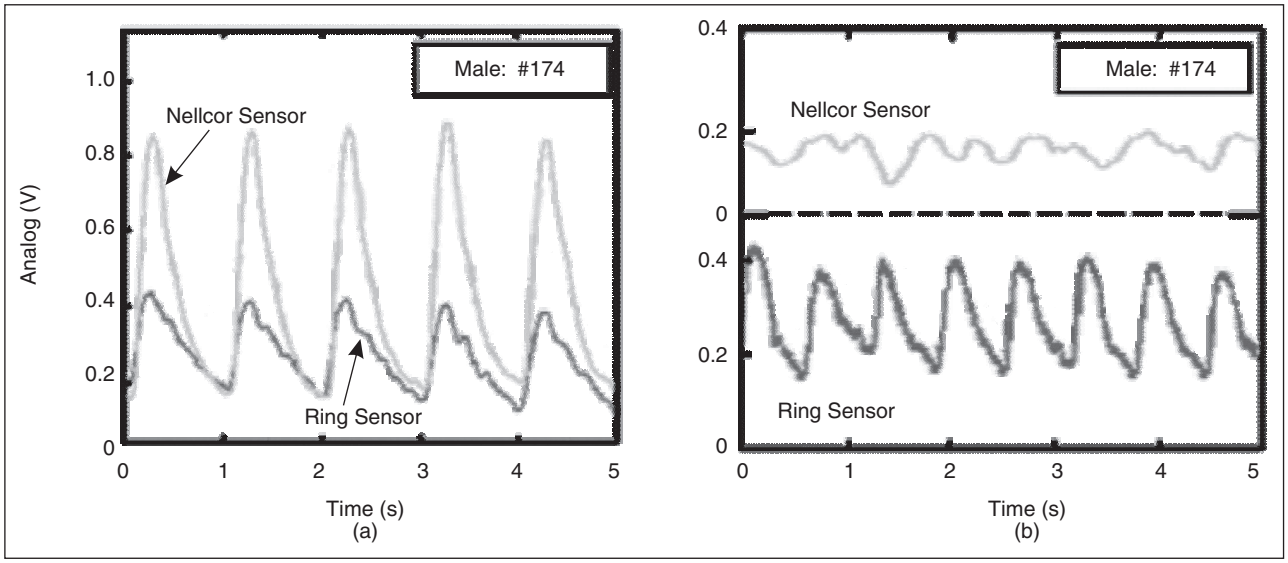

Fig. 13. Representative example of PPG benchmarking data acquired while (a) patient was at rest and (b) patient was riding a bicycle against a graded resistance.

ally benchmarked with both the Nellcor sensor and with arterial blood gas samples analyzed by a CO-Oximeter. The ring sensor data used for comparison were the raw, unprocessed sensor data. No additional postprocessing algorithms were used to improve the quality of the measured signals.

In general, it was found that the ring sensor and the Nellcor sensor had comparable stability and resolution while the patient was at rest. However, the ring sensor was found to have a significantly more stable signal than the Nellcor fingertip pulse oximeter while the patient was riding the bicycle (Figure 13).

In addition to added waveform stability, the ring sensor demonstrated superior performance under motion conditions while monitoring the patient's oxygen saturation as is shown in Figure 14. Further, each patient was asked to fill out a survey before, during, and after each trial. The survey consisted of a simple comfort rating system for the ring sensor. The patients indicated no discomfort (no worse than wearing a hat) at any time during the testing of the device.

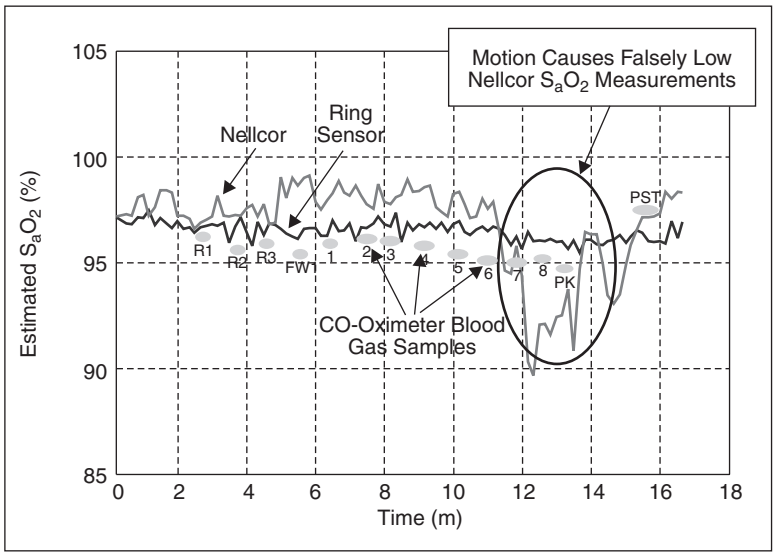

Fig. 14. Unlike the Nellcor sensor, the ring sensor was able to more accurately follow the oxygen saturation trend of the patient due to improved waveform stability during patient motion.

Prototype C

The local pressurization and motion detection methods described previously have been implemented for further improvement. Figure 15 shows the schematic of the Prototype C ring sensor. Both transmittal (PD-A) and reflective (PD-B) PPGs were mounted on the sensor band. The former is placed on top of a locally pressurizing mechanism with an adjustable setscrew. The latter is mounted on the low-pressure side in order to detect motion.

To evaluate how a pressure applied to the finger base interferes with blood circulation, the blood flow toward the fingertip was measured by using Nellcor's PPG sensor attached to the fingertip. For the purpose of comparing the local pressurization with the traditional cuff pressurization, a finger cuff that generates a uniform pressure all around the finger circumference has been built and used for experiments. Figure 16 shows the simultaneous measurements of the fingertip PPG and a finger base PPG using the pressure-controlled finger cuff. As the cuff pressure increased, the amplitude of the finger base PPG increased. The fingertip PPG (i.e., the blood circulation toward the fingertip) was not influenced up to a certain cuff pressure, but it sharply decreased when the cuff pressure exceeded a threshold level. This significant decrease happened for the cuff pressure between 80 mmHg and 120 mmHg. Figure 17 shows the same measurements using the Prototype C ring sensor with the local pressurization mechanism. As the local pressure increased, the ring sensor output increased in amplitude, but the fingertip PPG did not show any tangible difference. As the local pressure was further increased, the ring sensor output gradually decreased. The fingertip PPG did not change even for this excessive local pressure. The ex-

act value of the local pressure is not available due to difficulties of instrumentation, but the nominal pressure given by the normal force divided by the pressurized area was 120 mmHg when the maximum output amplitude was reached. Since the finger consists of a network of veins and arteries, pressurizing a small spot, 5 mm in diameter, at the finger base does not significantly affect the overall circulation within the finger.

These results clearly indicate that it is possible to achieve a design that can meet the critical, conflicting design requirements for out-of-hospital environments. By developing a thorough understanding of both the physiology of the relevant signals and the mechanisms through which these signals can be acquired, it is possible to design a wearable biosensor that can offer cost-effective, acceptable diagnostic test characteristics that are effective over a broad range of novel health applications outside of traditional clinical monitoring settings.

Survey of Applications for Ring Sensor Technology

There are a number of promising applications for PPG and pulse oximetry-related WBS technologies. Applications range from real-time catastrophe detection to management of chronic medical conditions and regimen compliance. The scope of these applications are described below, with focused consideration of surveillance for the catastrophe of Sudden Infant Death Syndrome (SIDS), as well as the long-term management of hypertension and chronic heart failure. Overall, WBS technology stands to make a major impact by taking surveillance for numerous cardiovascular/pulmonary conditions outside of traditional medical settings.

Catastrophe Detection

In one class of applications, the goal is to detect a physiologic catastrophe (meaning the development or progression of a dangerous or unstable state) and trigger a timely response that improves outcomes. WBS, in conjunction with diagnostic algorithms and some specific response (which might be human or automated in nature), stand to ameliorate physiologic catastrophes occurring outside conventional clinical environments. For instance, WBS can play an important role in the wireless surveillance of people during hazardous operations (military, fire-fighting, etc.), or such sensors can be dispensed during a mass civilian casualty occurrence. In an overcrowded Emergency Department, patients who are in the waiting room for hours with an undifferentiated medical complaint will receive state-of-the-art physiologic monitoring. For hospital inpatients who require CV monitoring, current biosensor technology typically tethers patients in a tangle of cables. For convalescing patients in a hospital, or a rehabilitation center, there would no longer be a dichotomy between optimal bed-bound monitoring and optimal rehabilitation consisting of ambulation and a full scope of physical activities. Given the physical freedom when monitored by WBS, inpatients may experience less physical deconditioning, and these two factors together may impact the not insignificant problem of dangerous inpatient falls in the elderly (an incidence on the order of 1-5% per admission [32], [33]).

WBS measuring circulation could also be used to monitor geriatric subjects living alone, offering an automatic 911 call in the event of a catastrophe and peace of mind for the subject and concerned family the rest of the time. The dissemination of new automated defibrillators for the home, such as the recently FDA-approved Philips Electronics' HeartStart model, means that the general public will be increasingly able to respond to victims of life-threatening arrhythmias when such catastrophes are detected. SIDS demonstrates the potential power and liability of WBS technology implemented in a home monitoring system. SIDS, the leading cause of death in infants less than 1 year of age, afflicts several thousand infants per year in this country [34], [35]. Unfortunately, the precise pathophysiology of SIDS remains unknown, and it is likely due to a range of etiologies that cannot be distinguished postmortem. Over 25 years ago, new initiatives were taken to implement home cardiopulmonary monitoring for high-risk infants [36], [37]. In one series, the impact of home monitoring appeared powerful, as 12 of 50 monitored high-risk infants received resuscitation for life-threatening events. At that time, though, there was a significant issue of false alarms due to imperfect technology solutions and inaccurate parental assessment of the infant's health [38], [39]. In the Collaborative Home Infant Monitoring Evaluation (CHIME) study, it was

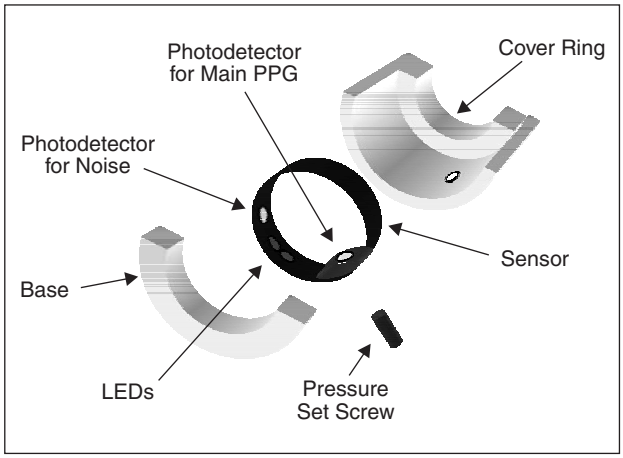

Fig. 15. The schematic of the Prototype C ring sensor.

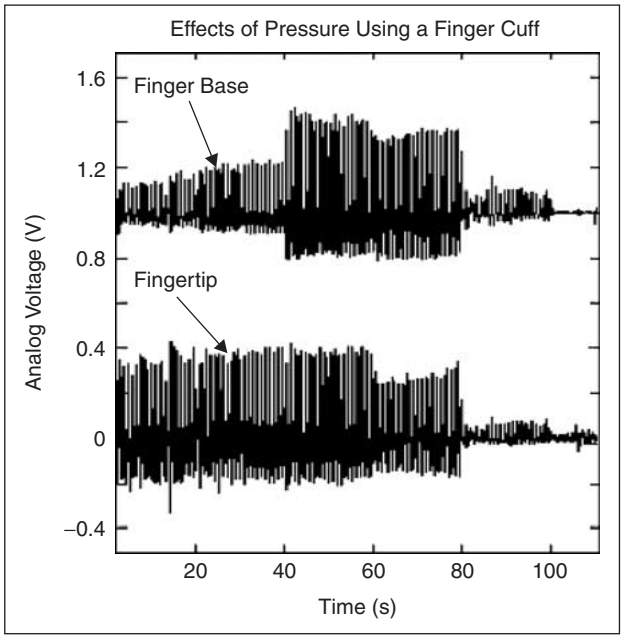

Fig. 16. The effects of cuff-induced pressure changes monitored at the fingertip and the finger base—cuff pressure changes completely occlude blood flow.

noted that apnea and bradycardia are relatively common events for healthy infants (this study of 1,079 infants was not large enough to address the impact on mortality of home monitoring on SIDS because the disease incidence is between 0.5 and 1.0 per 1,000) [40]. It seems that WBS technology might offer a powerful solution to the leading cause of death of U.S. infants, but it will require acceptable WBS hardware and diagnostic algorithms that identify endangered infants in time for their parents and/or emergency medical service to make a useful intervention. Such a system will also be judged on its rate of financially (and emotionally) expensive false alarms, since automated alarms will likely trigger expensive and stressful medical evaluations.

Chronic Medical Conditions

WBS may enable a new paradigm in the management of long-term CV disease, enhancing the titration of therapies and detecting disease progression. Moreover, it has been suggested that serious noncompliance occurs in from 30 to 60% of outpatients on a medication regimen [41], [42]. If there is a measurable physiologic signature of missed medications, a monitoring system could offer friendly reminders to patients when lapses are detected. Continuous monitoring also enables caregivers to gather accurate data about patients' home physiologic states, as it has been suggested that patients measuring their own blood pressure may leave out unsatisfactory numbers [43]. Similarly, measurement of heart rate changes indicative of exertion might serve to track compliance with an exercise regimen, thus motivating patient adherence to an exercise regimen, given the benefits of even low-level physical activity [44]. Potential utility of long-term WBS monitoring for management of hypertension and chronic heart failure are discussed below.

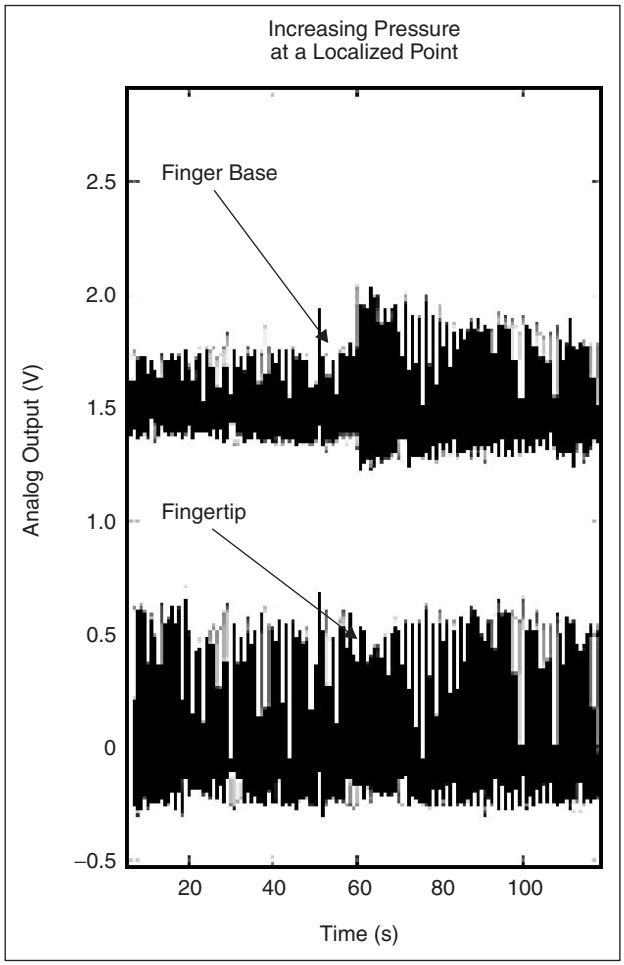

Fig. 17. The effects of local pressure changes monitored at the fingertip and the finger base—no significant change in the downstream circulation.

Hypertension

Hypertension is a major risk factor for cardiovascular (CV) disease, and though disease prevalence is quite subject to the diagnostic criteria used, hypertension afflicts on the order of 25% of the American population [45], [46]. Currently, the diagnosis of hypertension is made using discrete values of the waveform's peak (systolic) and trough (diastolic) pressure values, measured over a small number of cycles, which are assumed to be representative of the subject's chronic vascular state. Yet an approach relying on discrete ABP measurements, especially those acquired in a clinical setting, is problematic and often inaccurate [47], [48]. Despite the magnitude of the CV risks of hypertension, present medical approaches to treating the condition have not been shown to fully reduce the risk [49], [50]. The discrete approach for measuring ABP may very well put some patients at risk for undertreatment or overtreatment with medication [51]-[54]. It is possible that there are intrinsic limitations to the discrete approach to ABP characterization.

In contrast, multiple studies have suggested the benefit of ambulatory blood pressure measurement (the ABP is measured repeatedly in the outpatient setting to produce a 24-hour time-course) as compared to standard clinic and home measurements, for risk stratification and predicting morphologic changes in the left ventricle [55]-[58]. There is evidence that treatment is more effective when titrated to ambulatory blood pressure versus conventional measurement strategies [59]. Typically, though, a cuff-based technique is employed, which limits the subject's activities or limits the reliability of the measurements when the subject is active [60], [61]. In conjunction with novel diagnostic algorithms able to analyze long time-series of data, a truly wearable ABP biosensor stands to improve the efficacy of medical treatment. As noted in section 2.2, there is presently no adequate WBS solution for this application, but it has been demonstrated that measures of arterial compliance, closely related to hypertension, can be extracted from the plethysmograph and PPG [62]-[64]. Given the potential for the Asada group's ring sensor to meet the desirable design criteria necessary for a robust WBS modality, there is reason to give future attention to the PPG and other ABP surrogates in future studies of the efficacy of ambulatory and long-term ABP monitoring.

Congestive Heart Failure Management

Another potential application for chronic surveillance using WBS is the management of heart failure. This chronic disease is characterized by episodic, acute exacerbations that frequently lead to costly inpatient admissions. In the 1990s, an average hospitalization cost approximately US$10,000, versus US$4,000 for average annual outpatient care expenditures [65]. By the year 2007 heart failure is projected to afflict 10 million Americans [66]. Yet most patients admitted with acute heart failure have an identifiable precipitant, and it seems reasonable to hypothesize that a majority of these precipitants

(such as medication noncompliance, and dietary indiscretion, accounting for about 64% of the cases in one series [67]) might be detected by continuous home monitoring well before the exacerbation necessitated the costly hospital admission. There are a constellation of clinical symptoms associated with worsening heart failure, including increased dyspnea with exertion, increased dyspnea with recumbent positioning (orthopnea or paroxysmal nocturnal dyspnea), and increasing peripheral edema. Certainly it has been recognized that management of advanced heart failure patients calls for "intensive home monitoring" [68]. Ultimately, the utility of WBS in screening for heart failure exacerbation rests in the sensitivity of the sensor measurements to identify these aforementioned abnormalities using one or multiple modalities, including oximetry, plethysmography, extremity conductance, microphony, etc. Given that WBS technology enables continuous monitoring, one specific advantage is that it allows detection of transient phenomena, such as transient hypoxia with exertion or recumbent positioning. WBS technology is an appealing potential solution to intensive home monitoring, as abnormal sensor measurements could prompt further diagnostic and therapeutic measures.

Haruhiko Harry Asada is a Ford professor of mechanical engineering and director of the Brit and Alex d'Arbeloff Laboratory for Information Systems and Technology in the Department of Mechanical Engineering at Massachusetts Institute of Technology (MIT). He specializes in robotics, biomedical engineering, and system dynamics and control. His current research areas include wearable health monitoring, robotic aids for bedridden patients, vast DOF actuator systems, and multiphysics simulation. He received the B.S., M.S., and Ph.D. degrees in precision engineering in 1973, 1975, and 1979, respectively, all from Kyoto University, Japan. He was a visiting research scientist at the Robotics Institute of Carnegie-Mellon University from 1980 to 1981. He joined the Department of Mechanical Engineering at MIT as faculty in 1982 and became a full professor in 1989. He is a Fellow of ASME.

Phillip Shaltis received the B.A. degree in physics from Albion College, Albion, MI, in 1999 and the B.S. degree in mechanical engineering from the University of Michigan, Ann Arbor, MI in 2000. He will be finishing dual M.S. degrees in mechanical and electrical engineering at MIT in 2003 and plans to continue work towards the Ph.D. degree in mechanical engineering at MIT. His research interests include biomedical instrumentation, biomedical signal processing, analog circuit design, and system analysis and control.

Andrew Reisner received the B.S. in mechanical engineering and biological sciences at Stanford University in 1992, the M.D. from Harvard Medical School in 1997, and trained in emergency medicine at the Harvard-affiliated emergency medicine residency program. He is presently an attending physician at the Massachusetts General Hospital in the Department of Emergency Medicine, an instructor at Harvard Medical School, and a visiting scientist at MIT. Dr. Reisner's research is oriented toward the intersection of diagnostic expert systems, medical sensor technology, and the clinical problem of circulatory shock.

Sokwoo Rhee received the B.S. degree in mechanical engineering from Seoul National University, Seoul, South Korea, in 1995, and the M.S. and Ph.D. degrees in mechanical engineering from MIT in 1997 and 2000, respectively. He is currently the chief technology officer and vice president of technology at Millennial Net, Inc. in Cambridge, MA. He was also a postdoctoral research associate in the Department of Mechanical Engineering at MIT in 2000-2002. His research interests include biomedical instrumentation, ultra-low power wireless communication, system analysis, and control.

Reginald C. Hutchinson received the B.S. degree in mathematics from Morehouse College, Atlanta, GA; the B.S. degree in mechanical engineering from the Georgia Institute of Technology, Atlanta, Georgia, in 1999; and dual M.S. degrees in mechanical engineering and electrical engineering from MIT, Cambridge, MA, in 2002. He is currently working as a consultant for Accenture in New York City. His research interests include design, control of electromechanical systems, controls and system dynamics, and analog and digital signal processing.

Address for Correspondence: Harry Asada, Massachusetts Institute of Technology, Department of Mech. Engineering, d'Arbeloff Laboratory for Information, Systems and Technology, Cambridge, MA, 02139 USA. Tel: +1 617 258 0813. Fax: +1 617 258 6575. E-mail: asada@mit.edu. URL: http://www.mit.edu/people/pshaltis/home.html

References

[1] S. Rhee, B-H. Yang, and H. Asada, "Artifact-resistant, power-efficient design of finger-ring plethysmographic sensors," *IEEE Trans. Biomed. Eng.*, vol. 48, pp. 795-805, July 2001.

[2] M.L. Katcher, M.M. Shapiro, and C. Guist, "Severe injury and death associated with home infant cardiorespiratory monitors," *Pediatrics*, vol. 78, no. 5, pp. 775-779, Nov. 1986.

[3] M.J. Hayes and P.R. Smith, "Quantitative evaluation of photoplethysmographic artefact reduction for pulse oximetry in biomedical sensors, fibers and optical delivery systems," *Proc. SPIE*, vol. 3570, pp. 138-147, Stockholm, Sweden, 1999.

[4] A.B. Barreto, L.M. Vicente, and A. Taberner, "Adaptive pre-processing of photoplethysmographic blood volume pulse measurements," in *Proc. 1996 15th Southern Biomedical Eng. Conf.*, Dayton, Ohio, 1996, pp. 114-117.

[5] P.R. Lictenthal and L.D. Wade, "Evaluation of signal extraction technology (SET) in preventing false alarms when using pulse oximetry in the recovery room," *Anesthesiology*, vol. 86, no. 2S, pp. S278, 1996.

[6] I.G. Kestin, B.R. Miller, and C.H. Lockhart, "Auditory alarms during anesthesia monitoring," *Anesthesiology*, vol. 69, no. 1, pp. 106-109, July 1988.

[7] L.R. Bentt, T.A. Santora, B.J. Leverle, M LoBue, and MM Shabot, "Accuracy and utility of pulse oximetry in the surgical intensive care unit," *Curr. Surg.*, vol. 47, no. 4, pp. 267-268, July-Aug. 1990.

[8] G.A. Lanza, M. Lucente, A.G. Rebuzzi, M.C. Cortellessa, S. Tamburi, P. Mancuso, R. Neri, and U. Manzoli, "Accuracy in clinical arrhythmia detection of a real-time Holter system," *J. Electrocardiol.*, vol. 23, no. 4, pp. 301-306, Oct. 1990.

[9] D.H. Cooper, H.L. Kennedy, D.S. Lyyski, and M.K. Sprague, "Holter triage ambulatory ECG analysis. Accuracy and time efficiency," *J. Electrocardiol.*, vol. 29, no. 1, pp. 33-38, Jan. 1996.

[10] P.J. Zimetbaum and M.E. Josephson, "The evolving role of ambulatory arrhythmia monitoring in general clinical practice," *Ann. Intern. Med.*, vol. 130, no. 10, pp. 848-856, May 1999.

[11] J.L. Vincent, J.J. Moraine, and P. van der Linden, "Toe temperature versus transcutaneous oxygen tension monitoring during acute circulatory failure," *Intensive Care Med*., vol. 14, no. 1, pp. 64-68, 1988.
[12] R.J. Henning, F. Wiener, S. Valdes, and M.H. Weil, "Measurement of toe temperature for assessing the severity of acute circulatory failure," *Surg. Gynecol. Obstet.*, vol. 149, no. 1, pp. 1-7, July 1979.
[13] B.P. McGrath, "Ambulatory blood pressure monitoring," *Med. J. Aust*., vol. 176, no. 12, pp. 588-592, June 17, 2002.
[14] W.W. Nichols and D.A. McDonald, "Wave-velocity in the proximal aorta," *Med. Biol. Eng*., vol. 10, no. 3 pp. 327-335, 1972.
[15] M. Anliker, W.E. Moritz, and E. Ogden, "Transmission characteristics of axial waves in blood vessels," *J. Biomechanics*, vol. 1, pp. 235-246, 1968.
[16] D.G. Clayton, "Pulse oximeter probes. A comparison between finger, nose, ear and forehead probes under conditions of poor perfusion," *Anaesthesia*, vol. 46, no. 4, pp. 260-265, Apr. 1991.
[17] A. Guyton and J. Hall, *Textbook of Medical Physiology*, 9th ed. Philadelphia, PA: Saunders, 1996, pp. 187.
[18] M.S. Rendell and J.M. Wells, "Ischemic and pressure-induced hyperemia: A comparison," *Arch. Phys. Med. Rehab.*, vol. 79, no. 11, pp. 1451-1455, 1998.
[19] S. Feng, F. Zeng, and B. Chance, "Photon migration in the presence of a single defect: A perturbation analysis," *Appl. Opt*., vol. 34, no. 19, pp. 3826-3837, 1995.
[20] Y. Mendelson and B.D. Ochs, "Noninvasive pulse oximetry utilizing skin reflectance photoplethysmography," *IEEE Trans. Biomed. Eng.*, vol. 35, pp. 798-805, 1988.
[21] W. Feng, D. Haishu, T. Fenghua, Z. Jun, X. Qing, and T. Xianwu, "Influence of overlying tissue and probe geometry on the sensitivity of a near-infrared tissue oximeter," *Physiol. Meas.,* vol. 22, no. 1, pp. 201-208, 2001.
[22] G. Kumar and J.M. Schmitt, "Optimal probe geometry for near-infrared spectroscopy of biological tissue," *Appl. Opt.*, vol. 36, no. 10, pp. 2286-2293, Apr. 1997.
[23] P.A. Shaltis, H. Asada, and S. Rhee, "Artifact resistant, power efficient, high speed modulation design for photo plethysmographic ring sensors," *Ann. Biomed. Eng*., vol. 29, suppl. 1, pp. S-117, 2001.
[24] F.T. Kahveci, S. Gören, and B. Özcan, "A rare complication due to pulse oximetry in intensive care unit," *Ann. Med. Sci*., vol. 9, pp. 36-37, 2000.
[25] K.H. Wesseling, B. de Wit, G.M.A. van der Hoeven, J. van Goudoever, and J.J. Settels, "Physiocal, calibrating finger vascular physiology for Finapres," *Homeostatis*, vol. 36, no. 2-3, pp. 67-82, 1995.
[26] K. Yamakoshi, H. Shimazu, M. Shibata, and A. Kamiya, "New oscillometric method for indirect measurement of systolic and mean arterial pressure in the human finger. Part 1: Correlation study," *Med. Biol. Eng. Comput*., vol. 20, pp. 307-313, 1982.
[27] R.K. Daniel, D.L. Priest, and D.C. Wheatley, "Etiologic factors in pressure sores: An experimental model," *Arch. Physical Med. Rehab.*, vol. 62, no. 10, pp. 492–498, 1981.
[28] K. Yamakoshi, H. Shimazu, A. Kawarada, "Electric impedance cuff for the indirect measurement of blood pressure and volume elastic modulus in human limb and finger arteries," *Med. Biol. Eng. Comput.*, vol. 27, pp. 477-483, 1989.
[29] B. Widrow, J.R. Glover, J.M. McCool, J. Kaunitz, C.S. Williams, R.H. Hearns, J.R. Zeidler, E. Dong, Jr., and R.C. Goodlin, "Adaptive noise canceling: Principles and applications," *Proc. IEEE*, vol. 63, pp. 1692-1716, Dec. 1975.
[30] S. Rhee, B-H. Yang, and H. Asada, "Artifact-resistant, power-efficient design of finger-ring plethysmographic sensors. Part I: Design and analysis," *22nd Annu. Int. Conf. IEEE Engineering in Medicine and Biology Society*, pp. 2792-2795, Chicago, IL, July 23-28, 2000.
[31] S. Rhee, B-H. Yang, and H. Asada, "Design of a artifact-free wearable plethysmographic sensor," *21st Annu. Int. Conf. IEEE Engineering in Medicine and Biology Society*, Atlanta, GA, Oct. 13-16, 1999, pp. 786.
[32] D. Oliver, A. Hopper, and P. Seed, "Do hospital fall prevention programs really work? A systematic review," *J. Amer. Geriatr. Soc*., vol. 48, no. 12, pp. 1679-1689, Dec. 2000.
[33] M. Vassallo, T. Azeem, M.F. Pirwani, J.C. Sharma, and S.C. Allen, "An epidemiological study of falls on integrated general medical wards," *Int. J. Clin. Pract*., vol. 54, no. 10, pp. 654-657, Dec. 2000.
[34] P.A. Farrell, G.M. Weiner, and J.A. Lemons, "SIDS, ALTE, apnea, and the use of home monitors," *Pediatr. Rev.*, vol. 23, no. 1, pp. 3-9, Jan. 2002.
[35] C.E. Leach, P.S. Blair, P.J. Fleming, I.J. Smith, M.W. Platt, P.J. Berry, and J. Golding, "Epidemiology of SIDS and explained sudden infant deaths," *Pediatrics*, vol. 104, no. 4, pp. e43, 1999.
[36] A. Kahn and D. Blum, "Home monitoring of infants considered at risk for the sudden infant death syndrome. Four years' experience (1977-1981)," *Eur. J. Pediatrics*, vol. 139, no. 2, pp. 94-100, Oct. 1982.
[37] D.H. Kelly, "Home monitoring for the sudden infant death syndrome. The case for.," *Ann. NY Acad. Sci*., vol. 533, pp. 158-163, 1988.
[38] J.E. Hodgman and T. Hoppenbrouwers, "Home monitoring for the sudden infant death syndrome. The case against," *Ann. NY Acad. Sci*., vol. 533, pp. 164-175, 1988.
[39] E. Kongrad and L. O'Neill, "Near miss sudden death syndrome episodes? A clinical and eletrocardiographic correlation," *Pediatrics*, vol. 77, no. 6, pp. 811-815, 1986.
[40] R. Ramanathan, M.J. Corwin, C.E. Hunt, G. Lister, L.R. Tinsley, T. Baird, J.M. Silvestri, D.H. Crowell, D. Hufford, R.J. Martin, M.R. Neuman, D.E. Weese-Mayer, L.A. Cupples, M. Peucker, M. Willinger, and T.G. Keens, "Cardiorespiratory events recorded on home monitors: Comparison of healthy infants with those at increased risk for SIDS," *JAMA*, vol. 285, no. 17, pp. 2199-2207, May 2, 2001.
[41] R.B. Stewart and G.J. Caranasos, "Medication compliance in the elderly," *Med. Clin. North Amer.*, vol. 73, no. 6, pp. 1551-1563, Nov. 1989.
[42] J. Dunbar-Jacob and M.K. Mortimer-Stephens, "Treatment adherence in chronic disease," *J. Clin. Epidemiol*., vol. 54, suppl. 1, pp. S57-60, Dec. 2001.
[43] B.L. Carter, "Blood pressure as a surrogate end point for hypertension," *Ann. Pharmacother.*, vol. 36, no. 1, pp. 87-92, Jan. 2002.
[44] F.B. Hu, "Walking compared with vigorous physical activity and risk of type 2 diabetes in women: A prospective study," *JAMA*, vol. 282, no. 15, pp. 1433-1439, Oct. 20, 1999.
[45] M.H. Alderman**,** "How prevalence of hypertension varies as diagnostic criteria change," *Amer. J. Med. Sci*., vol. 271, no. 3, pp. 343-349, May-Jun. 1976.
[46] American Heart Association, *Heart and Stroke Statistical Update*. Dallas, TX: American Heart Association, 1999.
[47] P. Froom, M. Bar-David, J. Ribak, D. Van Dyk, B. Kallner, and J. Benbassat, "Predictive value of systolic blood pressure in young men for elevated systolic blood pressure 12 to 15 years later," *Circulation*, vol. 68, no. 3, pp. 467-469, 1983.
[48] A.D. Mejia, B.M. Egan, N.J. Schork, and A.J. Zweifler, "Artifacts in measurement of blood pressure and lack of target organ involvement in the assessment of patients with treatment-resistant hypertension," *Ann. Intern. Med*., vol. 112, no. 4, pp. 270-277, 1990.
[49] L.H. Lindholm and L. Werkö, "Comparing hypertension guidelines. Cost effectiveness analyses have been carried out in Sweden," *BMJ*, vol. 313, no. 7066, pp. 1203-1204, Nov. 9, 1996.
[50] C.G. Isles, L.M. Walker, G.D. Beevers, I. Brown, H.L. Cameron, J. Clarke, V. Hawthorne, D. Hole, A.F. Lever, and J.W. Robertson, "Mortality in patients of the Glasgow Blood Pressure Clinic," *J. Hypertens*., vol. 4, no. 2, pp. 141-156, Apr. 1986.
[51] L. Hansson, "How far should blood pressure be lowered? What is the role of the J-curve?" *Amer. J. Hypertens*., vol. 3, no. 9, pp. 726-729, discussion 730-732, Sept. 1990.
[52] M.H. Alderman, W.L. Ooi, S. Madhavan, and H. Cohen, "Treatment-induced blood pressure reduction and the risk of myocardial infarction," *JAMA*, vol. 262, no. 7, pp. 920-924, Aug. 18, 1989.
[53] O. Samuelsson, L. Wilhelmsen, O.K. Andersson, K. Pennert, and G. Berglund, "Cardiovascular morbidity in relation to change in blood pressure and serum cholesterol levels in treated hypertension. Results from the primary prevention trial in Göteborg, Sweden," *JAMA*, vol. 258, no. 13, pp. 1768-1776, Oct. 2, 1987.
[54] L. Hansson, A. Zanchetti, S.G. Carruthers, B. Dahlof, D. Elmfeldt, S. Julius, J. Menard, K.H. Rahn, H. Wedel, and S. Westerling, "Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: Principal results of the Hypertension Optimal Treatment (HOT) randomized trial," *Lancet*, vol. 351, no. 9118, pp. 1755, 1998.
[55] L.M. Prisant and A.A. Carr, "Ambulatory blood pressure monitoring and echocardiographic left ventricular wall thickness and mass," *Amer. J. Hypertens*., vol. 3, no. 2, pp. 81-89, 1990.
[56] P. Verdacchia, D. Clement, R. Fagard, P. Palantini, and G. Parati, "Blood pressure monitoring. Task force III. Target organ damage, morbidity, and mortality," *Blood Press. Monit.*, vol. 4, no. 6, pp. 303-317, Dec. 1999.
[57] G. Mancia, A. Zanchetti, E. Agabiti-Rosei, G. Benemio, R. De Cesaris, R. Fogari, A. Pessina, C. Porcellati, A. Rappelli, A. Salvetti, B. Trimarco, E. Agebiti-Rosei, and A. Pessino, "Ambulatory blood pressure is superior to clinic blood pressure in predicting treatment-induced regression of left ventricular hypertrophy. SAMPLE Study Group, Study on Ambulatory Monitoring of Blood Pressure and Lisinopril Evaluation," *Circulation*, vol. 95, no. 6, pp. 1464-1470, Mar. 18, 1997.
[58] P. Verdecchia, "Prognostic value of ambulatory blood pressure," *Hypertension*, vol. 35, no. 3, pp. 844-851, Mar. 2000.
[59] J.A. Staessen, L. Thijs, R. Fagard, E.T. O'Brien, D. Clement, P.W. de Leeuw, G. Mancia, C. Nachev, P. Palatini, G. Parati, J. Tuomilehto, and J. Webster, "Predicting cardiovascular risk using conventional vs ambulatory blood pressure in older patients with systolic hypertension. Systolic hypertension in Europe trial investigators," *JAMA,* vol. 282, no. 6, pp. 539-546, Aug. 11, 1999.
[60] B.P. McGrath, "Ambulatory blood pressure monitoring," *Medical J. Aust*., vol. 176, no. 12, pp. 588-592, Jun. 17, 2002.
[61] H.A. Punzi, "Why ambulatory blood pressure monitoring?," *Amer. J. Health Syst. Pharm*., vol. 55, suppl. 3, pp. S12-16, Nov. 15, 1998.
[62] Y. Iketani, T. Iketani, K. Takazawa, and M. Murata**,** "Second derivative of photoplethysmogram in children and young people," *Jpn. Circ. J.*, vol. 64, no. 2, pp. 110-116, Feb. 2000.
[63] D.H. Fitchett, "Forearm arterial compliance: A new measure of arterial compliance?," *Cardiovasc. Res*., vol. 18, no. 11, pp. 651-656, Nov. 1984.
[64] J.B. O'Connell and M.R. Bristow, "Economic impact of heart failure in the United States: Time for a different approach," *J. Heart Lung Transplant*, vol. 13, no. 4, pp. S107-112, 1994.
[65] M.W. Rich, "Epidemiology, pathophysiology, and etiology of congestive heart failure in older adults," *J. Amer. Geriatr. Soc.*, vol. 45, no. 8, pp. 968-974, 1997.
[66] J.K. Ghali, S. Kadakia, R. Cooper, and J. Ferlinz, "Precipitating factors leading to decompensation of heart failure. Traits among urban blacks," *Arch. Intern. Med.*, vol. 148, no. 9, pp. 2013-2016, 1988.
[67] B.M. Massie and N.B. Shah, "Evolving trends in the epidemiologic factors of heart failure: Rationale for preventive strategies and comprehensive disease management," *Amer. Heart J.*, vol. 133, no. 6, pp. 703-712, 1997.