absorbance change in an underlying artery (e.g., in the finger) caused by the propagating pressure pulse.

[0003] Typical PTT measurements determine the time separating a maximum point on the QRS complex (indicating the peak of ventricular depolarization) and a portion of the PPG waveform (indicating the arrival of the pressure pulse). PTT depends primarily on arterial compliance, the propagation distance of the pressure pulse (which is closely approximated by the patient's arm length), and blood pressure. To account for patient-specific properties, such as arterial compliance, PTT-based measurements of blood pressure are typically 'calibrated' using a conventional blood pressure cuff. Typically during the calibration process the blood pressure cuff is applied to the patient, used to make one or more blood pressure measurements, and then removed. Going forward, the calibration measurements are used, along with a change in PTT, to determine the patient's blood pressure and blood pressure variability. PTT typically relates inversely to blood pressure, i.e., a decrease in PTT indicates an increase in blood pressure.

[0004] A number of issued U.S. Patents describe the relationship between PTT and blood pressure. For example, U.S. Patents 5,316,008; 5,857,975; 5,865,755; and 5,649,543 each describe an apparatus that includes conventional sensors that measure ECG and PPG waveforms, which are then processed to determine PTT.

SUMMARY OF THE INVENTION

[0005] This invention provides a technique for continuous measurement of blood pressure (cNIBP), based on PTT, which features a number of improvements over conventional PTT measurements. Referred to herein as the 'Composite Method', the invention uses a body-worn monitor that measures cNIBP and other vital signs, and wirelessly transmits them to a remote monitor, such as a tablet PC, workstation at a nursing station, personal digital assistant (PDA), or cellular telephone. The body-worn monitor features a wrist-worn transceiver that receives and processes signals generated by a network of body-worn sensors. During a measurement these sensors are typically placed on the patient's arm and chest and measure time-dependent ECG, PPG, pressure, and accelerometer waveforms. Sensors within the network typically include a cuff with an inflatable air bladder, at least three electrical sensors (e.g. ECG electrodes), three accelerometers, and an optical sensor (e.g., a light source and photodiode) typically worn around the patient's thumb. They measure signals that are processed according to the

[0010] Pressure-dependent measurements performed on inflation have several advantages to similar measurements performed on deflation, which are convention. For example, inflation-based measurements are relatively fast and comfortable compared to those made on deflation. Most conventional cuff-based systems using deflation-based oscillometry take roughly 4 times longer than the Composite Method's pressure-dependent measurement. Inflation-based measurements are possible because of the Composite Method's relatively slow inflation speed (typically 5 – 10 mmHg/second) and high sensitivity of the pressure sensor used within the body-worn monitor. Moreover, measurements made during inflation can be immediately terminated once systolic blood pressure is calculated. In contrast, conventional cuff-based measurements made during deflation typically apply a pressure that far exceeds the patient's systolic blood pressure; pressure within the cuff then slowly bleeds down below DIA to complete the measurement.

[0011] Pressure-free measurements immediately follow the pressure-dependent measurements, and are typically made by determining PTT with the same optical and electrical sensors used in the pressure-dependent measurements. Specifically, the body-worn monitor processes PTT and other properties of the PPG waveform, along with the patient-specific slope and measurements of SYS, DIA, and MAP made during the pressure-dependent measurement, to determine cNIBP.

[0012] In addition to blood pressure, the body-worn monitor measures heart rate (HR), SpO2, and respiratory rate from components of the ECG, PPG, and accelerometer waveforms. A body-worn thermocouple measures temperature. These measurements, along with those used to process accelerometer waveforms to determine motion, posture, and activity level, are made using algorithms described below.

[0013] In one aspect, the invention provides a body-worn monitor, described in detail below, which measures cNIBP from an ambulatory patient according to the Composite Method. The body-worn monitor features: (1) a pressure-delivery and sensor system that applies a variable pressure to the patient's arm and, in response, measures a time-dependent pressure waveform; (2) a first sensor (e.g. an optical sensor) that generates a first time-dependent waveform representing a flow of blood within the patient; and (3) a second sensor (e.g. an ECG circuit and electrodes) that generates a second time-dependent waveform representing contractile properties of the patient's heart. A

represents a pulse transit time determined before *PTT* (and typically immediately before the pressure-dependent indexing measurement), $m_{femoral}$ represents a mathematical slope representing a relationship between $MAP_{femoral}$ and *PTT*, and MAP_{INDEX} represents a mean arterial pressure determined from the time-dependent pressure waveform. In the Equation above, $m_{femoral}$ is typically determined by collectively processing the first, second, and pressure waveforms. For example, it can be determined by processing a set of PTT values measured while time-dependent pressure is applied to the patient's arm, and then fitting the set with a linear equation to estimate a patient-specific relationship between PTT and MAP. This relationship, which is determined during the pressure-dependent indexing measurement, forms part of a 'calibration' for cuffless, PTT-based cNIBP measurement made afterwards. Other calibration parameters determined during the indexing measurement are SYS, DIA, and relationships between these parameters and MAP. These values are determined directly from a pressure waveform, typically measured during inflation using techniques derived from oscillometry. In embodiments, during an indexing measurement a digital filter, typically implemented with a software-based algorithm, processes the time-dependent pressure waveform to determine a 'processed pressure waveform'. The digital filter, for example, can be a 2-stage filter featuring a digital bandpass filter, followed by a digital low-pass filter. From the processed pressure waveform SYS, DIA, and MAP can be determined.

[0016] In other embodiments, the relationship between SYS, DIA, and MAP depends on the patient's HR, which is typically determined from either the ECG or PPG waveform. In still other embodiments, the relationship between PTT and MAP is non-adjustable and determined beforehand, e.g. from a group of patients in a clinical study. During an actual measurement, such a relationship is typically used as a default case when a patient-specific relationship cannot be accurately determined (because, e.g., of PPG or ECG waveforms corrupted by motion-related noise). Typically the relationship between PTT and MAP in the patient's femoral artery is between 0.5 mmHg/ms and 1.5 mmHg/ms.

[0017] In another aspect, the patient-specific indexing measurement involves estimating an 'effective MAP' in the patient's arm that varies with pressure applied by the pressure-delivery system. The effective MAP is the difference between MAP determined during the inflation in the indexing measurement and a pressure-induced blood pressure

change, caused by an arm-worn cuff featuring an inflatable bladder. In embodiments, the pressure-induced blood pressure change is defined by the following equation or a mathematical derivative thereof:

$$\Delta MAP(P) = F \times \left(P_{applied} - DIA_{INDEX}\right)$$

where $\Delta MAP(P)$ is the pressure-induced blood pressure change, $P_{applied}$ is pressure applied by the pressure-delivery system during inflation, DIA_{INDEX} is the diastolic pressure determined from the processed pressure waveform during the indexing measurement, and F is a mathematical constant.

[0018] In embodiments, the indexing measurement is performed once every 4 hours or more, and a PTT-based cNIBP measurement is performed once every 1 second or less. Typically, PTT values are averaged from a set of values collected over a time period between, typically ranging from 10 to 120 seconds. The average is typically a 'rolling average' so that a new value, determined over the averaging period, can be displayed relatively frequently (e.g. every second).

[0019] In another aspect, the invention provides a method for monitoring a blood pressure value from a patient, which features determining a PTT value from a patient, as described above, from PPG and ECG waveforms. Additionally, HR is determined by analyzing QRS complexes in the ECG waveform. During the measurement, the processing component determines a mathematical relationship between HR (or a parameter calculated therefrom), and PTT (or a parameter calculated therefrom). At a later point in time, the processing component uses the mathematical relationship and a current value of HR to estimate PTT and, ultimately, a based blood pressure value. This method would be deployed, for example, when motion-related noise corrupts the PPG waveform (which is relatively sensitive to motion), but not the ECG waveform (which is relatively immune to motion).

[0020] In embodiments, the method measures a first set of HR values and a second set of PTT values, and then processes the first and second sets to determine the mathematical relationship between them. The first and second sets are typically measured prior to measuring the HR used to estimate PTT, and are typically collected over a time period ranging between 5 and 60 seconds. Paired HR/PTT values collected during the time period are then analyzed, typically by fitting them using a linear regression algorithm, to determine a mathematical relationship relating HR to PTT.

Alternatively a non-linear fitting algorithm, such as the Levenburg-Marquardt algorithm, can be used to determine a non-linear relationship between HR and PTT. The non-linear relationship can be characterized, e.g., by a second or third-order polynomial, or by an exponential function.

[0021] As described above, this algorithm is typically performed when a patient's motion makes it difficult or impossible to accurately calculate PTT from the PPG waveform. The algorithm can be initiated when analysis of a pulse in the PPG waveform indicates PTT cannot be measured. Alternatively, the algorithm is initiated when analysis of at least one 'motion waveform' (e.g. an accelerometer waveform generated from one or more signals from an accelerometer) indicates that the PPG waveform is likely corrupted by motion. Analysis of the motion waveform can involve comparing a portion of it to a predetermined threshold, or analyzing it with a mathematical model, to determine if an accurate PTT can be calculated.

[0022] In a related aspect, the invention provides another algorithm that allows PTT-based cNIBP to be determined in the presence of motion. In this case, rather than estimating PTT from HR using a mathematical model, the algorithm 'reconstructs' motion-corrupted pulses in the PPG waveform through analysis of separate PPG waveforms measured simultaneously with two separate light sources. A pulse oximeter sensor, such as that included in the body-worn monitor described in detail below, includes a first light source operating in a red spectral region (between 590 and 700 nm, and preferably about 660 nm), and a second light source operating in the infrared spectral region (between 800 and 1000 nm, and preferably around 905 nm), and can therefore be used for this purpose.

[0023] The algorithm features: 1) collectively processing unique PPG waveforms to generate a processed signal; 2) processing the processed signal with a digital filter to generate a filtered signal; 3) analyzing the filtered signal to determine a feature related to blood pressure; and 4) analyzing the feature related to blood pressure to determine the blood pressure value. In embodiments, the processing component is programmed to collectively process the first and second signals by subtracting one signal from the other, or dividing one signal into the other, to generate the processed signal. This signal is then filtered with a digital bandpass filter, typically characterized by a passband between 0.01→5.0 Hz, to generate the filtered signal. The filtered signal is typically relatively

free of motion artifacts, and yields an onset point which can be combined with an ECG QRS complex to determine PTT and then cNIBP. As described above, this algorithm can be initiated by processing an accelerometer waveform which indicates that a patient is moving, or by processing the PPG waveforms to determine that they are corrupted in any way. In other embodiments, steps in the algorithm are rearranged so that the corrupted PPG waveforms are first filtered with a digital bandpass filter, and then these filtered waveforms are subtracted from each other or divided into each other, and then processed to determine an onset point.

[0024] In another aspect, the body-worn monitor's optical sensor described above features a detector that includes at least two pixel elements, each configured to generate a unique signal. A processing component within the monitor is configured to: (1) analyze a signal generated by a first pixel element; (2) analyze a signal generated by a second pixel element; (3) analyze a signal indicating motion, e.g. an accelerometer waveform; (4) based on analysis of the motion signal, select a signal from at least one of the pixel elements characterized by a relatively low degree of motion corruption; and (5) analyze the selected signal to determine a vital sign value, e.g. cNIBP.

[0025] In embodiments, the multi-pixel detector features at least a 3x3 array of pixels, each containing a photodetector. In this case the optical sensor is integrated with a circuit configured to de-multiplex signals from the multi-pixel detector. The processor in the body-worn monitor can be programmed to analyze the motion signal and a signal from each pixel element to determine the signal that has the lowest correlation to the motion signal, indicating that the signal is characterized by a relatively low degree of motion corruption. Correlation, for example, can be determined using standard algorithms known in the art, such as algorithms that determine cross-correlation between two sequences of data points. Such algorithms can yield a Gaussian-type waveform, with the amplitude of the waveform increasing with correlation. The waveform can then be compared to a series of metrics to determine a numerical figure of merit indicating the degree of correlation. Alternatively, the processor is programmed to analyze the motion signal to determine a measurement period when patient movement is relatively low, and then measure a signal from each pixel element. In both cases, the signal from each pixel element represents a PPG waveform featuring a sequence of pulses, each characterized by an onset point. When combined with an ECG QRS complex, this waveform can yield a

[0044] Fig. 16 shows a graph of a time-dependent PPG waveform measured with and without motion using an IR LED (top trace), a RED LED (second trace), the waveform measured with the RED LED subtracted from the waveform measured with the IR LED (third trace), and the third trace processed with a digital bandpass filter (fourth trace);

[0045] Fig. 17 shows a graph of a time-dependent PPG waveform measured with and without motion using an IR LED and processed with a digital bandpass filter (top trace), a RED LED and processed with a digital bandpass filter (second trace), and the second trace subtracted from the first trace (third trace);

[0046] Fig. 18 shows a schematic drawing indicating an algorithm that allows cNIBP measurements to be made in both the presence and absence of motion;

[0047] Fig. 19 shows a graph of time-dependent PTT and HR measurements, and how these can be processed with the algorithm shown in Fig. 18 to measure cNIBP in presence of motion;

[0048] Figs. 20A and 21A show, respectively, time-dependent SYS waveforms made using a femoral A-line (dark gray) and reconstructed using the algorithm shown in Figs. 18 and 19 to yield the best and worst results for the 23 clinical subjects;

[0049] Figs. 20B and 21B show, respectively, correlation plots generated using data from Figs. 20A and 21A;

[0050] Fig. 22 shows a schematic view of a patient and a coordinate axis used with an algorithm and accelerometer waveforms to determine the patient's posture;

[0051] Fig. 23A shows a graph of time-dependent accelerometer waveforms measured from a patient's chest during different postures;

[0052] Fig. 23B shows a graph of time-dependent postures determined by processing the accelerometer waveforms of Fig. 23A with an algorithm and the coordinate axis shown in Fig. 22;

[0053] Figs. 24A and 24B show, respectively, a three-dimensional image of the body-worn monitor of the invention attached to a patient during and after an initial indexing measurement;

[0054] Fig. 25 shows a three-dimensional image of the wrist-worn transceiver used with the body-worn monitor of Figs. 24A and 24B;

[0055] Fig. 26 shows an image of a patient wearing a head-mounted sensor featuring a multi-pixel array photodetector for measuring a PPG waveform according to an alternate embodiment of the invention;

[0056] Fig. 27 shows a plan view of the multi-pixel array photodetector of Fig. 26;

[0057] Figs. 28A and 28B show a bolus of blood passing through a detecting area of a conventional single-pixel photodetector for measuring a PPG waveform;

[0058] Figs. 29A and 29B show a bolus of blood passing through a detecting area of the multi-pixel array photodetector of Figs. 26 and 27; and

[0059] Fig. 30 shows a flow chart for measuring cNIBP, SpO2, respiration rate, heart rate, temperature, and motion according to the invention.

DETAILED DESCRIPTION OF THE INVENTION

[0060] Theory of the Composite Method

[0061] Figs. 1A and 1B show schematic drawings of the Composite Method's pressure-free (Fig. 1A) and pressure-dependent (Fig. 1B) measurements. Working in concert, these measurements accurately determine the patient's cNIBP for an extended time without requiring an external calibration device, e.g., a conventional blood pressure cuff. During a measurement, the patient wears a body-worn monitor attached to a disposable cuff and collection of optical, electrical, motion, and temperature sensors. These sensors measure signals for both the pressure-dependent and pressure-free measurements. The co-pending patent applications, the contents of which are fully incorporated herein by reference, describe earlier embodiments of this measurement: DEVICE AND METHOD FOR DETERMINING BLOOD PRESSURE USING 'HYBRID' PULSE TRANSIT TIME MEASUREMENT (U.S.S.N. 60/943,464; filed June 12, 2007), VITAL SIGN MONITOR FOR CUFFLESSLY MEASURING BLOOD PRESSURE USING A PULSE TRANSIT TIME CORRECTED FOR VASCULAR INDEX (U.S.S.N. 60/943,523; filed June 12, 2007); and VITAL SIGN MONITOR FOR MEASURING BLOOD PRESSURE USING OPTICAL, ELECTRICAL, AND PRESSURE WAVEFORMS (U.S.S.N 12/138, 194; filed June 12, 2008). A microprocessor in the body-worn monitor processes the PPG and ECG waveforms to determine PTT, which is used in both measurements of the Composite Method to determine cNIBP, as is described in more detail below.

[0062] The cuff includes an air bladder which, when pressurized with a pneumatic system, applies a pressure 107 to an underlying artery 102, 102'. An electrical system featuring at least 3 electrodes coupled to an amplifier/filter circuit within cabling attached to the wrist-worn transceiver measures an ECG waveform 104, 104' from the patient. Three electrodes (two detecting positive and negative signals, and one serving as a ground) are typically required to detect the necessary signals to generate an ECG waveform with an adequate signal-to-noise ratio. At the same time, an optical system featuring a transmissive or, optionally, reflective optical sensor measures a PPG waveform 105, 105' featuring a series of 'pulses', each characterized by an amplitude of $AMP_{1/2}$, from the patient's artery. The preferred measurement site is typically near small arteries in the patient's thumb, such as the princeps pollicis artery. A microprocessor and analog-to-digital converter within the wrist-worn transceiver detects and analyzes the ECG 104, 104' and PPG 105, 105' waveforms to determine both PTT_1 (from the pressure-free measurement) and PTT_2 (from the pressure-dependent measurement). Typically the microprocessor determines both PTT_1 and PTT_2 by calculating the time difference between the peak of the QRS complex in the ECG waveform 104, 104' and the foot (i.e. onset) of the PPG waveform 105, 105'.

[0063] The invention is based on the discovery that an applied pressure (indicated by arrow 107) during the pressure-dependent measurement affects blood flow (indicated by arrows 103, 103') in the underlying artery 102, 102'. Specifically, the applied pressure has no affect on either PTT_2 or AMP_2 when it is less than a diastolic pressure within the artery 102, 102'. When the applied pressure 107 reaches the diastolic pressure it begins to compress the artery, thus reducing blood flow and the effective internal pressure. This causes PTT_2 to systematically increase relative to PTT_1, and AMP_2 to systematically decrease relative to AMP_1. PTT_2 increases and AMP_2 decreases (typically in a linear manner) as the applied pressure 107 approaches the systolic blood pressure within the artery 102, 102'. When the applied pressure 107 reaches the systolic blood pressure, AMP_2 is completely eliminated and PTT_2 consequently becomes immeasurable.

[0064] During a measurement the patient's heart generates electrical impulses that pass through the body near the speed of light. These impulses accompany each heartbeat, which then generates a pressure wave that propagates through the patient's vasculature at a significantly slower speed. Immediately after the heartbeat, the pressure wave leaves

elevated compared to both cNIBP and femoral blood pressures. Additionally, blood pressure at the radial artery tends to be relatively volatile compared to the other blood pressures. Without being bound to any theory, this too may also be due to pulse pressure amplification. Correlation between radial blood pressure and cNIBP is notably worse than that between cNIBP and femoral blood pressure, with both STDEV (9.3 mmHg) and BIAS (-12.8 mmHg) for the paired values falling outside of the FDA's guidelines. Data similar to that shown in Fig. 10 was collected from 23 subjects in a recent study using the device and method according to the invention.

[0113] Fig. 11 shows typical correlation between both SYS and DIA measured with the Composite Method and a femoral A-line. Data were collected in the same manner described above. Blood pressure was measured over a 4-hour period with only a single indexing measurement performed at the beginning of the study. cNIBP measurements for both SYS and DIA in Fig. 11, like that described above in Fig. 10, correlate well with pressures measured at the femoral artery, and comfortably meet the guidelines required by the FDA. Fig. 12, for example, shows blood pressure correlations (shown as standard deviation) from a cohort of 23 subjects measured in two different ICUs using both the Composite Method and a femoral A- line. All subjects were measured under essentially identical conditions to those described above. The figure shows a histogram that graphs standard deviation values between the two measurements for both SYS (dark gray bars) and DIA (light gray bars). The histogram indicates that, for all measurements collected from 23 subjects, only a single measurement (for SYS) falls outside the FDA's guidelines of 8 mmHg for STDEV. All other measurements are comfortably within this limit, and as expected show Gaussian-type distributions, with the distributions peaked near 3 and 4 mmHg for, respectively, SYS and DIA.

[0114] Fig. 13 shows the collective, intra-subject statistics determined for all 23 subjects for the above-described study. Statistics were determined using two independent techniques. The first technique, called 'analysis of variance' or 'ANOVA', tests statistical variance for a set of repeated measures, like those used in the ICU study. ANOVA models for STDEV and BIAS are commonly used for analysis of data collected in clinical trials, like the one described herein. The second technique shown in Fig. 13 simply calculates the STDEV and BIAS for each subject in the study over the 4-hour measurement period, and then calculates the average of each of these parameters for the

[0127] The relationship between HR and PTT determined with the linear model is most accurate when the HR and PTT data points are collected immediately prior to the period of motion. If patient motion continues, then this model can be used along with HR for a period of time of up to 5 minutes to calculate cNIBP values. If patient motion persists past this period, then cNIBP cannot typically be accurately calculated, and this methodology should not be used. Typically this approach works best if correlation between HR and PTT, as indicated by $r^2_{HR/PTT,i}$, is relatively strong. In preferred embodiments, $r^2_{HR/PTT,i}$ is greater than about 0.5 for the algorithm to be implemented. If $r^2_{HR/PTT,i}$ is less than this value the algorithm is not implemented, and a blood pressure value is assumed to be corrupted by motion, and thus not reported.

[0128] Figs. 20A,B and 21A,B indicate the efficacy of this approach. Figs. 20A and 21A show time-dependent traces of SYS, measured with a femoral A-line, and a 'reconstructed' SYS determined using Equation (11). These graphs were generated using data measured during the 23-subject ICU study, described above. Figs. 20B and 21B plot the same data in Figs. 20A and 21A in a different way, showing a point-to-point correlation between SYS measured with the femoral arterial line and 'reconstructed' SYS measured with the method according to the invention. As is clear from these graphs, reconstructing SYS values using this approach yields better agreement and higher correlation when the subject's blood pressure undergoes only small amounts of volatility. For example, Figs. 20A,B show the 'best' results from the group of 23 subjects. Here, the subject's blood pressure is relatively stable, and the reconstructed SYS agrees extremely well with SYS measured using the femoral arterial line (STDEV = 2.0 mmHg; BIAS = 0.2 mmHg). Figs. 21A,B show data from a subject with highly volatile blood pressure. This case represents the 'worst' agreement for the 23 subjects, likely because the volatility in cNIBP also results in a corresponding volatility in cardiac output. This, in turn, makes it more difficult to accurately reconstruct the subject's cNIBP, and results in slightly worse correlation (STDEV = 15.8 mmHg; BIAS = 0.6 mmHg) between arterial line and reconstructed SYS.

[0129] Processing Accelerometer Waveforms to Determine Posture

[0130] In addition to motion, a patient's posture can influence how the above-described system generates alarms/alerts from cNIBP and other vital signs. For example, the alarms/alerts related to cNIBP may vary depending on whether the patient is lying

What is claimed is:

1. A method for monitoring a blood pressure value from a patient, comprising:

(a) applying a variable pressure to the patient's arm using a pressure-delivery system;

(b) detecting a time-dependent pressure waveform representing the pressure applied to the patient's arm;

(c) detecting a first time-dependent waveform comprising a first feature induced by the patient's heartbeat with a first sensor configured to attach to the patient;

(d) detecting a second time-dependent waveform comprising a second feature induced by the patient's heartbeat with a second sensor configured to attach to the patient;

(e) determining a pulse transit time which is a measure of a separation in time between the first feature of the first time-dependent waveform and the second feature of the second time-dependent waveform;

(f) determining a variation in the pulse transit time as a function of the pressure applied to the patient's arm;

(g) processing the variation in pulse transit time to determine a relationship between pulse transit time and blood pressure;

(h) digitally filtering a portion of the time-dependent pressure waveform to determine a processed pressure waveform;

(i) analyzing the processed pressure waveform to determine values for systolic blood pressure, diastolic blood pressure, and mean arterial pressure; and

(j) analyzing a pulse transit time, the relationship between pulse transit time and blood pressure, and blood pressure values determined from the processed pressure waveform to determine a blood pressure value when no pressure is applied to the patient's arm with the pressure delivery system.

2. A method for monitoring a blood pressure value from a patient, comprising:

(a) applying a variable pressure to the patient's arm using a pressure-delivery system;

(b) detecting a time-dependent pressure waveform representing the pressure applied to the patient's arm during inflation of the pressure-delivery system;

(c) detecting a first time-dependent waveform comprising a first feature induced by the patient's heartbeat with a first sensor configured to attach to the patient;

(d) detecting a second time-dependent waveform comprising a second feature induced by the patient's heartbeat with a second sensor configured to attach to the patient;

(e) determining a pulse transit time which is a measure of a separation in time between the first feature of the first time-dependent waveform and the second feature of the second time-dependent waveform;

(f) determining a variation in the pulse transit time as a function of the pressure applied to the patient's arm during inflation of the pressure-delivery system;

(g) processing the variation in pulse transit time to determine a relationship between pulse transit time and blood pressure;

(h) digitally filtering a portion of the time-dependent pressure waveform measured during inflation to determine a processed pressure waveform;

(i) analyzing the processed pressure waveform to determine values for systolic blood pressure, diastolic blood pressure, and mean arterial pressure; and

(j) analyzing a pulse transit time, the relationship between pulse transit time and blood pressure, and blood pressure values determined from the processed pressure waveform to determine a blood pressure value when no pressure is applied to the patient's arm with the pressure delivery system.

3. A method for monitoring a blood pressure value from a patient, comprising:

(a) detecting a time-dependent pressure waveform representing pressure applied to the patient's arm during inflation of a pressure-delivery system;

(b) determining a pulse transit time between a first feature of a first time-dependent waveform and a second feature of a second time-dependent waveform, both the first and second waveforms measured from the patient;

(c) determining a variation in the pulse transit time as a function of the pressure applied to the patient's arm during inflation of the pressure-delivery system; and

(d) analyzing a pulse transit time along with a calibration determined from the variation in pulse transit time to determine a blood pressure value.

4. A method for monitoring a blood pressure value from a patient, comprising:

(a) detecting a time-dependent pressure waveform representing pressure applied to the patient's arm during inflation of a pressure-delivery system;

(b) determining a pulse transit time between a first feature of a first time-dependent waveform and a second feature of a second time-dependent waveform, both the first and second waveforms measured from the patient;

(c) digitally filtering a portion of the time-dependent pressure waveform to determine a processed pressure waveform measured during inflation; and

(d) analyzing a pulse transit time along with a calibration determined from a relationship between pulse transit time and blood pressure determined from parameters measured during inflation to determine a blood pressure value after inflation.

5. The method of claim 1, wherein step (g) further comprises processing the variation in pulse transit time to determine a relationship between pulse transit time and mean arterial pressure.

6. The method of claim 5, wherein step (g) further comprises processing the variation in pulse transit time with a mathematical model that estimates an effective mean arterial pressure in the patient's arm that varies with pressure applied by the pressure-delivery system.

7. The method of claim 6, wherein the effective mean arterial pressure is the difference between the mean arterial pressure determined during step (i) and a pressure-induced blood pressure change.

8. The method of claim 7, wherein the pressure-induced blood pressure change is defined by the following equation or a mathematical derivative thereof:

$$\Delta MAP(P) = F \times \left(P_{applied} - DIA_{INDEX}\right)$$

where $\Delta MAP(P)$ is the pressure-induced blood pressure change, $P_{applied}$ is pressure applied by the pressure-delivery system during inflation, DIA_{INDEX} is the diastolic pressure determined from the processed pressure waveform, and F is a mathematical constant.

9. The method of claim 1, wherein step (b) further comprises detecting the time-dependent pressure waveform representing the pressure applied to the patient's arm while the pressure-delivery system is inflating.

10. The method of claim 9, wherein step (h) further comprises digitally filtering a portion of the time-dependent pressure waveform measured during inflation to determine a processed pressure waveform.

11. The method of claim 10, wherein step (h) further comprises digitally filtering a portion of the time-dependent pressure waveform measured during inflation with: 1) a digital bandpass filter; and then 2) a digital low-pass filter to determine the processed pressure waveform.

12. The method of claim 11, wherein step (i) further comprises analyzing the processed pressure waveform to determine a ratio between systolic and mean arterial blood pressure.

13. The method of claim 12, wherein step (j) further comprises processing the ratio between systolic and mean arterial blood pressure, along with pulse transit time and the relationship between pulse transit time and blood pressure, to determine systolic blood pressure value when no pressure is applied to the patient's arm with the pressure delivery system.

14. The method of claim 11, wherein step (i) further comprises analyzing the processed pressure waveform to determine a ratio between diastolic and mean arterial blood pressure.

15. The method of claim 14, wherein step (j) further comprises processing the ratio between diastolic and mean arterial blood pressure, along with pulse transit time and the relationship between pulse transit time and blood pressure, to determine diastolic blood pressure value when no pressure is applied to the patient's arm with the pressure delivery system.

16. The method of claim 1, wherein the pressure-delivery system comprises a cuff comprising an inflatable bladder.

17. The method of claim 16, wherein the pressure-delivery system comprises a pneumatic system connected to the cuff and configured to inflate the cuff.

18. The method of claim 1, wherein step (a) is performed once every 4 hours or more.

19. The method of claim 1, wherein step (j) is performed once every 1 second or less.

20. The method of claim 19, wherein step (j) further comprises determining an average pulse transit time from a set of pulse transit times collected over a time period.

21. The method of claim 20, wherein the time period is between 10 and 120 seconds.

22. The method of claim 1, wherein both the first and second sensors are selected from the group comprising an optical sensor, a pressure sensor, an electrical impedance sensor, an ECG waveform sensor, and a transducer.

23. A system for monitoring a patient's blood pressure, the system comprising: a pressure-delivery system for applying a variable pressure to the patient's arm; a pressure sensor for measuring a time-dependent pressure waveform representing the pressure applied to the patient's arm; an optical sensor configured to attach to the patient and generate a time-dependent optical waveform representing a flow of blood within the patient; an electrode system configured to attach to the patient and generate a time-dependent electrical waveform representing activity of the patient's heart; and,
a processing component programmed to: i) determine a pulse transit time which is a measure of a separation in time of a first feature of the time-dependent electrical waveform and a second feature of the time-dependent optical waveform; ii) processing the pressure, optical, and electrical waveforms to determine a relationship between pulse transit time and blood pressure in the patient's core region; and iii) analyze a pulse transit time and the relationship between pulse transit time and blood pressure in the patient's core region with a mathematical model configured to generate a blood pressure indicative of the patient's core region.

24. A method for monitoring a blood pressure value from a patient, comprising:

(a) detecting a time-dependent optical waveform comprising a pulse induced by the patient's heartbeat with an optical sensor configured to attach to the patient;

(b) detecting a time-dependent electrical waveform comprising a QRS complex induced by the patient's heartbeat with an electrical sensor configured to attach to the patient;

(c) determining a pulse transit time which is a measure of a separation in time between a portion of the pulse comprised by the time-dependent optical waveform and a portion of the QRS complex comprised by the time-dependent electrical waveform;

(d) determining a heart rate from portions of QRS complexes in the time-dependent electrical waveform;

(e) determining a mathematical relationship between heart rate, or a first parameter calculated therefrom, and pulse transit time, or a second parameter calculated therefrom;

(f) determining an estimated pulse transit time from a heart rate and the mathematical relationship between heart rate and pulse transit time; and

(g) analyzing the estimated pulse transit time and a blood pressure calibration to determine a blood pressure value.

absorbance change in an underlying artery (e.g., in the finger) caused by the propagating pressure pulse.

[0003] Typical PTT measurements determine the time separating a maximum point on the QRS complex (indicating the peak of ventricular depolarization) and a portion of the PPG waveform (indicating the arrival of the pressure pulse). PTT depends primarily on arterial compliance, the propagation distance of the pressure pulse (which is closely approximated by the patient's arm length), and blood pressure. To account for patient-specific properties, such as arterial compliance, PTT-based measurements of blood pressure are typically 'calibrated' using a conventional blood pressure cuff. Typically during the calibration process the blood pressure cuff is applied to the patient, used to make one or more blood pressure measurements, and then removed. Going forward, the calibration measurements are used, along with a change in PTT, to determine the patient's blood pressure and blood pressure variability. PTT typically relates inversely to blood pressure, i.e., a decrease in PTT indicates an increase in blood pressure.

[0004] A number of issued U.S. Patents describe the relationship between PTT and blood pressure. For example, U.S. Patents 5,316,008; 5,857,975; 5,865,755; and 5,649,543 each describe an apparatus that includes conventional sensors that measure ECG and PPG waveforms, which are then processed to determine PTT.

SUMMARY OF THE INVENTION

[0004a] The invention is defined in the independent claim. Some optional features of the invention are defined in the independent claims.

[0005] The exemplary disclosures herein may provide a technique for continuous measurement of blood pressure (cNIBP), based on PTT, which features a number of improvements over conventional PTT measurements. Referred to herein as the 'Composite Method', there is a disclosure relating to a body-worn monitor that measures cNIBP and other vital signs, and wirelessly transmits them to a remote monitor, such as a tablet PC, workstation at a nursing station, personal digital assistant (PDA), or cellular telephone. The body-worn monitor features a wrist-worn transceiver that receives and processes signals generated by a network of body-worn sensors. During a measurement these sensors are typically placed on the patient's arm and chest and measure time-dependent ECG, PPG, pressure, and accelerometer waveforms. Sensors within the network typically include a cuff with an inflatable air bladder, at least three electrical sensors (e.g. ECG electrodes), three accelerometers, and an optical sensor (e.g., a light source and photodiode) typically worn around the patient's thumb. They measure signals that are processed according to the

[0010] Pressure-dependent measurements performed on inflation have several advantages to similar measurements performed on deflation, which are convention. For example, inflation-based measurements are relatively fast and comfortable compared to those made on deflation. Most conventional cuff-based systems using deflation-based oscillometry take roughly 4 times longer than the Composite Method's pressure-dependent measurement. Inflation-based measurements are possible because of the Composite Method's relatively slow inflation speed (typically 5 – 10 mmHg/second) and high sensitivity of the pressure sensor used within the body-worn monitor. Moreover, measurements made during inflation can be immediately terminated once systolic blood pressure is calculated. In contrast, conventional cuff-based measurements made during deflation typically apply a pressure that far exceeds the patient's systolic blood pressure; pressure within the cuff then slowly bleeds down below DIA to complete the measurement.

[0011] Pressure-free measurements immediately follow the pressure-dependent measurements, and are typically made by determining PTT with the same optical and electrical sensors used in the pressure-dependent measurements. Specifically, the body-worn monitor processes PTT and other properties of the PPG waveform, along with the patient-specific slope and measurements of SYS, DIA, and MAP made during the pressure-dependent measurement, to determine cNIBP.

[0012] In addition to blood pressure, the body-worn monitor measures heart rate (HR), SpO2, and respiratory rate from components of the ECG, PPG, and accelerometer waveforms. A body-worn thermocouple measures temperature. These measurements, along with those used to process accelerometer waveforms to determine motion, posture, and activity level, are made using algorithms described below.

[0013] In one exemplary technique, there is a body-worn monitor, described in detail below, which measures cNIBP from an ambulatory patient according to the Composite Method. The body-worn monitor features: (1) a pressure-delivery and sensor system that applies a variable pressure to the patient's arm and, in response, measures a time-dependent pressure waveform; (2) a first sensor (e.g. an optical sensor) that generates a first time-dependent waveform representing a flow of blood within the patient; and (3) a second sensor (e.g. an ECG circuit and electrodes) that generates a second time-dependent waveform representing contractile properties of the patient's heart. A

represents a pulse transit time determined before *PTT* (and typically immediately before the pressure-dependent indexing measurement), $m_{femoral}$ represents a mathematical slope representing a relationship between $MAP_{femoral}$ and *PTT*, and MAP_{INDEX} represents a mean arterial pressure determined from the time-dependent pressure waveform. In the Equation above, $m_{femoral}$ is typically determined by collectively processing the first, second, and pressure waveforms. For example, it can be determined by processing a set of PTT values measured while time-dependent pressure is applied to the patient's arm, and then fitting the set with a linear equation to estimate a patient-specific relationship between PTT and MAP. This relationship, which is determined during the pressure-dependent indexing measurement, forms part of a 'calibration' for cuffless, PTT-based cNIBP measurement made afterwards. Other calibration parameters determined during the indexing measurement are SYS, DIA, and relationships between these parameters and MAP. These values are determined directly from a pressure waveform, typically measured during inflation using techniques derived from oscillometry. In embodiments, during an indexing measurement a digital filter, typically implemented with a software-based algorithm, processes the time-dependent pressure waveform to determine a 'processed pressure waveform'. The digital filter, for example, can be a 2-stage filter featuring a digital bandpass filter, followed by a digital low-pass filter. From the processed pressure waveform SYS, DIA, and MAP can be determined.

[0016] In other embodiments, the relationship between SYS, DIA, and MAP depends on the patient's HR, which is typically determined from either the ECG or PPG waveform. In still other embodiments, the relationship between PTT and MAP is non-adjustable and determined beforehand, e.g. from a group of patients in a clinical study. During an actual measurement, such a relationship is typically used as a default case when a patient-specific relationship cannot be accurately determined (because, e.g., of PPG or ECG waveforms corrupted by motion-related noise). Typically the relationship between PTT and MAP in the patient's femoral artery is between 0.5 mmHg/ms and 1.5 mmHg/ms.

[0017] In another exemplary technique, the patient-specific indexing measurement involves estimating an 'effective MAP' in the patient's arm that varies with pressure applied by the pressure-delivery system. The effective MAP is the difference between MAP determined during the inflation in the indexing measurement and a pressure-induced blood pressure

change, caused by an arm-worn cuff featuring an inflatable bladder. In embodiments, the pressure-induced blood pressure change is defined by the following equation or a mathematical derivative thereof:

$$\Delta MAP(P) = F \times \left(P_{applied} - DIA_{INDEX}\right)$$

where $\Delta MAP(P)$ is the pressure-induced blood pressure change, $P_{applied}$ is pressure applied by the pressure-delivery system during inflation, DIA_{INDEX} is the diastolic pressure determined from the processed pressure waveform during the indexing measurement, and F is a mathematical constant.

[0018] In embodiments, the indexing measurement is performed once every 4 hours or more, and a PTT-based cNIBP measurement is performed once every 1 second or less. Typically, PTT values are averaged from a set of values collected over a time period between, typically ranging from 10 to 120 seconds. The average is typically a 'rolling average' so that a new value, determined over the averaging period, can be displayed relatively frequently (e.g. every second).

[0019] In another exemplary technique, there is provided a method for monitoring a blood pressure value from a patient, which features determining a PTT value from a patient, as described above, from PPG and ECG waveforms. Additionally, HR is determined by analyzing QRS complexes in the ECG waveform. During the measurement, the processing component determines a mathematical relationship between HR (or a parameter calculated therefrom), and PTT (or a parameter calculated therefrom). At a later point in time, the processing component uses the mathematical relationship and a current value of HR to estimate PTT and, ultimately, a based blood pressure value. This method would be deployed, for example, when motion-related noise corrupts the PPG waveform (which is relatively sensitive to motion), but not the ECG waveform (which is relatively immune to motion).

[0020] In embodiments, the method measures a first set of HR values and a second set of PTT values, and then processes the first and second sets to determine the mathematical relationship between them. The first and second sets are typically measured prior to measuring the HR used to estimate PTT, and are typically collected over a time period ranging between 5 and 60 seconds. Paired HR/PTT values collected during the time period are then analyzed, typically by fitting them using a linear regression algorithm, to determine a mathematical relationship relating HR to PTT.

Alternatively a non-linear fitting algorithm, such as the Levenburg-Marquardt algorithm, can be used to determine a non-linear relationship between HR and PTT. The non-linear relationship can be characterized, e.g., by a second or third-order polynomial, or by an exponential function.

[0021] As described above, this algorithm is typically performed when a patient's motion makes it difficult or impossible to accurately calculate PTT from the PPG waveform. The algorithm can be initiated when analysis of a pulse in the PPG waveform indicates PTT cannot be measured. Alternatively, the algorithm is initiated when analysis of at least one 'motion waveform' (e.g. an accelerometer waveform generated from one or more signals from an accelerometer) indicates that the PPG waveform is likely corrupted by motion. Analysis of the motion waveform can involve comparing a portion of it to a predetermined threshold, or analyzing it with a mathematical model, to determine if an accurate PTT can be calculated.

[0022] In a related technique, there is another algorithm that allows PTT-based cNIBP to be determined in the presence of motion. In this case, rather than estimating PTT from HR using a mathematical model, the algorithm 'reconstructs' motion-corrupted pulses in the PPG waveform through analysis of separate PPG waveforms measured simultaneously with two separate light sources. A pulse oximeter sensor, such as that included in the body-worn monitor described in detail below, includes a first light source operating in a red spectral region (between 590 and 700 nm, and preferably about 660 nm), and a second light source operating in the infrared spectral region (between 800 and 1000 nm, and preferably around 905 nm), and can therefore be used for this purpose.

[0023] The algorithm features: 1) collectively processing unique PPG waveforms to generate a processed signal; 2) processing the processed signal with a digital filter to generate a filtered signal; 3) analyzing the filtered signal to determine a feature related to blood pressure; and 4) analyzing the feature related to blood pressure to determine the blood pressure value. In embodiments, the processing component is programmed to collectively process the first and second signals by subtracting one signal from the other, or dividing one signal into the other, to generate the processed signal. This signal is then filtered with a digital bandpass filter, typically characterized by a passband between 0.01→5.0 Hz, to generate the filtered signal. The filtered signal is typically relatively

free of motion artifacts, and yields an onset point which can be combined with an ECG QRS complex to determine PTT and then cNIBP. As described above, this algorithm can be initiated by processing an accelerometer waveform which indicates that a patient is moving, or by processing the PPG waveforms to determine that they are corrupted in any way. In other embodiments, steps in the algorithm are rearranged so that the corrupted PPG waveforms are first filtered with a digital bandpass filter, and then these filtered waveforms are subtracted from each other or divided into each other, and then processed to determine an onset point.

[0024] In another arrangement, the body-worn monitor's optical sensor described above features a detector that includes at least two pixel elements, each configured to generate a unique signal. A processing component within the monitor is configured to: (1) analyze a signal generated by a first pixel element; (2) analyze a signal generated by a second pixel element; (3) analyze a signal indicating motion, e.g. an accelerometer waveform; (4) based on analysis of the motion signal, select a signal from at least one of the pixel elements characterized by a relatively low degree of motion corruption; and (5) analyze the selected signal to determine a vital sign value, e.g. cNIBP.

[0025] In embodiments, the multi-pixel detector features at least a 3x3 array of pixels, each containing a photodetector. In this case the optical sensor is integrated with a circuit configured to de-multiplex signals from the multi-pixel detector. The processor in the body-worn monitor can be programmed to analyze the motion signal and a signal from each pixel element to determine the signal that has the lowest correlation to the motion signal, indicating that the signal is characterized by a relatively low degree of motion corruption. Correlation, for example, can be determined using standard algorithms known in the art, such as algorithms that determine cross-correlation between two sequences of data points. Such algorithms can yield a Gaussian-type waveform, with the amplitude of the waveform increasing with correlation. The waveform can then be compared to a series of metrics to determine a numerical figure of merit indicating the degree of correlation. Alternatively, the processor is programmed to analyze the motion signal to determine a measurement period when patient movement is relatively low, and then measure a signal from each pixel element. In both cases, the signal from each pixel element represents a PPG waveform featuring a sequence of pulses, each characterized by an onset point. When combined with an ECG QRS complex, this waveform can yield a

[0044] Fig. 16 shows a graph of a time-dependent PPG waveform measured with and without motion using an IR LED (top trace), a RED LED (second trace), the waveform measured with the RED LED subtracted from the waveform measured with the IR LED (third trace), and the third trace processed with a digital bandpass filter (fourth trace);

[0045] Fig. 17 shows a graph of a time-dependent PPG waveform measured with and without motion using an IR LED and processed with a digital bandpass filter (top trace), a RED LED and processed with a digital bandpass filter (second trace), and the second trace subtracted from the first trace (third trace);

[0046] Fig. 18 shows a schematic drawing indicating an algorithm that allows cNIBP measurements to be made in both the presence and absence of motion;

[0047] Fig. 19 shows a graph of time-dependent PTT and HR measurements, and how these can be processed with the algorithm shown in Fig. 18 to measure cNIBP in presence of motion;

[0048] Figs. 20A and 21A show, respectively, time-dependent SYS waveforms made using a femoral A-line (dark gray) and reconstructed using the algorithm shown in Figs. 18 and 19 to yield the best and worst results for the 23 clinical subjects;

[0049] Figs. 20B and 21B show, respectively, correlation plots generated using data from Figs. 20A and 21A;

[0050] Fig. 22 shows a schematic view of a patient and a coordinate axis used with an algorithm and accelerometer waveforms to determine the patient's posture;

[0051] Fig. 23A shows a graph of time-dependent accelerometer waveforms measured from a patient's chest during different postures;

[0052] Fig. 23B shows a graph of time-dependent postures determined by processing the accelerometer waveforms of Fig. 23A with an algorithm and the coordinate axis shown in Fig. 22;

[0053] Figs. 24A and 24B show, respectively, a three-dimensional image of the body-worn monitor attached to a patient during and after an initial indexing measurement;

[0054] Fig. 25 shows a three-dimensional image of the wrist-worn transceiver used with the body-worn monitor of Figs. 24A and 24B;

[0055] Fig. 26 shows an image of a patient wearing a head-mounted sensor featuring a multi-pixel array photodetector for measuring a PPG waveform;

[0056] Fig. 27 shows a plan view of the multi-pixel array photodetector of Fig. 26;

[0057] Figs. 28A and 28B show a bolus of blood passing through a detecting area of a conventional single-pixel photodetector for measuring a PPG waveform;

[0058] Figs. 29A and 29B show a bolus of blood passing through a detecting area of the multi-pixel array photodetector of Figs. 26 and 27; and

[0059] Fig. 30 shows a flow chart for measuring cNIBP, SpO2, respiration rate, heart rate, temperature and motion.

DETAILED DESCRIPTION OF THE INVENTION

[0060] Theory of the Composite Method

[0061] Figs. 1A and 1B show schematic drawings of the Composite Method's pressure-free (Fig. 1A) and pressure-dependent (Fig. 1B) measurements. Working in concert, these measurements accurately determine the patient's cNIBP for an extended time without requiring an external calibration device, e.g., a conventional blood pressure cuff. During a measurement, the patient wears a body-worn monitor attached to a disposable cuff and collection of optical, electrical, motion, and temperature sensors. These sensors measure signals for both the pressure-dependent and pressure-free measurements. The co-pending patent applications, the contents of which are fully incorporated herein by reference, describe earlier embodiments of this measurement: DEVICE AND METHOD FOR DETERMINING BLOOD PRESSURE USING 'HYBRID' PULSE TRANSIT TIME MEASUREMENT (U.S.S.N. 60/943,464; filed June 12, 2007); VITAL SIGN MONITOR FOR CUFFLESSLY MEASURING BLOOD PRESSURE USING A PULSE TRANSIT TIME CORRECTED FOR VASCULAR INDEX (U.S.S.N. 60/943,523; filed June 12, 2007); and VITAL SIGN MONITOR FOR MEASURING BLOOD PRESSURE USING OPTICAL, ELECTRICAL, AND PRESSURE WAVEFORMS (U.S.S.N 12/138, 194; filed June 12, 2008). A microprocessor in the body-worn monitor processes the PPG and ECG waveforms to determine PTT, which is used in both measurements of the Composite Method to determine cNIBP, as is described in more detail below.

[0062] The cuff includes an air bladder which, when pressurized with a pneumatic system, applies a pressure 107 to an underlying artery 102, 102'. An electrical system featuring at least 3 electrodes coupled to an amplifier/filter circuit within cabling attached to the wrist-worn transceiver measures an ECG waveform 104, 104' from the patient. Three electrodes (two detecting positive and negative signals, and one serving as a ground) are typically required to detect the necessary signals to generate an ECG waveform with an adequate signal-to-noise ratio. At the same time, an optical system featuring a transmissive or, optionally, reflective optical sensor measures a PPG waveform 105, 105' featuring a series of 'pulses', each characterized by an amplitude of $AMP_{1/2}$, from the patient's artery. The preferred measurement site is typically near small arteries in the patient's thumb, such as the princeps pollicis artery. A microprocessor and analog-to-digital converter within the wrist-worn transceiver detects and analyzes the ECG 104, 104' and PPG 105, 105' waveforms to determine both PTT_1 (from the pressure-free measurement) and PTT_2 (from the pressure-dependent measurement). Typically the microprocessor determines both PTT_1 and PTT_2 by calculating the time difference between the peak of the QRS complex in the ECG waveform 104, 104' and the foot (i.e. onset) of the PPG waveform 105, 105'.

[0063] The techniques disclosed herein are based on the discovery that an applied pressure (indicated by arrow 107) during the pressure-dependent measurement affects blood flow (indicated by arrows 103, 103') in the underlying artery 102, 102'. Specifically, the applied pressure has no affect on either PTT_2 or AMP_2 when it is less than a diastolic pressure within the artery 102, 102'. When the applied pressure 107 reaches the diastolic pressure it begins to compress the artery, thus reducing blood flow and the effective internal pressure. This causes PTT_2 to systematically increase relative to PTT_1, and AMP_2 to systematically decrease relative to AMP_1. PTT_2 increases and AMP_2 decreases (typically in a linear manner) as the applied pressure 107 approaches the systolic blood pressure within the artery 102, 102'. When the applied pressure 107 reaches the systolic blood pressure, AMP_2 is completely eliminated and PTT_2 consequently becomes immeasurable.

[0064] During a measurement the patient's heart generates electrical impulses that pass through the body near the speed of light. These impulses accompany each heartbeat, which then generates a pressure wave that propagates through the patient's vasculature at a significantly slower speed. Immediately after the heartbeat, the pressure wave leaves

elevated compared to both cNIBP and femoral blood pressures. Additionally, blood pressure at the radial artery tends to be relatively volatile compared to the other blood pressures. Without being bound to any theory, this too may also be due to pulse pressure amplification. Correlation between radial blood pressure and cNIBP is notably worse than that between cNIBP and femoral blood pressure, with both STDEV (9.3 mmHg) and BIAS (-12.8 mmHg) for the paired values falling outside of the FDA's guidelines. Data similar to that shown in Fig. 10 was collected from 23 subjects in a recent study using the device and method disclosed herein.

[0113] Fig. 11 shows typical correlation between both SYS and DIA measured with the Composite Method and a femoral A-line. Data were collected in the same manner described above. Blood pressure was measured over a 4-hour period with only a single indexing measurement performed at the beginning of the study. cNIBP measurements for both SYS and DIA in Fig. 11, like that described above in Fig. 10, correlate well with pressures measured at the femoral artery, and comfortably meet the guidelines required by the FDA. Fig. 12, for example, shows blood pressure correlations (shown as standard deviation) from a cohort of 23 subjects measured in two different ICUs using both the Composite Method and a femoral A- line. All subjects were measured under essentially identical conditions to those described above. The figure shows a histogram that graphs standard deviation values between the two measurements for both SYS (dark gray bars) and DIA (light gray bars). The histogram indicates that, for all measurements collected from 23 subjects, only a single measurement (for SYS) falls outside the FDA's guidelines of 8 mmHg for STDEV. All other measurements are comfortably within this limit, and as expected show Gaussian-type distributions, with the distributions peaked near 3 and 4 mmHg for, respectively, SYS and DIA.

[0114] Fig. 13 shows the collective, intra-subject statistics determined for all 23 subjects for the above-described study. Statistics were determined using two independent techniques. The first technique, called 'analysis of variance' or 'ANOVA', tests statistical variance for a set of repeated measures, like those used in the ICU study. ANOVA models for STDEV and BIAS are commonly used for analysis of data collected in clinical trials, like the one described herein. The second technique shown in Fig. 13 simply calculates the STDEV and BIAS for each subject in the study over the 4-hour measurement period, and then calculates the average of each of these parameters for the

[0127] The relationship between HR and PTT determined with the linear model is most accurate when the HR and PTT data points are collected immediately prior to the period of motion. If patient motion continues, then this model can be used along with HR for a period of time of up to 5 minutes to calculate cNIBP values. If patient motion persists past this period, then cNIBP cannot typically be accurately calculated, and this methodology should not be used. Typically this approach works best if correlation between HR and PTT, as indicated by $r^2_{HR/PTT,i}$, is relatively strong. In preferred embodiments, $r^2_{HR/PTT,i}$ is greater than about 0.5 for the algorithm to be implemented. If $r^2_{HR/PTT,i}$ is less than this value the algorithm is not implemented, and a blood pressure value is assumed to be corrupted by motion, and thus not reported.

[0128] Figs. 20A,B and 21A,B indicate the efficacy of this approach. Figs. 20A and 21A show time-dependent traces of SYS, measured with a femoral A-line, and a 'reconstructed' SYS determined using Equation (11). These graphs were generated using data measured during the 23-subject ICU study, described above. Figs. 20B and 21B plot the same data in Figs. 20A and 21A in a different way, showing a point-to-point correlation between SYS measured with the femoral arterial line and 'reconstructed' SYS measured with the method disclosed herein. As is clear from these graphs, reconstructing SYS values using this approach yields better agreement and higher correlation when the subject's blood pressure undergoes only small amounts of volatility. For example, Figs. 20A,B show the 'best' results from the group of 23 subjects. Here, the subject's blood pressure is relatively stable, and the reconstructed SYS agrees extremely well with SYS measured using the femoral arterial line (STDEV = 2.0 mmHg; BIAS = 0.2 mmHg). Figs. 21A,B show data from a subject with highly volatile blood pressure. This case represents the 'worst' agreement for the 23 subjects, likely because the volatility in cNIBP also results in a corresponding volatility in cardiac output. This, in turn, makes it more difficult to accurately reconstruct the subject's cNIBP, and results in slightly worse correlation (STDEV = 15.8 mmHg; BIAS = 0.6 mmHg) between arterial line and reconstructed SYS.

[0129] Processing Accelerometer Waveforms to Determine Posture

[0130] In addition to motion, a patient's posture can influence how the above-described system generates alarms/alerts from cNIBP and other vital signs. For example, the alarms/alerts related to cNIBP may vary depending on whether the patient is lying

What is claimed is:

1. A method for monitoring a blood pressure value from a patient, comprising:

(a) applying a variable pressure to the patient's arm using a pressure-delivery system;

(b) detecting a time-dependent pressure waveform representing the pressure applied to the patient's arm;

(c) digitally filtering a portion of the time-dependent pressure waveform to determine a processed pressure waveform;

(d) analyzing the processed pressure waveform to determine values for systolic blood pressure, diastolic blood pressure, and mean arterial pressure;

(e) detecting a first time-dependent waveform comprising a first feature induced by the patient's heartbeat with a first sensor configured to attach to the patient;

(f) detecting a second time-dependent waveform comprising a second feature induced by the patient's heartbeat with a second sensor configured to attach to the patient;

(g) determining a pulse transit time from a separation in time between the first feature and the second feature, wherein determining the pulse transit time comprises a measure of a separation in time between the first feature and the second feature;

(h) determining a variation in the pulse transit time as a function of the pressure applied to the patient's arm;

(i) processing the variation in pulse transit time to determine a relationship between pulse transit time and mean arterial pressure using a mathematical model that estimates an effective mean arterial pressure in the patient' s arm that varies with pressure applied by the pressure-delivery system;

wherein the effective mean arterial pressure is the difference between the mean arterial pressure determined during step (d) and a pressure-induced blood pressure change,

wherein the pressure-induced blood pressure change is defined by the following equation or a mathematical derivative thereof:

$$\Delta MAP(P)=F\times(P_{applied}-DIA_{INDEX})$$

where $\Delta MAP(P)$ is the pressure-induced blood pressure change, $P_{applied}$ is pressure applied by the pressure-delivery system during inflation, DIA_{INDEX} is the diastolic pressure determined from the processed pressure waveform, and F is a mathematical constant; and

(j) analyzing a pulse transit time determined when no pressure is applied to the patient's arm with the pressure delivery system, the relationship between pulse transit time and mean arterial blood pressure, and the blood pressure values determined from the processed pressure waveform in step (d) to determine a blood pressure value when no pressure is applied to the patient's arm with the pressure delivery system.

2. The method of claim 1, wherein step (b) comprises detecting the time-dependent pressure waveform representing the pressure applied to the patient's arm while the pressure-delivery system is inflating.

3. The method of claim 2, wherein step (c) comprises digitally filtering a portion of the time-dependent pressure waveform measured during inflation to determine the processed pressure waveform.

4. The method of claim 3, wherein step (c) comprises digitally filtering a portion of the time-dependent pressure waveform measured during inflation with: 1) a digital bandpass filter; and then 2) a digital low-pass filter to determine the processed pressure waveform.

5. The method of claim 1, wherein the pressure-delivery system comprises a cuff comprising an inflatable bladder.

6. The method of claim 5, wherein the pressure-delivery system comprises a pneumatic system connected to the cuff and configured to inflate the cuff.

7. The method of claim 1, wherein step (a) is performed once every 4 hours or more.

8. The method of claim 1, wherein step (j) is performed once every 1 second or less.

9. The method of claim 8, wherein step (j) further comprises determining an average pulse transit time from a set of pulse transit times collected over a time period.

10. The method of claim 9, wherein the time period is between 10 and 120 seconds.

11. The method of claim 1, wherein both the first and second sensors are selected from the group comprising an optical sensor, a pressure sensor, an electrical impedance sensor, an ECG waveform sensor, and a transducer.