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(54) **METHOD OF CALIBRATING A BLOOD PRESSURE MEASUREMENT DEVICE**

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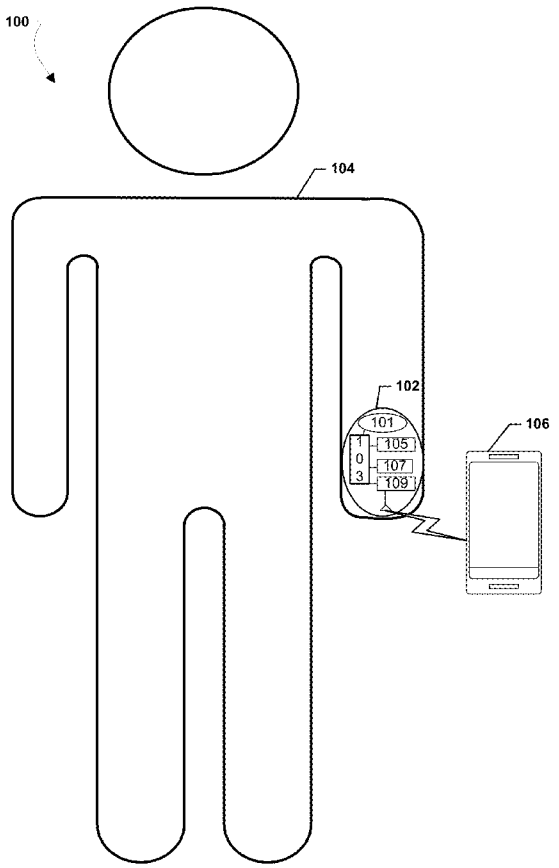
(57) **ABSTRACT**

Systems, methods, and devices of the various embodiments enable calibration of continuous non-interfering blood pressure measurement devices. The measured quantity may be related to an arterial lumen or arterial cross sectional area. The arterial cross-sectional area may be related to transmural pressure, and thus the measured quantity may be related to transmural pressure by applying the first relationship to the second relationship. Sensor outputs may be obtained at a number of different heights, while the blood pressure measurement device is attached to the limb of a patient. The obtained sensor outputs may be used to determine a set of unknown parameters associated with the relationship of the transmural pressure to the sensor output. Upon determination of the parameters, the relationship of the transmural pressure to the sensor output may be used to obtain blood pressure measurements.



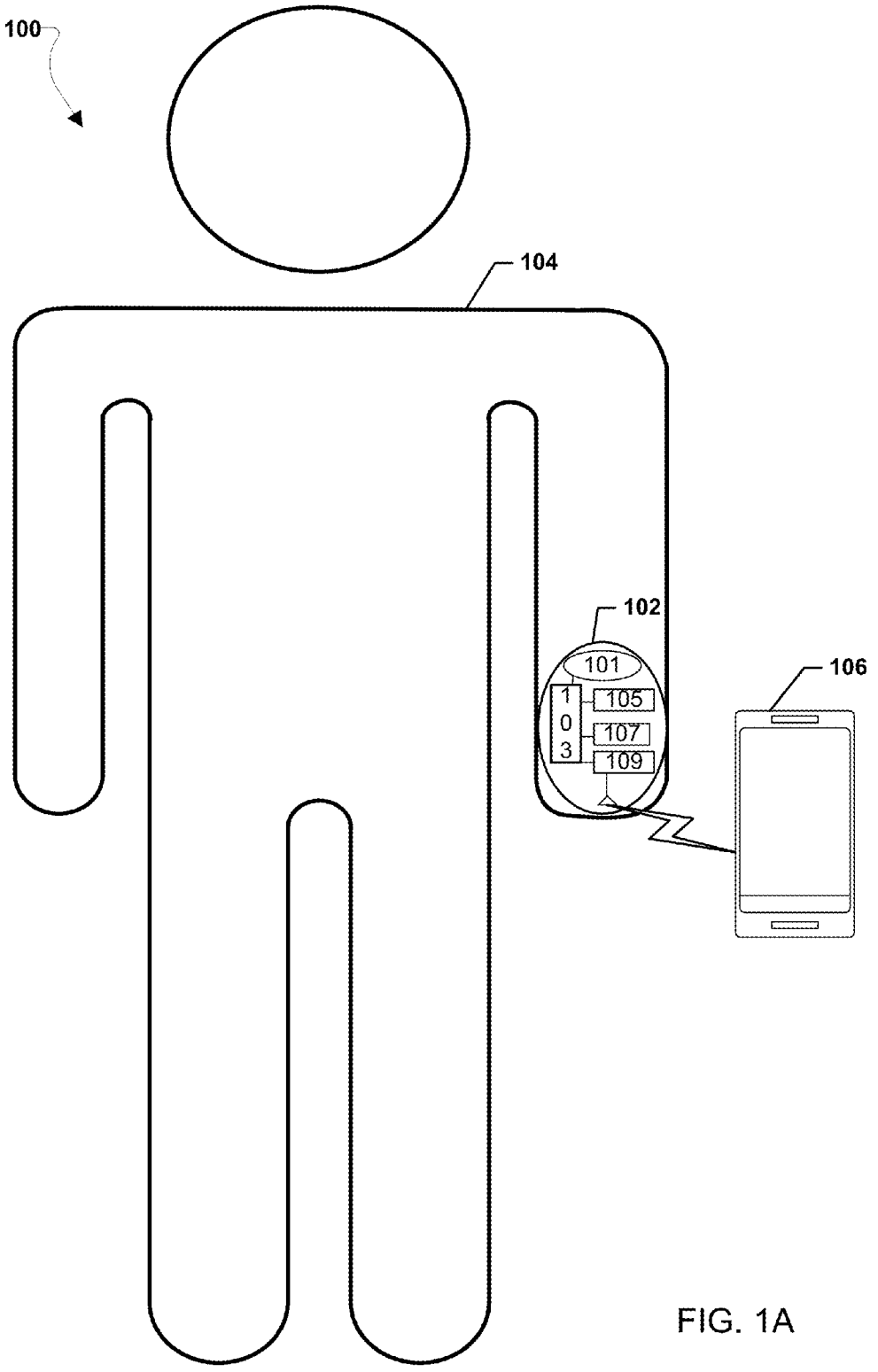


FIG. 1A

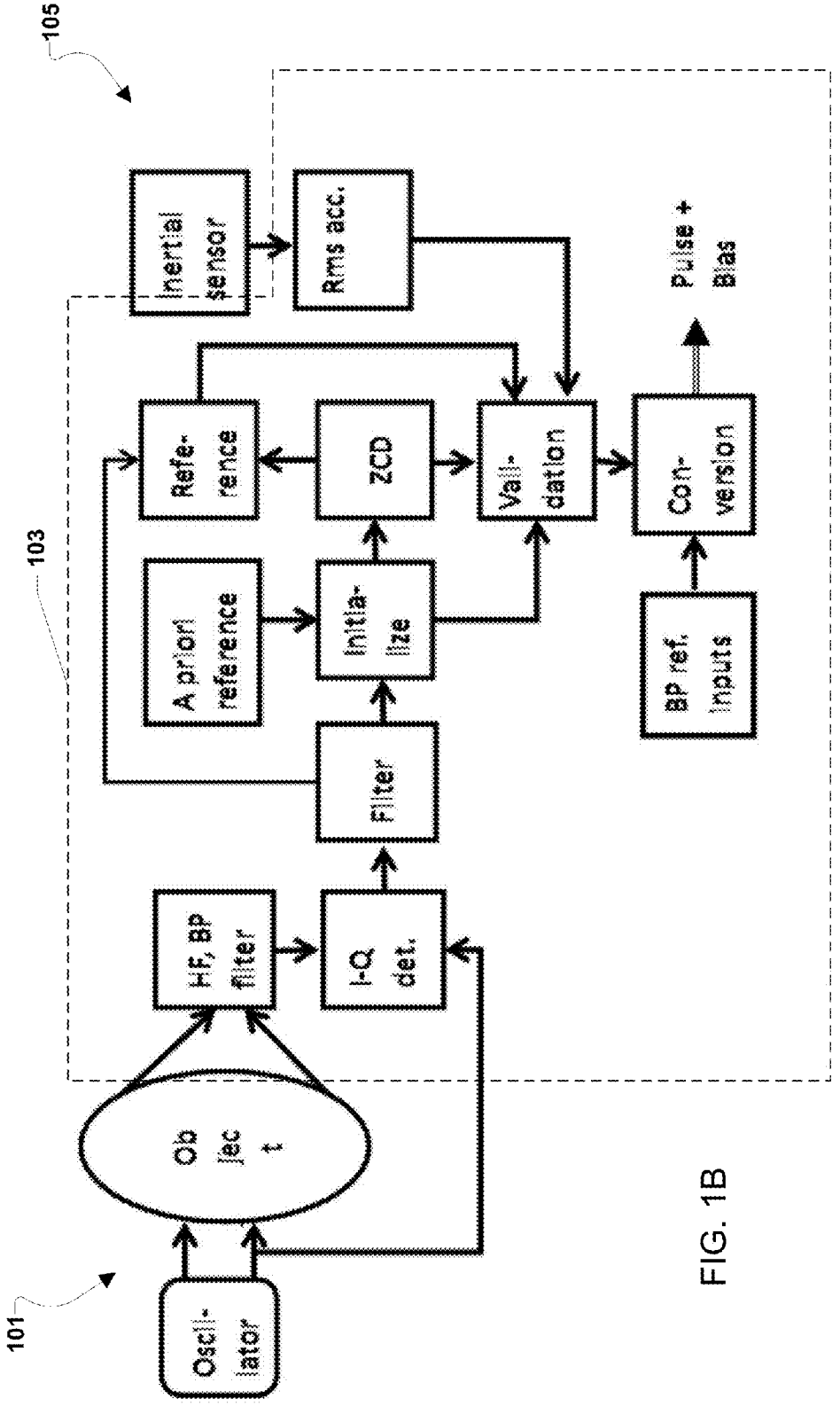

105
Inertial sensor
Rms acc.
Pulse + Bias
Refe-rence
ZCD
Vali-dation
Con-version
103
A priori reference
Initia-lize
BP ref. inputs
Filter
HF, BP filter
I-Q det.
Ob jec t
Oscil-lator
101

FIG. 1B

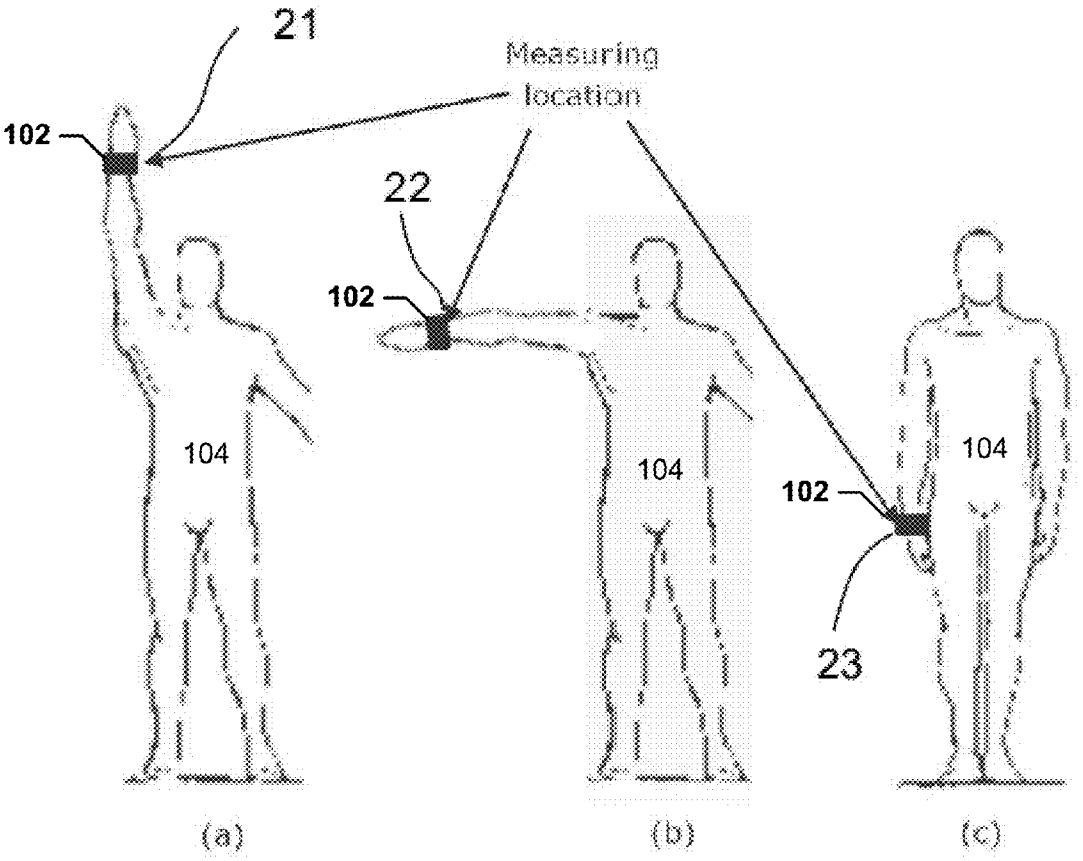


FIG. 2

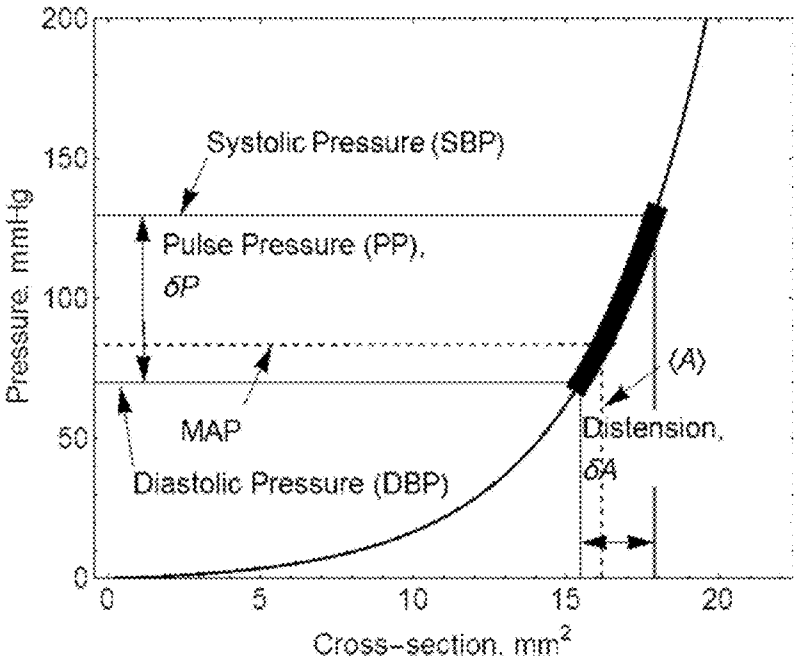

200
150
100
50
0
Pressure, mmHg
Systolic Pressure (SBP)
Pulse Pressure (PP),
δP
MAP
Diastolic Pressure (DBP)
⟨A⟩
Distension,
δA
0
5
10
15
20
Cross-section, mm²

FIG. 3A

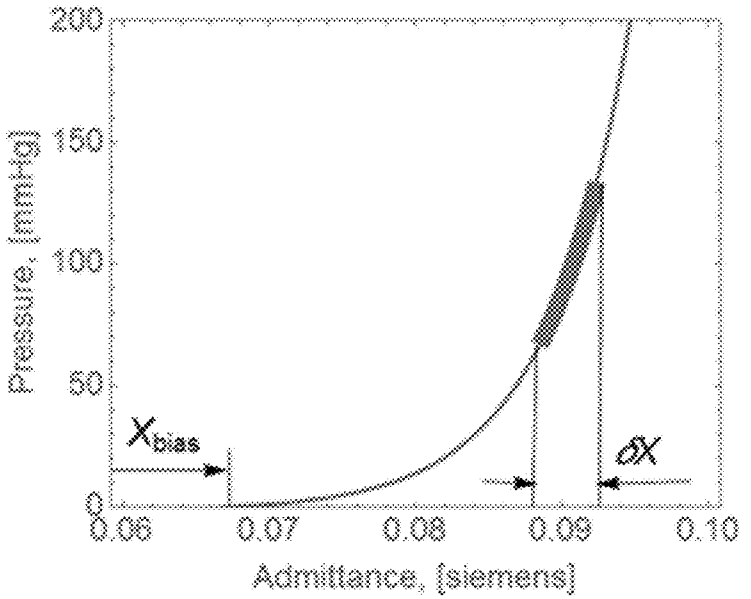

200
150
100
50
0
Pressure, [mmHg]
X_bias
δX
0.06
0.07
0.08
0.09
0.10
Admittance, [siemens]

FIG. 3B

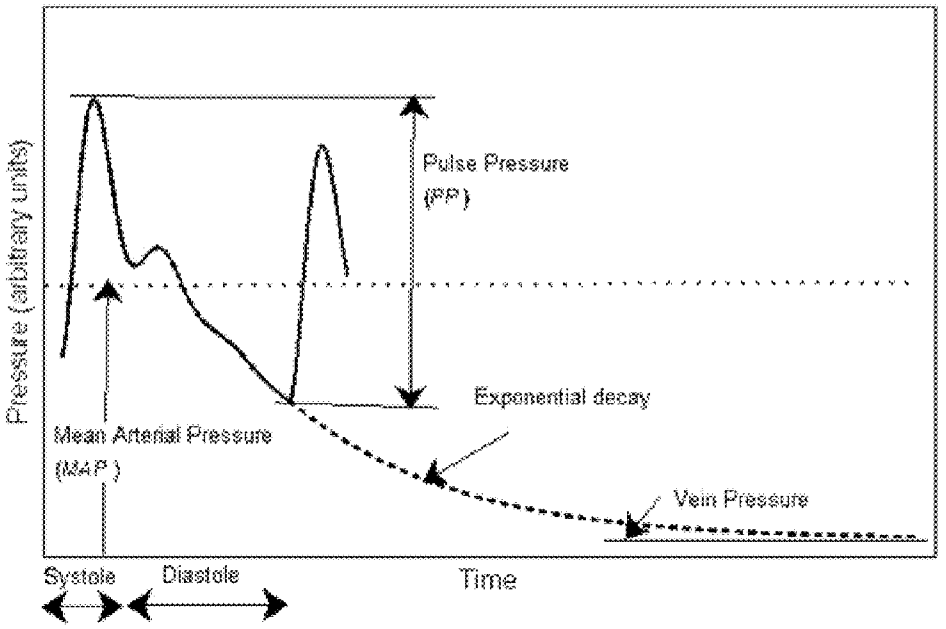

Pressure (arbitrary units)
Pulse Pressure
(PP)
Exponential decay
Mean Arterial Pressure
(MAP)
Vein Pressure
Systole
Diastole
Time

FIG. 3C

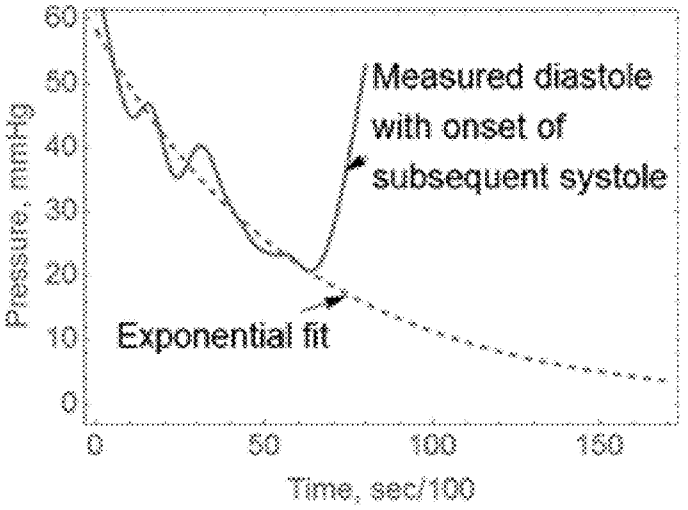

60
50
40
30
20
10
0
Pressure, mmHg
Measured diastole
with onset of
subsequent systole
Exponential fit
0
50
100
150
Time, sec/100

FIG. 3D

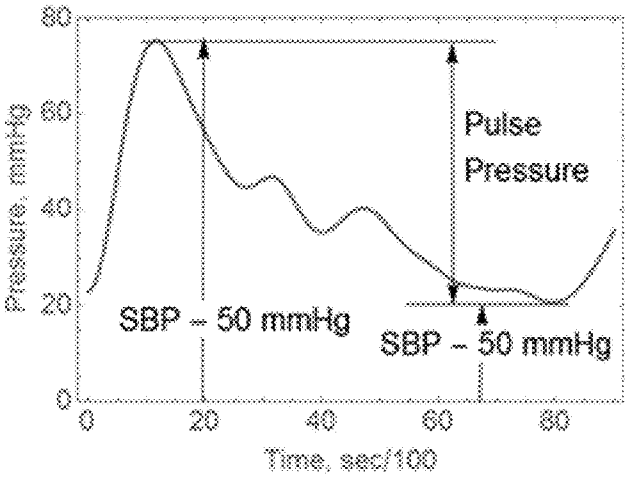

80
60
40
20
0
Pressure, mmHg
Pulse
Pressure
SBP – 50 mmHg
SBP – 50 mmHg
0
20
40
60
80
Time, sec/100

FIG. 3E

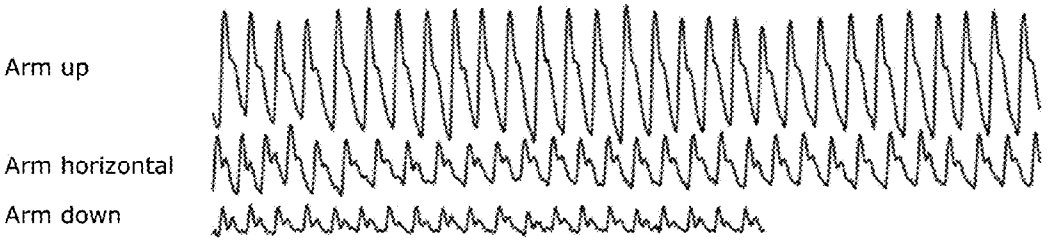

Arm up
Arm horizontal
Arm down

FIG. 4

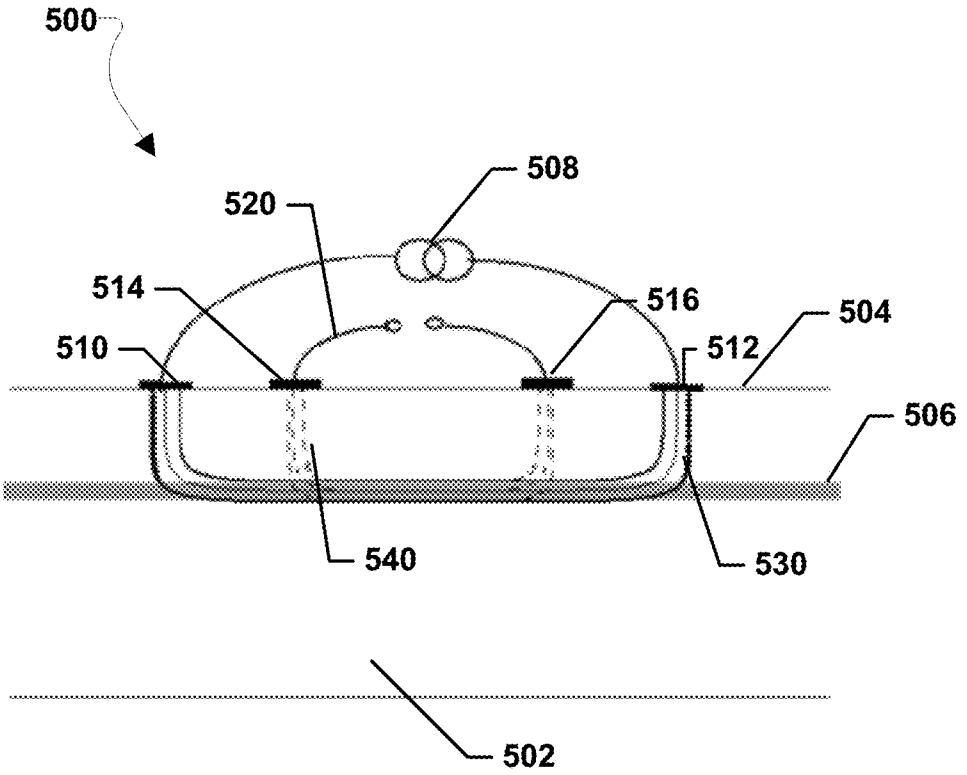


FIG. 5

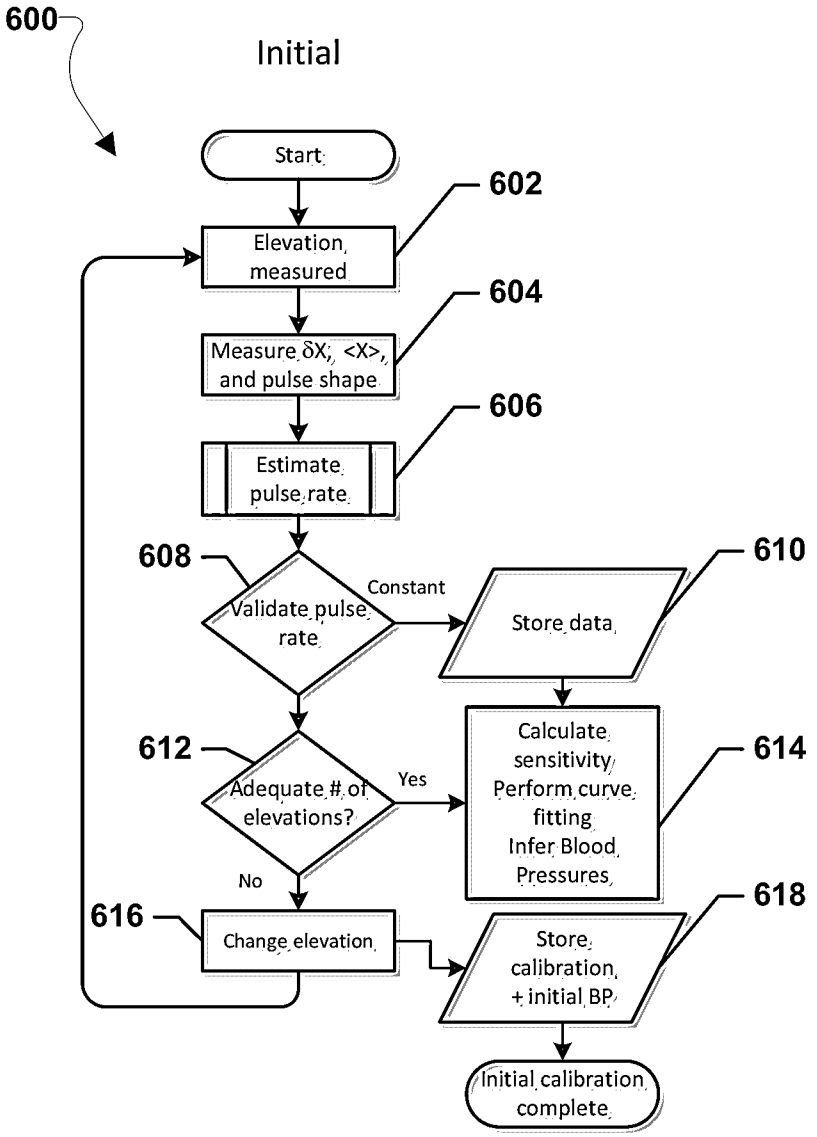

600
Initial
Start
602
Elevation measured
604
Measure δX, <X>, and pulse shape
606
Estimate pulse rate
608
Validate pulse rate
Constant
610
Store data
612
Adequate # of elevations?
Yes
614
Calculate sensitivity Perform curve fitting Infer Blood Pressures
No
616
Change elevation
618
Store calibration + initial BP
Initial calibration complete

FIG. 6A

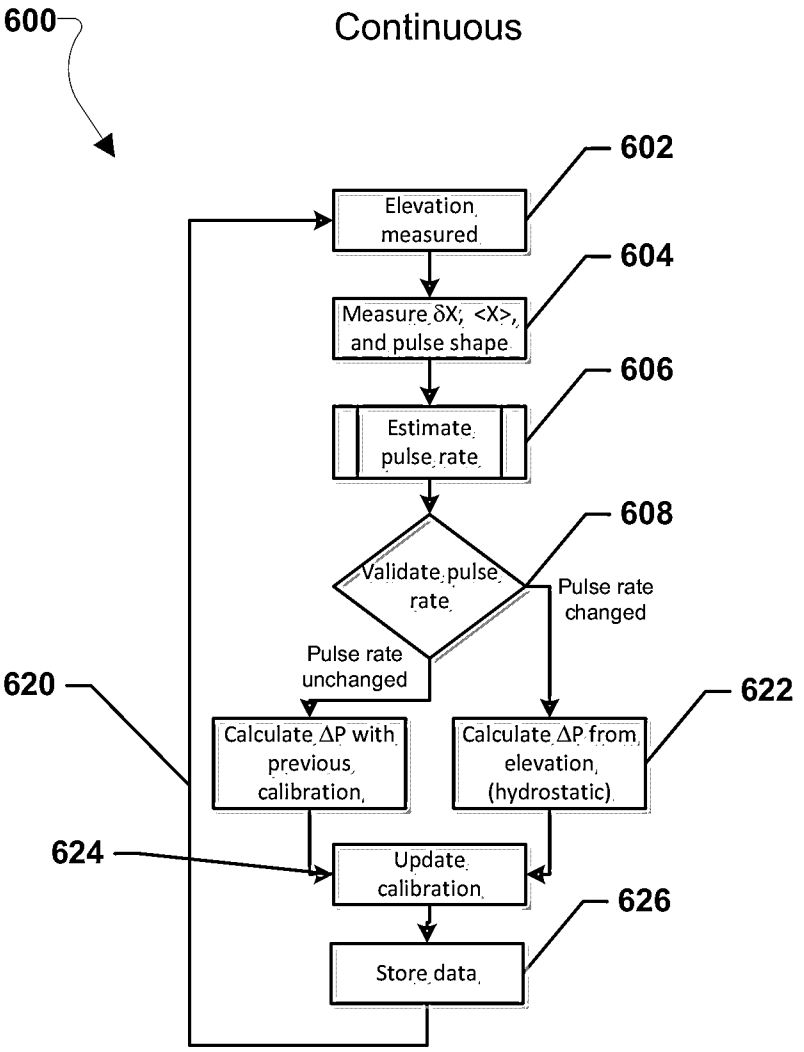

600
Continuous
602
Elevation measured
604
Measure δX, <X>, and pulse shape
606
Estimate pulse rate
608
Validate pulse rate
Pulse rate changed
Pulse rate unchanged
620
622
Calculate ΔP with previous calibration
Calculate ΔP from elevation (hydrostatic)
624
Update calibration
626
Store data

FIG. 6B

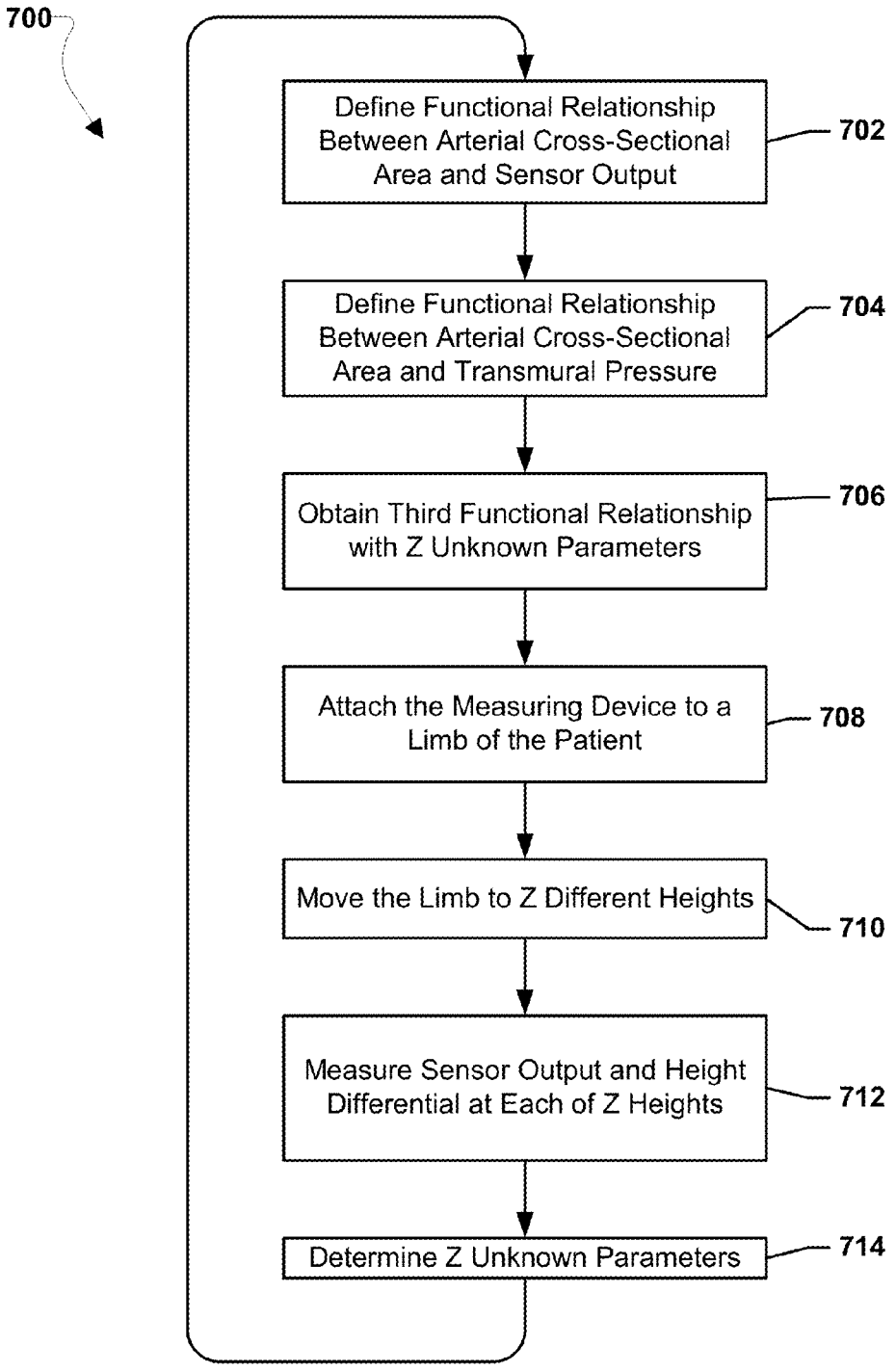

700
Define Functional Relationship Between Arterial Cross-Sectional Area and Sensor Output
702
Define Functional Relationship Between Arterial Cross-Sectional Area and Transmural Pressure
704
Obtain Third Functional Relationship with Z Unknown Parameters
706
Attach the Measuring Device to a Limb of the Patient
708
Move the Limb to Z Different Heights
710
Measure Sensor Output and Height Differential at Each of Z Heights
712
Determine Z Unknown Parameters
714

FIG. 7

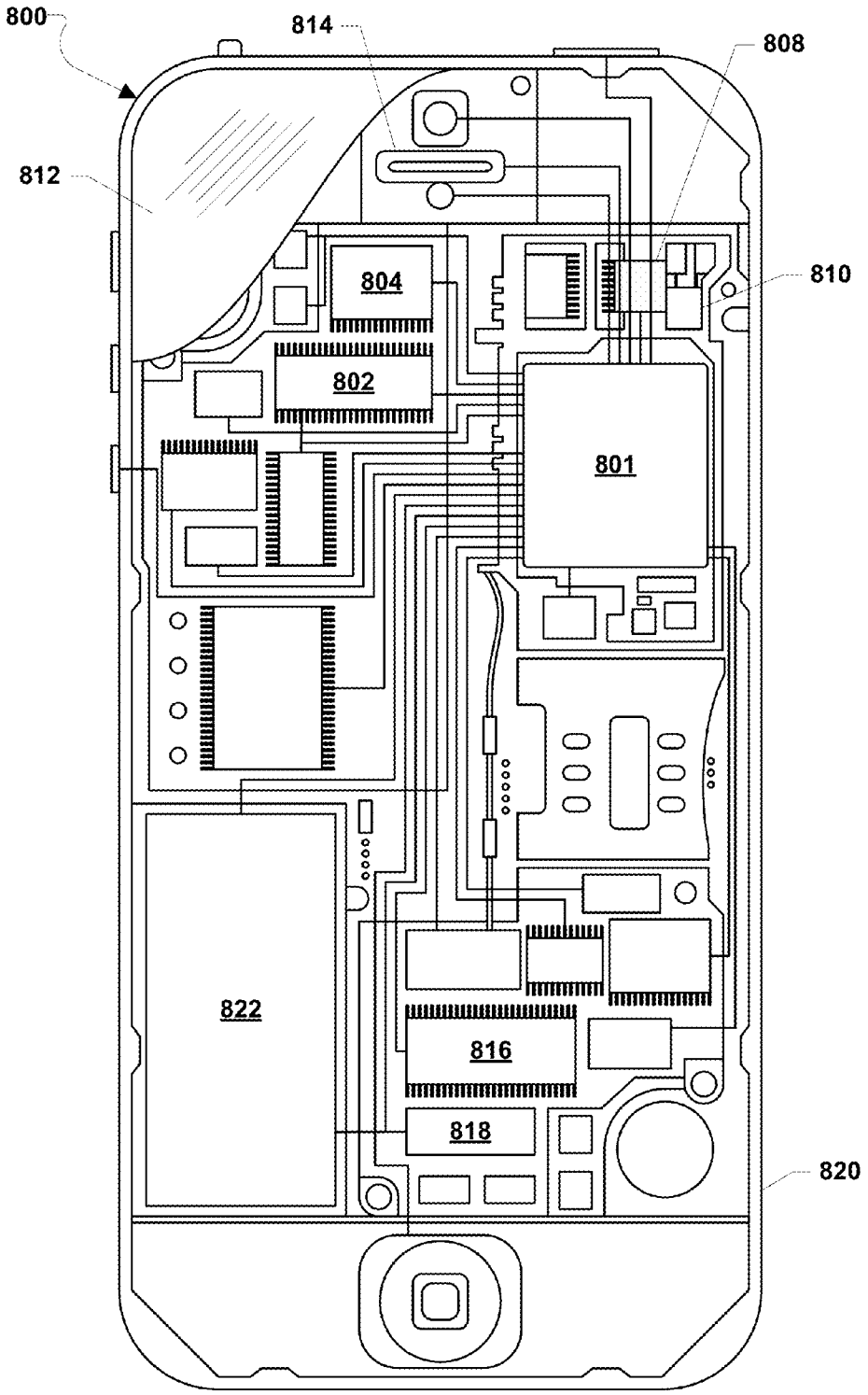


FIG. 8

METHOD OF CALIBRATING A BLOOD PRESSURE MEASUREMENT DEVICE

RELATED APPLICATIONS

[0001] This application claims the benefit of priority to U.S. Provisional Application No. 62/000,078 entitled "Method of Calibrating a Non-Interfering Continuous Blood Pressure Measurement Device" filed May 19, 2014; U.S. Provisional Application No. 62/072,568 entitled "Continuous Calibration of Non-Interfering Blood Pressure Device" filed Oct. 30, 2014; and U.S. Provisional Application No. 62/072,601 entitled "A Method of Estimating the Transmural Pressure in an Artery of a Subject with a Non-Interfering Continuous Blood Pressure Measuring Device" filed Oct. 30, 2014, the entire contents of each of which are hereby incorporated by reference.

BACKGROUND

[0002] Devices for measuring cardiovascular properties suffer from the problem that the measurement itself interferes strongly with the state of the subject, thereby leading to erroneous results. This is especially the case for current cuff-based methods that may impart a significant physiological impact. In current cuff-based methods, the systolic blood pressure is obtained by completely or at least substantially blocking an artery, which in most cases is the brachial artery in the upper arm. Blocking the artery affects pulse pressure propagation and pulse pressure shapes, which may only be tolerated in the peripheral system. Further, the diastolic pressure is derived from measurements obtained when the transmural pressure (pressure difference between the outside and the inside of an artery) is close to zero, which implies those measurements are made under conditions that are far from normal.

[0003] It is also well recognized that traditional methods based on inflatable cuffs and measurements performed in a clinical environment may have strong psychological effects causing elevation of blood pressure. The phenomenon is commonly called "white coat syndrome" or "white coat hypertension." So-called "masked hypertension" is a contrasting phenomenon in which blood pressure is elevated during normal daily activities but not in a medical office setting.

[0004] Additionally, blood pressure often exhibits considerable variability over time. Thus, identifying diurnal or other temporary variations in blood pressure may be very important for proper diagnosis of hypertension. It has also recently been shown that performing ambulatory blood pressure measurements is overall cost-effective.

[0005] It is therefore desirable to provide a device for measuring blood pressure that does not interfere with the normal bodily functions or at least does not perturb an artery being measured and that may measure blood pressure continuously and over a longer period of time.

SUMMARY

[0006] The systems, methods, and devices may include embodiments directed to the calibration of a continuous non-interfering blood pressure measurement device. Various embodiment methods may include determining, by an elevation sensor, an elevation of the blood pressure measuring device, determining, by an arterial measurement sensor, distension of an artery, determining, by a processor of the blood pressure measuring device, a pulse shape, determining, by the processor, whether a change in distension of an artery and elevation of a measurement device occurred between two observation times, determining, by the processor, whether a change in pulse rate has occurred between the two observation times in response to determining that a change in distension of an artery and elevation of a measurement device occurred between two observation times, storing, in a memory, the pulse shape, distension, and elevation in response to determining that the pulse rate is constant, determining, by the processor, a coefficient fitting an exponentially decaying function with an additive bias and representing an exponential decay of a portion of a diastolic phase to diastolic parts of measured pulses, an determining, by the processor, a calibration of the arterial measurement sensor based at least in part on the exponentially decaying function and the incremental variation between the two observation times.

[0007] In some embodiments, determining a calibration of the arterial measurement sensor may include determining an initial calibration of the arterial measurement sensor. Such embodiments may include determining an initial calibration of the arterial measurement sensor, which may be performed prior to each measuring session.

[0008] In some embodiments, determining distension of an artery may include measuring one or more of bioimpedance, impedance plethysmography, photoplethsmography, ultrasound, and surface pressure sensing.

[0009] Embodiments include a computing device having a processor configured with processor-executable instructions to perform operations of one or more of the embodiment methods described above.

[0010] Embodiments include a non-transitory processor-readable medium having stored thereon processor-executable software instructions to cause a processor to perform operations of one or more of the embodiment methods described above.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] The accompanying drawings, which are incorporated herein and constitute part of this specification, illustrate exemplary embodiments of the claims, and together with the general description given above and the detailed description given below, serve to explain the features of the claims.

[0012] FIG. **1**A is a block diagram of an embodiment system including an embodiment blood pressure measuring device placed on a subject.

[0013] FIG. **1**B is a component block diagram of an embodiment blood pressure measuring device.

[0014] FIG. **2** is a block diagram illustrating movement of a subject's limb and an embodiment blood pressure measuring device.

[0015] FIG. **3**A is a graph of a stress-strain relationship for an artery and illustrates transmural pressure P versus the arterial cross-sectional area, A.

[0016] FIG. **3**B is a graph of a stress-strain relationship for an artery and illustrates transmural pressure P versus a measured quantity X respectively.

[0017] FIG. **3**C shows a graph of a pressure pulse versus time.

[0018] FIG. **3**D is a graph illustrating details of fitting an exponential decay curve to the diastolic part of a measured pulse.

[0019] FIG. **3**E is a graph illustrating a measured pulse. FIG. **4** is a graph illustrating differences in distension relating to elevation of a measurement location.

[0020] FIG. **5** is an exemplary in-line bioelectric impedance sensing configuration in accordance with various embodiments.

[0021] FIGS. **6**A-B are process flow diagrams of embodiment methods for obtaining calibrated blood pressure values.

[0022] FIG. **7** is a process flow diagram illustrating an embodiment method for calibrating a non-interfering continuous blood pressure measurement device.

[0023] FIG. **8** is a component block diagram of a computing device suitable for use with the various embodiments.

DETAILED DESCRIPTION

[0024] The various embodiments will be described in detail with reference to the accompanying drawings. Wherever possible, the same reference numbers will be used throughout the drawings to refer to the same or like parts. References made to particular examples and implementations are for illustrative purposes, and are not intended to limit the scope of the claims.

[0025] The various embodiments provide methods and devices for continuous calibration of non-interfering blood-pressure devices to enable non-invasive monitoring of blood pressure with a minimum of interference to the measurement. The various embodiments may enable non-interfering measurements of blood pressure.

[0026] The word "exemplary" is used herein to mean "serving as an example, instance, or illustration." Any implementation described herein as "exemplary" is not necessarily to be construed as preferred or advantageous over other implementations.

[0027] The terms "computing device" are used herein to refer to any one or all of cellular telephones, smart-phones, web-pads, tablet computers, Internet enabled cellular telephones, Wi-Fi enabled electronic devices, laptop computers, personal computers, dedicated healthcare electronic devices, and similar electronic devices equipped with at least a processor and configured to communicate with a blood pressure measuring device described herein, such as a negligible interfering and negligible perception configuration or form blood pressure measuring device (e.g., a wearable patch, bracelet, anklet, watch, etc.).

[0028] The terms "sensing device", "sensor" or "transducer" are used interchangeably herein to refer to a device that performs a measurement of a biometric. Some non-limiting examples of a sensor may include devices utilizing ultrasound, applanation tonometery, light scattering and extinction, and electrical bioimpedance. Some of these methods are sometimes referred to as plethysmography, i.e. measurements which measure changes in volume within an organ or part of the body (usually resulting from fluctuations in the amount of contained blood or oxygen).

[0029] The term "monotonic relationship" refers to a relationship between an arterial cross-section and a pressure such that an increase in cross-sectional area is always accompanied by an increase in pressure.

[0030] The various embodiments may include methods, systems, and devices for calibrating a blood pressure measuring device. Initial calibration of a blood pressure measuring device may be performed exclusively on the basis of the hydrostatic pressure, which may be determined at different elevations of a blood pressure measuring location (e.g., an arm, a wrist, a finger, etc.). The initial calibration of a blood pressure measuring device may be performed without requiring a reference device. Subsequent re-calibration of the blood pressure measuring device may commence continuously or at pre-determined intervals by monitoring the instantaneous elevation of the measuring location and re-evaluating the corresponding hydrostatic pressure. In some embodiments, the calibration requires no special action from the subject and the adaptation provides no sensation to the subject.

[0031] In various embodiments a blood pressure measuring device may provide an output that varies proportionally with the variations of the cross-sectional area of an artery at a location of the measurement. In some embodiments, the proportionality may be for incremental changes or fluctuations and not for the absolute values because of the bias terms discussed further below. The various embodiments may provide outputs associated with the area or lumen of an artery, and thus to the square of the diameter. Cross-sectional area and lumen (volume) may be proportional because expansion in the direction of the artery may be negligible. The placement of the blood pressure measuring device and/or the location of the measurement may be at any location on a patient, such as a limb (e.g., an arm, a wrist, a finger, etc.).

[0032] The various embodiments may measure arterial lumen or cross-sectional area with a bias term. In order to convert such measurements to pressure, the sensitivity of blood pressure measuring device, as well as the arterial stiffness, may be needed and a bias term may be determined. In the various embodiments, variations of the hydrostatic pressure (for example an elevation difference of 60 cm may correspond to a 47 mmHg pressure change, while the Mean Arterial Pressure at heart level may be around 100 mmHg) may be continuously monitored along with outputs from an elevation sensor such as a 3D accelerometer with measurements integrated in order to detect position changes, a high resolution barometer configured to output the elevation or change in elevation of the measuring location, etc. When the pulse rate is constant, the "driving pulse pressure" may be assumed to be unchanged and the pulse pressure may be assumed to be constant, and thus the only pressure change may be caused by the change of the hydrostatic pressure due to changes in elevation of the measuring location. This presumption that the only cause of the change in pressure is the change of the hydrostatic pressure may enable a method of calibration for incremental changes.

[0033] The absolute pressure may be evaluated through analysis of the exponential decay of the diastolic part of the pulse (i.e., the last part of the pulse), which converges towards the venous pressure, generally a few mmHg, a fitting procedure may give a correction to the bias term. Thus, in the various embodiments both pulse pressure and mean arterial pressure may be estimated. Using these estimates, systolic and diastolic pressures may be determined with a temporal resolution unattainable by traditional cuff-based devices and without any interference of the artery on which measurements may be performed. Additionally, the various embodiments may eliminate the need for measuring local Pulse Wave Velocity and arterial diameter to determine blood pressure.

[0034] In the various embodiments, variations of the measured quantity may be generally proportional to the variations of the cross-sectional area of the artery, but may include an unknown additive bias term. The proportionality constant and the bias may change, but typically over time scales much longer than the duration of a single pulse. The duration of a single pulse is typically about one second, but the length of a single pulse may vary over time and from individual to individual.

[0035] The arterial pressure P and the artery cross-sectional area may be related by a stress-strain relation that generally may be assumed to be exponential. The pressure pulses associated with the beating of the heart may be smaller than the mean pressure and a local linear relation between pressure variations and cross-sectional area variations of the artery can be assumed. The gradient of the relation may define the instantaneous incremental arterial stiffness or elasticity. The stiffness may not be constant, and the stiffness may continuously adapt to the state of the subject (i.e., patient). The response time may typically be in the order of minutes or longer, but may be much shorter in cases of extraordinary changes of the environment to which the subject is exposed. Incremental pressure and lumen changes may be related by the gradient of the stress-strain relation. In general, the lumen and the cross-sectional area of peripheral arteries may be proportional since the variations in the direction of the artery may be negligible: The elastic properties of peripheral arteries may be predominantly given by smooth muscles arranges in a spiral pattern—presumably arranged in such a way that the arterial expansion upon a pressure increase predominantly may be in the radial direction and negligible in the longitudinal direction.

[0036] In the various embodiments, the pressure pulse occurring after each contraction of the left heart ventricle can be considered to include three parts. The first part may be the immediate rise of the pressure as a consequence of the ejection from the heart, i.e., the systole phase. The second part may include an exponentially decaying pressure occurring in the diastole phase. The decay may asymptotically approach the venous pressure, which may be only a few mmHg, but may be terminated by the occurrence of the subsequent pulse. The exponential decay may be caused by the arterial system being connected with the veins through capillary network with a high fluid-flow resistivity and the veins being much more elastic than the arteries. Thus, the venous system may essentially behave in a manner that can be represented as a capacitor. Propagation effects may play an insignificant role for the decay since the time constant of the decay may be much larger than the pulse propagation time through the arterial system. The third part may represent reflections from discontinuities in the arterial system, such as bifurcations or diameter changes in the arterial system, particularly in the vicinity of a sensor.

[0037] In the various embodiments, the pulse rate averaged over time, such as averaged over about one minute of measurements, may play an important role. There may be an inverse relationship between heart rate and central blood pressure, but often a positive correlation is encountered between heart rate and peripheral blood pressure. It may be assumed that if the heart rate is constant—except for the very short term heart rate variability—then the pulse pressure may also be constant. In various embodiments, the cross-section of an artery may be a function of a measured quantity, a constant and a bias term. The arterial cross-section "A" may be expressed in terms of a sensor output "X" (e.g., a measured quantity), scaling constant "k" and bias "X_{bias}". Thus, the relationship of arterial cross-section to sensor output may be expressed by the function:

$$A=k(X-X_{bias})$$

[0038] In some embodiments, the constant k may be evaluated on the basis of the physics and geometry of the sensor configuration whereas it may not be possible to determine X_{bias} a priori.

[0039] In various embodiments, the arterial cross-section "A" and arterial transmural pressure "P" (e.g., the pressure across the arterial wall) may be related by a stress-strain relation that generally may be assumed to be exponential. For positive transmural pressures (e.g., uncollapsed arteries) the transmural pressure "P" may be expressed in terms of artery-dependent parameters "P_o" and "A_o", and arterial cross-section "A". The cross-sectional area "A", of the artery may be measured with several different non-interfering sensing devices. Thus, transmural pressure for $A \geq A_0$ may be expressed by the function:

$$P=P_o(e^{A/A_o}-1)$$

[0040] Further, the transmural pressure "P" may be functionally related to sensor output "X" by substituting the expression of arterial cross-section to sensor output for the arterial cross-section term in the transmural pressure expression.

$$P = P_0\left(\exp\left(\frac{k(X - X_{bias})}{A_0}\right) - 1\right) = P_0(\exp(k_1(X - X_{bias})) - 1)$$

where $\{P_0, k_1, X_{bias}\}$ are parameters that may be determined during calibration. As will be described in greater detail below, determination of these parameters during calibration may enable subsequent direct determination of transmural pressure using the measured quantity. In some embodiments, other stress-strain relationships may be employed so long as the arterial cross-section and arterial pressure have a monotonic relationship.

[0041] In some embodiments, conversion between transmural pressure and arterial cross-section may be possible by finding the gradient of the stress-strain relationship at a mean arterial cross-sectional area. For most of the range of pulse pressure, a straight line may be used to approximate the local stress-strain relationship. However, if the pulse pressure extends over a range where significant changes of the gradient occur, the full nonlinear stress-strain relation must be applied.

[0042] In various embodiments, the pressure in an extended system may be affected both by the system itself and by gravity. The hydrostatic pressure affecting the blood pressure in an artery may be exclusively given by the elevation of a location relative to a reference point if it is assumed that the fluid in the system is incompressible, i.e. its density is constant, and that the gravitation acceleration is constant. The change in hydrostatic pressure P_{hs} encountered by moving a measuring location from one position to another position separated by a distance h in the direction of gravity (i.e., height) may simply be given by:

$$P_{hs}=\rho g h$$

where ρ is the density of the fluid and g is the gravitational acceleration. For example, the difference in hydrostatic pressure at the wrist of an arm of length 60 cm raised to a straight upward position and a horizontal position, respectively, may be 47.4 mmHg, which may be significant relative to the mean arterial pressure at the elevation of the heart (typically around 100 mmHg). The siphon effect may be neglected if the fluid system is terminated into a very high fluid impedance unit, which is the case for most of the arterial systems in which the high resistance capillary network provides the connection from arteries to veins.

[0043] During calibration the sensor output may be measured at multiple different elevations of the limb supporting the non-interfering blood pressure measuring device. A mean sensor output may be calculated at each elevation. The "mean" may be an average over a time period. For example, the time period may be at least as long as the duration of one pulse, but may be as long as one respiration period in order to eliminate the modulation of the blood pressure resulting from respiration. An upper limit for the averaging time period may be the time within which the pulse pressure stays constant. This time can be inferred from the variability of the pulse rate as described herein.

[0044] In various embodiments, the difference in heights (h_2-h_1) may be used to calculate transmural pressure, rendering measurement of the absolute height position of each measurement unnecessary. For example, transmural pressure may be expressed in terms of the difference between three measurement points 1, 2, 3 by the series of functions:

$$\begin{aligned}\rho g(h_1-h_2) &= P_0(\exp(k_1(X_1-X_0))-\exp(k_1(X_2-X_0)))\rho g(h_1-h_3)\\ &= P_0(\exp(k_1(X_1-X_0))-\exp(k_1(X_3-X_0)))\rho_g(h_2-h_3)\\ &= P_0(\exp(k_1(X_2-X_0))-\exp(k_1(X_3-X_0)))\end{aligned}$$

Solving the system of questions during calibration may enable determination of the parameters $\{P_0, k_1, X_0\}$. Once these parameters are determined, subsequent sensor outputs may be directly related to transmural pressure.

[0045] Various embodiments, may include recording sets of data relating to the hydrostatic pressure relative to the heart level along with the mean sensor output at several different elevation positions. Thus, each elevation position may have an associated data set $\{P_{hsi}, X_i\}$, where the index "i" indicates the specific elevation.

[0046] Each artery may have a mean transmural pressure "MAP_R" at the reference point. The reference point may for example be the level of the heart. Hydrostatic pressure may be represented by P_{hs}, where the separation distance h is an offset in the direction of gravitational force, relative to the reference point. During the calibration procedure, the MAP_R may be assumed to be constant so long as the vascular properties other than hydrostatic pressure do not change during the time period needed for calibration. For example, the calibration time period during which vascular properties are unchanging is typically in the order of one minute for healthy individuals, but will be even larger for other subjects. Thus, the transmural pressure may be expressed in terms of the hydrostatic pressure and the mean arterial pressure by the function:

$$P=MAP_R+P_{hs}=MAP_R+\rho gh$$

or

$$P=P_{heart}+P_{hs} \text{ where } MAP_R=P_{heart}$$

[0047] Some embodiments may include the mean arterial pressure at a reference point as a fourth unknown parameter. The reference point may be set at a patient's heart level. Thus, the height h would be equal to zero when the sensing device is level with a patient's heart, negative when the sensing device is vertically positioned lower than heart level and positive when the sensing device is raised above heart level. In such embodiments, the transmural pressure may P may be written in terms of the mean arterial pressure as discussed above:

$$MAP_R+\rho gh=P_0(\exp(k_1(X-X_0))-1)$$

$$\rho gh=P_0(\exp(k_1(X-X_0))-1)-MAP_R$$

[0048] In this way, the MAP at the level of the heart may be determined during the calibration process. However, if the MAP_R value is not specifically desired, then the sensing device may be started at any reference point. Thereby enabling a generic calibration procedure. The specific value for the MAP at heart level may be calculated at a later time by measuring the pressure pulse with the sensing device maintained at the level of the heart.

[0049] In various embodiments, the pulse pressure, δP, may be inferred by measuring the dynamic part of the sensor output, δX, which may be converted to pressure as discussed above.

[0050] In various embodiments, the values used during the calibration procedure may be the average values for at least one pulse. However, once the calibration procedure has been performed then the instantaneous values may subsequently be found. The Systolic Blood Pressure (SBP) may be given by the maximum of the pressure and the Diastolic Blood Pressure (DBP) is given by the minimum pressure, in both cases when corrected for the hydrostatic pressure. The MAP may be approximated by the expression:

$$MAP\cong(1/3)SBP+(2/3)DBP$$

[0051] The true MAP, in contrast to the approximate MAP may be obtained by averaging the pressure over an entire pulse. This average may depend on the pulse shape. The above MAP approximation may hold true for healthy patients, but may produce less reliable results for patients with blood pressure problems.

[0052] The various embodiments may include methods, devices, and systems for calibrating a non-interfering blood pressure device including the determination of $\{P_0, k_1, X_0\}$. The various embodiments may include a sensor that may measure a quantity monotonically related to the cross-sectional area of an artery positioned beneath the sensing device. Embodiments may include non-interfering blood pressure measurement devices that may be attached to varied points on a patient's body. The examples and illustrations described herein refer to a non-interfering blood pressure measurement device positioned along the wrist of a patient, however numerous other positioning may be employed in accordance with the various methods, devices, and systems. For example, embodiments may include the measurement device along the upper arm, as is the case for traditional cuff-based blood pressure measuring devices. In such embodiments, the change in elevation due to motion of the arm may be lower, resulting in a reduce impact on the hydrostatic pressure during motion. Thus, greater demands may be placed on the accuracy of the sensor measurements. However, the effect of gravity during normal use may be less than that experienced by wrist based measuring devices because the measurement location will be closer to the heart during normal use.

[0053] In various embodiments, the sensing device may obtain and record sensor output for at least three different elevations of the patient's wrist with respect to a reference position. For example, the measured quantity may be obtained with the arm positioned straight upright, horizontal, and straight downward. Some embodiments may include a

reference point that is laterally aligned with a patient's heart and may use such a reference point as a zero point.

[0054] Various embodiments may include using the obtained measured quantities to determine a set of unknown parameters $\{P_0, k_1, X_0\}$ characterizing the relationship between arterial transmural pressure P and the measured quantity X. In some embodiments, the determination of these parameters may enable subsequent determination of transmural pressure using only a measured quantity as a function of time. By measuring the sensor output over an entire pulse, the pressure over an entire pulse can be determined. From the pressure signal over an entire pulse, it is possible to determine traditional blood pressure parameters such as Pulse Pressure (PP), Mean Arterial Pressure (MAP), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP).

[0055] The systems, methods, and devices of the various embodiments may enable calibration of a continuous non-interfering blood pressure device based on measured bio-impedance over time. The various embodiments may calibrate a blood pressure monitoring device based on measured bioimpedance to determine changes of the arterial properties of a patient (i.e., subject), over time, in such a way that no special action may be required by the patient and no sensation may be felt by the patient.

[0056] In the various embodiments, when a change ΔX of the measured quantity X is observed jointly with a possible change of elevation of the measuring site, the expected change in blood pressure, caused by the change of hydrostatic pressure, may be evaluated. Further, if the change ΔX and possible change of elevation of the measuring site occur during a time interval in which the pulse rate is constant, then the only cause of change in blood pressure at the measuring site is the change in hydrostatic pressure. This may provide for an estimate of the current relation between incremental pressure change ΔP and incremental change of measured quantity ΔX, i.e. for determining k in the equation:

$$\Delta P = k \times \Delta X.$$

[0057] Knowing the incremental sensitivity, the pulse pressure may be determined. The absolute pressure may be obtained by fitting the diastole to the exponential decay function. The fitted exponentially decaying function may asymptotically approach the pressure in the veins.

[0058] In various embodiments, a blood pressure measuring device may initially be calibrated and set for the correct arterial properties when a measuring session is started. In various embodiments, a blood pressure measuring device may initially be calibrated in any manner that may enable the blood pressure measuring device to be set for the correct arterial properties for a patient at an initial time. For example, a blood pressure measuring device may be calibrated to measure a quantity (X) monotonically related to the cross sectional area (A) of an artery arranged in the vicinity of a sensor of the blood pressure measuring device by: providing a first model that describes the relationship between the output (X) of the sensor and the cross sectional area (A) of the artery and representing the first model with a first equation ($A=f(X)$) having a first number of unknown parameters; providing a second model that describes the relationship between the cross sectional area (A) of an artery and the transmural pressure (P) in the artery and representing the second model with a second equation ($P=g(A)$) having a second number of unknown parameters; substituting the first equation (f) into the second equation (g) to get a third equation, $P=c(X)$, representing the relationship between the output of the sensor and the transmural pressure in the artery, the third equation (c) having a number (z) of unknown parameters; attaching the blood pressure measuring device to a limb of a subject such that the sensor is arranged in the vicinity of an artery in the limb of the subject; placing the limb of the subject into z positions so that the measurement location of the sensor arrives at z different heights with regard to a reference height; at each of the z different heights, measuring and recording the average value of the output of the sensor together with the height of the measurement location of the sensor relative to the reference height; and using the known effect of the hydrostatic force on the transmural pressure at the different heights of the measurement location of the sensor to find the unknown parameters of the third equation (c).

[0059] In the various embodiments, a sensor, such as an arterial measurement sensor, may provide an output, X that is proportional to the instantaneous arterial cross-sectional area, but that may also include an unknown additive bias term. The variations of the sensor output may provide the equivalent variations of the arterial cross-section. One problem to be solved is to convert the sensor output to properly calibrated blood pressure. The conversion is in general not static because of the varying arterial stiffness. The measuring bias may change as a consequence of movements of the limb on which the measurement is performed, which may correspond to elevation changes at the measurement site. Bias changes may not occur immediately with elevation changes. Rather, in various embodiments bias changes may be assumed to be relatively slow, e.g., on time scales of at least several minutes which may be caused by relatively slow variations of the properties of the veins of a subject. The incremental conversion from sensor signal to lumen may also change as a consequence of changing posture/position of the patient.

[0060] In the various embodiments, an elevation sensor may provide an output that may be continuously converted to a measure of the elevation of the measuring location. For example, the elevation sensor may be a 3D inertial sensor such as an accelerometer, where elevation changes may be inferred from integration of the accelerometer output. As other examples, the elevation sensor may be a barometer, magnetic near-field device, or any other type sensor configured to measure of the elevation or changes in elevation of the measuring location.

[0061] Individual pulses may exhibit considerable variability both in amplitude, pulse shape, and in pulse length. In order to obtain a characteristic pulse, conditional averaging may be applied in various embodiments. A conditional average may be obtained by averaging a set of numbers in which a given condition has to be fulfilled for each of the numbers. In an embodiment, it may be the amplitudes $X(t_{i,j})$ where the first index i represents a fixed time from a reference time of the pulse. The reference time may be defined by the time in which the largest positive slope of the pulse is observed. For example, the reference time may be at the first zero-crossing of the high-pass filtered pulse. If a number of pulses are recorded then the second index j may be the pulse number. In an embodiment, each of the i values of a pulse may be averaged over all pulses, that is over j. The result may be a pulse representing the average pulse averaged over all the recorded pulses.

[0062] In an embodiment, a method for measuring blood pressure may include selecting a location on the body for the measurement, such as a wrist, a finger, or some other location

where arteries are identified. The selected location may be fitted with a blood pressure measuring device including an artery measurement sensor, such as a non-interfering sensing device, which may measure a quantity proportional to the distension of the artery right below the sensor and an elevation sensor, such as a 3D inertial sensor, which may be supported by a tilt sensor. In an embodiment, the outputs of the sensor (e.g., the arterial measurement sensor) and the elevation sensor may be recorded continuously. The pulse rate may be measured and averaged continuously over a sliding window of a width of from 0.5 minute to about 2 minutes. The elevation may be continuously evaluated and averaged over a few seconds.

[0063] In an embodiment, sequences with a constant pulse rate may be selected. The mean of the sensor output may be evaluated for these sequences. The incremental sensitivity (or variation) may then be found to be $k=\Delta P_{hs}/\Delta X$ where ΔP_{hs} is the change in hydrostatic pressure from one observation time to another observation time and ΔX is the change of the mean output of the artery measurement sensor between the two observation times.

[0064] In an embodiment, the diastolic parts of measured pulses recorded between the two observation times may be fitted to an exponential function with an additive bias, e.g. to

$$y = a\exp\left(-\frac{t}{t_0}\right) + b$$

[0065] The parameter a is defined by the distension amplitude of the diastolic part of the pulse and b is the bias term caused by the possible contributions from tissues other than the artery and by a possible off-set of the measuring electronics. Time is denoted t and the time-constant of the decay is denoted t_0, which is given by the resistance of the capillary network connecting artery with veins in conjunction with the capacity of the arteries.

[0066] In an embodiment, diastolic parts may be fitted to the exponential function on each individual pulse and the fitting parameters may then be averaged over a series of pulses, such as 60 pulses or any other number of pulses. Alternatively the fitting may be performed on pulses obtained by conditional averaging over a series of pulses, such as up to 60 pulses. The diastole may be defined as starting at the time instance after the first dip of the pulse in which the second derivative of the measured pulse waveform with respect to time is positive and ending at the onset of the subsequent pulse.

[0067] In an embodiment, the parameters a and b may be converted to pressure parameters by multiplication with k. In an embodiment, the diastolic pressure (DBP) may be estimated by evaluation of the first part of the equation at the end of the diastole, multiplying with k and adding the vein pressure, which may be assumed to be 4 mmHg with an uncertainty of 2 mmHg. The diastolic blood pressure estimate may be performed on the individual pulses with and averaging the values of a number of pulses. The number of pulses may be from one to 60 or more. Generally 60 pulses may be used since short term fluctuations may be minimized and arterial properties may be generally constant over a period of 60 pulses. The diastolic blood pressure estimate may also be obtained from the pulse obtained by conditional averaging. In a similar manner, the pulse pressure (PP) may be simply obtained with averaging as described above.

[0068] In an embodiment, the systolic blood pressure (SBP) may be given by:

$$SBP=DB+PP.$$

[0069] In an embodiment, the Mean Arterial Pressure (MAP) may be obtained by finding the mean of the pulse pressure from the start of the systole to the end of the diastole, scaled with k, and with the bias term determined above. Alternatively, the often used approximation

$$MAP = \frac{2}{3}DBP + \frac{1}{3}SBP$$

may be applied. Alternatively, to perform a fitting over the whole pulse length where the initial sharp rise during the systolic phase as well as the oscillatory components of the pulse are included. A dynamic part of a function that accommodates this may be as follows:

$$[a(1-\exp(-t/t_a))]\cos(\omega_r t)\exp(-t/t_0)$$

[0070] Continuous measurement instructions to the subject may only be feasible at the initialization of a measuring session, as measuring sessions may last 24 hours or longer. Updating the calibration may be needed in the course of a measuring session, which may be achieved by measuring the distension signal, the pulse rate, and the elevation of the measuring location continuously. In response to determining that the elevation changes with a constant pulse rate and the accordingly calculated change of pressure deviates from a threshold value, such as a pressure value associated with the actual measured distension, an update calibration condition may be determined and the device may enter a calibration mode.

[0071] In an embodiment, a sensor exploiting bioimpedance variations and preferably with a tetrapolar configuration and an electrode configuration as disclosed in W02012110042A1 may be utilized to determine blood pressure. In another embodiment, electrodes may be applied to a patient placed in a line right on top of the radial artery and aligned with the direction of the selected artery. At the wrist this may be the radial artery or the ulnar artery. A first set of two electrodes may be placed with a separation somewhat larger than the depth at which the artery is embedded in the limb. At the wrist this may be about 1 cm, but the separation may be considerably larger only confined by the length of the limb. A second set of two electrodes may be placed with a closer separation than in the first set and between the electrodes of the first set. The separation of the electrodes of the second set may be at a minimum given by the depth at which the artery is located but preferably larger. At the wrist this may be a separation of from 5 mm to several centimeters. The sizes of the electrodes may be smaller than the separations, such as 1 mm, 2 mm, or larger. A current oscillating at a frequency, which may be in the range of 10 kHz to 100 MHz, may be injected into the limb. The magnitude of the current may be in the range of 0.1 μA to 2 mA. The field lines associated with the current may be essentially perpendicular close to the skin, because the skin and the subcutaneous fat may have low conductivities. In the artery the electric field lines may become aligned with the direction of the blood filled artery because blood has a relatively high conductivity.

[0072] In the various embodiments, an elevation sensor may provide an output that may be continuously converted to

a measure of the elevation of the measuring location. For example, the elevation sensor may be a 3D inertial sensor such as an accelerometer.

[0073] FIG. **1**A illustrates an embodiment system **100** including an embodiment blood pressure measuring device **102** placed on a subject **104**. In an embodiment, the blood pressure measuring device **102** may include a processor **103** connected to one or more artery measurement sensors **101**, one or more elevation sensor **105**, a power source **107**, and a radio module **109** connected to an antenna. The one or more artery measurement sensors **101** may be any type sensor or combination of sensors that may measure arterial properties of the patient **104** either directly or indirectly. As an example, the one or more artery measurement sensors **101** may be electrical tissue and blood impedance measurement sensors that inject an AC current by one set of electrodes and detect the voltage with another set of electrodes to measure bioimpedance. As another example, the one or more artery measurement sensors **101** may be optical sensors, such as photoplethysmographic sensors including pulse oximeters. As a further example, the one or more artery measurement sensors **101** may be ultrasound sensors. As yet another example, the one or more artery measurement sensors **101** may be surface arterial measurement sensors. As a still further example, the one or more artery measurement sensors **101** may be impedance sensors, such as impedance plethysmography sensors. The one or more artery measurement sensors **101** may output measurements of arterial properties to the processor **103** of the blood pressure measurement device **102**.

[0074] The one or more elevation sensors **105** may be any type sensor or combination of sensors that may measure the elevation of the blood pressure measuring device **102** and the limb or other location of the subject **104** to which the blood pressure measuring device **102** may be attached. As examples, the one or more elevation sensors may be three dimensional inertial sensors (e.g., accelerometers, etc.), GPS sensors. The one or more elevation sensors **105** may output elevation measurements to the processor **103** of the blood pressure measurement device **102**.

[0075] In an embodiment, via the radio module **109** and antenna, the processor **103** of the blood pressure measuring device **102** may establish a wireless connection with a computing device **106**, such as a smart phone. In this manner, via the wireless connection with the computing device **106**, the processor **103** of the blood pressure measuring device **102** may exchange data with the computing device **106**.

[0076] In the various embodiments, the blood pressure measuring device **102** may be of any type configuration or form. In an embodiment, the blood pressure measuring device **102** may be a negligible interfering and negligible perception configuration or form device, such as a wearable patch, bracelet, anklet, watch, etc.

[0077] FIG. **1**B is a component block diagram of an embodiment blood pressure measuring device, such as blood pressure measuring device **102** described above with reference to FIG. **1**A, illustrating various processing modules of the processor **103**. In an embodiment, the blood pressure measuring device illustrated in FIG. **1**B may measure blood pressure based on bioimpedances. The artery measurement sensor **101** may include a signal generator, such as an oscillator, configured to apply an excitation signal, such as oscillating current, sinusoidal current, etc., via excitation electrodes to an object, such as an artery, and detection electrodes to measure the resulting voltage and provide the voltage to the processor **103**. The elevation sensor **105** may comprise an inertial sensor that may be configured to output acceleration measurements to the processor **103**.

[0078] In an embodiment, the processor **103** of the blood pressure measuring device illustrated in FIG. **1**B may measure bioimpedances by controlling the artery measurement sensor **101** to apply an oscillating current to the excitation electrodes. Outputs from the processor may be pulses and MAP in units of mmHg or in some other selected pressure unit. For example, the pulses and MAP may be transmitted from the processor **103** via a radio module to a computing device, such as a smartphone, for further processing and/or display.

[0079] In an embodiment, the data from the inertial sensor may be supported by signals from a level detector in such a way that the first and last positions require a vertical orientation of the arm (limb), and the measurement between requires a horizontal orientation. FIG. **2** illustrates movement of a subject's limb and an embodiment blood pressure measuring device **102** moving from a first elevation in an upward vertical orientation (**21**) to a second elevation in a horizontal orientation (**22**), to a third elevation in a straight downward vertical orientation (**23**).

[0080] In various embodiments, the blood pressure measuring device having an accelerometer and a sensor may be attached to a patient's wrist. An accelerometer reading may be integrated twice to obtain the current limb position. During the calibration process, the patient may lift and lower the wrist to different positions. The blood pressure measuring device may calculate the height for all the positions via the twice integrated accelerometer reading. At each position, the blood pressure measuring device may also record the sensor output (e.g., the measured quantity). In some embodiments, the patient may move the limb freely through a range of positions, thereby enabling collection of a large number of points for the fitting procedure in a simple manner.

[0081] Accelerometer readings may further be used to validate sensor outputs (e.g., measured quantity). For example, if an accelerometer measures accelerations over a certain threshold, such as 0.2 G, then the blood pressure measuring device may determine that the limb is actively in motion. Measurements taken during time periods of active motion may be automatically filtered out, to reduce error resulting from blood pressure changes during the active motion. The filtering threshold for accelerometer readings may be reduced during the calibration process because the patient may be required to move the pertinent limb. For example, accelerometer signals occurring at accelerations over 0.1 G may be ignored during calibration, while only signals occurring at accelerations over 0.2 G may be ignored during normal operation.

[0082] In some embodiments, the blood pressure measuring device may include a level detector or elevation sensor. The level detector may determine when the patient's wrist (limb) is in a vertical or horizontal position. Determining that a patient's limb has moved from a first vertical position to a second vertical position may imply that the wrist has moved through the range of positions needed for calibration. For example, the blood pressure measuring device may be preprogrammed to begin and end measurement collection at a first and second vertical orientation of the limb respectively. The level detector may determine when the wrist (limb) is in a vertical position and may signal the blood pressure device that calibration may begin. Measurements may be obtained at

specific positions (e.g., a horizontal position), or may occur continuously until the second vertical orientation is detected by the level detector. In this way, the blood pressure measuring device may ensure that calibration occurs over the full range of desired positions.

[0083] In an embodiment, the measurement may be taken with the wrist (limb) in three different elevation positions, such as those depicted in **21**, **22**, **23**. Taking measurements at three elevation positions provides a series of three pressure equations and thereby enables determination of the three unknown parameters. In some embodiments, such as those utilizing ultrasound sensors, a more direct relationship between sensor output and arterial cross-sectional area may be provided, reducing the number of unknown parameters in the P(X) relationship by one. Therefore the number of unknown parameters may be reduced to two, and only two measurement elevation positions are needed to inform a system of equations adequate to determine the unknowns. Conversely, in embodiments in which the type of sensor employed results in a more complex relationship between sensor output and arterial cross-sectional area, the number of unknown parameters in the P(X) relationship may be greater than three. In such embodiments, the number of measurement positions needed to determine the unknown parameters may be greater than three. In general, the number of measurement positions should be equal to or greater than the number of unknowns.

[0084] The number of measurement positions employed during calibration is not restricted to the number of unknown parameters. Although the number of measurement positions needed to sufficiently calibrate the device may be defined by the number of unknown parameters in the sensor output to arterial cross-sectional area relationship, more measurements may be used to increase fitting accuracy. Obtaining additional sensor outputs during calibration may reduce the significance of any single instance of measurement error thereby reducing overall reliance on accuracy of detailed sensor output.

[0085] Characteristics of the body may change over time and the arterial stress strain relationship may change accordingly. Similarly, the relationship between cross-sectional area and sensor output may also change over time. Therefore, embodiments may include to recalibrating the blood pressure measuring device at regular intervals. Furthermore, due to the potential for changes in body characteristics, some embodiments may include performing the calibration procedure within a limited amount of time. For example, the bias term X_0 may be affected by the state of the veins in the pertinent limb. The veins are more elastic than the arteries and the relevant dynamics of the veins is slower than that of the arteries. Therefore, performing measurements within a limited time period may ensure that the characteristics of the veins are essentially constant. Exemplary time periods for performing the calibration procedure may include less than 10 minutes, less than 5 minutes, less than 2.5 minutes or less than 1 minute. An actual time period may be set by the patient or patient's healthcare provider and may depend on the health of the patient. In young, healthy individuals, body characteristics may change quite quickly as the body adapts to changing environments and activity levels, thereby requiring regular recalibration of the blood pressure measuring device. Conversely, patients with hypertension and/or stiff arteries, relevant body characteristics may change much more slowly, thus enabling less frequent recalibration of the blood pressure measuring device.

[0086] In some embodiments, the blood pressure measuring device may initiate the automatic cessation of sensor output and recalibration of the device after a predetermined time period. The time period may be preprogrammed by a medical professional and may depend on a patient's individual health and medical history. Alternatively, the time period may be determined using statistical data such as age, weight, height, and BMI. In some embodiments, the blood pressure measuring device may emit an alert to indicate that the predetermined time period has elapsed and recalibration is needed. Alerts may include any or all of audible, visual, and tactile notifications.

[0087] In various embodiments, sensor output (e.g., the measured quantity) may compensate for effects of hydrostatic pressure to ensure accuracy. Such compensation may include requiring the patient to hold the pertinent wrist (limb) at one position, such as at heart level, for a predetermined time period. In some embodiments, the level of the device relative to the heart may be determined continuously to enable the sensor output to compensate for hydrostatic pressure. In a simple embodiment, only a single accelerometer is used.

[0088] FIG. **3**A is a graph of a stress-strain relationship for an artery. FIG. **3**A defines the quantities that may be inferred by the various embodiments, including Systolic Blood Pressure (SBP), Pulse Pressure (PP), δP, MAP, Diastolic Blood Pressure (DBP), Distension, δA, and $\langle A \rangle$.

[0089] FIG. **3**B is a graph of a stress-strain relationship for an artery and illustrates transmural pressure P versus a measured quantity X respectively.

[0090] FIG. **3**C is a graph illustrating changes in a typical pressure pulse over time. A dashed line indicates the exponential decay of the pressure during the diastole. The decay is interrupted by the emergence of a subsequent pulse.

[0091] FIG. **3**D is a graph illustrating the fitting of an exponential decay curve to a measure pulse.

[0092] FIG. **3**E is a graph illustrating a measured pulse. The measurement is scaled and displaced to provide pressure values. The resulting values may be in good agreement with values obtained by a reference device on the alternate arm.

[0093] FIG. **4** is a graph of measurements taken from an exemplary subject and calibrated according to the various methods, devices, and systems. The readings are focused on the mean arterial pressure MAP, which was 105 mmHg. The graph illustrates the distension signal, which may be proportional to the arterial cross-section, versus time. The distension signal is provided for three different measurement location elevations. The changes of distension amplitudes with elevation may be in good agreement with the exponential stress-strain relation and the assumption of a constant pulse pressure.

[0094] FIG. **5** illustrates an embodiment in-line sensor configuration for an exemplary non-interfering blood pressure measuring device in accordance with the various embodiments. A patient's limb **502** may have a skin surface **504** and underlying artery **506**. A current generator **508** may be electrically connected to the two outermost excitation electrodes **510**, **512**. The outermost excitation electrodes may be positioned lying on the skin surface **504** to enable an excitation signal **520** to reach an underlying artery **506**. Voltage detection may be facilitated by the two innermost detecting electrodes **514**, **516**, which may also lie on the skin surface **504** and may be electrically connected to the current generator **508**. The excitation field lines **530** are illustrated as solid lines and the detection field lines **540** are illustrated as dashed lines.

[0095] Measurements may be performed on the radial artery or ulnar artery within the wrist. A first set of excitation electrodes **510**, **512** may be placed with a separation distance (i.e., the distance between positions of the electrodes) greater than the depth at which the underlying artery **506** is embedded in the limb **502**. At the wrist this depth is less than 1 cm, but the separation may be considerably larger, and may only be constrained by the length of the user's limb **502**. A second set of detecting electrodes **514**, **516** may have a smaller separation distance (i.e., the distance between positions of the electrodes) than the first set and is placed between the electrodes of the first set. The separation distance of the electrodes **514**, **516** of the second set may be at least as large as the depth at which the underlying artery **506** is located, and may be larger. At the wrist this may be a separation of from 5 mm to several centimeters. For example, the separation of the second set of electrodes **514**, **516** may be about 2.5 cm and the separation of the first set of electrodes is **510**, **512** may be about 5 cm.

[0096] The size of the electrodes is typically smaller than the respective separation distances. For example, each electrode may be as small as 1 mm or larger. A current oscillating at a frequency, which is in the range of 10 kHz to 10 MHz, may be injected into the limb **502**. The magnitude of the current may be in the range of 0.1 mA to 2 mA. The field lines associated with the current may be essentially perpendicular close to the skin surface **504**, because the skin **504** and the subcutaneous fat have low conductivities; close to the artery **506**. In the artery **506** the field lines may be aligned in the direction of the blood filled artery because blood has a relatively high conductivity.

[0097] FIG. **6**A illustrates an embodiment method **600** for the initial calibration of non-interfering blood pressure measuring device. In an embodiment, the operations of the method **600** may be performed by a processor of a blood pressure measuring device, such as the blood pressure measuring device **102** described above. In an embodiment, the operations of the method **600** may be performed by a processor as an initial calibration procedure to measure a quantity X monotonically related to an arterial cross-sectional area A lying in proximity to the position of the blood pressure measuring device, to set the correct arterial properties for the blood pressure measuring device prior to the beginning of a measuring session

[0098] In block **602**, the processor may determine a current elevation of the non-interfering blood pressure measuring device, supported by the limb of a patient user. Elevation sensors such as 3D inertial accelerometers and barometers may be used to obtain a current elevation output.

[0099] In block **604**, the processor may obtain a current value for a measured quantity X (i.e., sensor output) via a sensor integrated into the non-interfering blood pressure measuring device. A difference between the current sensor output and the previous sensor output may be calculated and stored. The processor may further determine a current pulse shape. In block **606**, a current pulse rate may be estimated and then validated in block **608**. If the validated pulse rate is constant, then the current sensor output, pulse shape, pulse rate, and difference in measured quantity may be stored in block **610**. If the pulse rate is not constant then the processor may determine whether additional measurements are needed.

[0100] In block **612**, the processor may determine whether measurements have been obtained at a sufficient number of measurement elevations. In block **616**, the processor may continue taking measurements at differing elevations until a sufficient number of measurements are obtained. The number of measurements required for sufficient confidence in calibration may be pre-determined prior to beginning calibration. Once a sufficient number of measurements have been obtained, the processor may fit the data to a function such as an exponential decay function to produce blood pressure estimates in block **614**. Parameter values may be determined during the data fitting, and may be stored, along with the blood pressure estimates in block **618**. Upon completion of the initial blood pressure measurement reading, the device may be ready to commence a measuring session.

[0101] FIG. **6**B illustrates an embodiment method **600** for continuous calibration of a non-interfering blood pressure measuring device during a measurement session. In an embodiment, the operations of the method **600** may be performed by a processor of a blood pressure measuring device, such as the blood pressure measuring device **102** described above. In an embodiment, the operations of the method **600** may be performed by a processor as an initial calibration procedure to measure a quantity X monotonically related to an arterial cross-sectional area A lying in proximity to the position of the blood pressure measuring device, to set the correct arterial properties for the blood pressure measuring device during an active measuring session

[0102] In blocks **602** through **606**, the processor may obtain measurements of elevation, measured quantity, and pulse shape in the manner described with reference to FIG. **6**A above.

[0103] In block **608**, the processor may determine whether the patient's pulse rate is constant, and if the pulse rate is positive, may begin determining whether a change in pressure has occurred since the last calibration. If there has been no change in transmural pulse pressure since the last calibration (i.e., block **608** evaluates to "No") then in block **620**, the processor may calibrate using the stored previous calibration information (i.e., the information stored in block **618**). If a change in transmural pulse pressure has occurred since the last calibration (i.e., block **608** evaluates to "Yes"), then in block **622**, the processor may calculate a change in hydrostatic pressure using elevation outputs. The resulting pressure changes may be used to update the calibration values in block **624** and stored for later comparison in block **626**.

[0104] FIG. **7** illustrates an embodiment method **700** for calibrating a blood pressure measuring device based on incremental variations of arterial properties. In an embodiment, the operations of method **700** may be performed by a processor of a blood pressure measuring device, such as blood pressure measuring device **102** described above. In an embodiment, the operations of method **700** may be performed by a processor as an initial calibration procedure to measure a quantity X monotonically related to an arterial cross-sectional area A lying in proximity to the position of the blood pressure measuring device, to set the correct arterial properties for the blood pressure measuring device prior to the beginning of a measuring session.

[0105] In block **702**, the processor may define a first functional relationship that describes the relationship between the sensor output (e.g., measured quantity) X, and the cross-sectional area A of an artery embedded in the limb to which the blood pressure measuring device is secured. In some embodiments, the functional relationship may be represented by the expression ($A=f(X)$). This expression may have a

number of unknown parameters, the quantity of which may depend on the type of sensor included in the blood pressure measuring device.

[0106] In block **704**, the processor may define a second functional relationship that describes the relationship between the cross-sectional area A of an artery and the transmural pressure P across the artery walls. In some embodiments, the second functional relationship may be represented by an expression (P=g(A)), which may have a second number of unknown parameters

[0107] In block **706**, the processor may substitute the first equation (*f*) into the second equation (g). A result of this substitution may be a third expression P=c(X), representing the relationship between the sensor output X and the transmural pressure P within the artery upon which measurements are taken. In some embodiments, the third equation (c) may have a number Z of unknown parameters.

[0108] In block **708**, the blood pressure measuring device may be attached to the limb (e.g., the wrist) of a patient, in preparation for obtaining measurements. The blood pressure measuring device may be attached to the limb (e.g., the wrist) in the vicinity of an artery embedded in the limb. In some embodiments, the blood pressure measuring device may be attached to the limb (e.g., the wrist) of a patient prior to defining the first functional relationship as in block **702**.

[0109] In block **710**, the blood pressure measuring device may be moved to Z distinct height positions. In some embodiments, the patient may move his or her limb through at least Z different positions having Z different vertical positions. In some embodiments, the patient's limb may be mechanically moved through a series of Z positions.

[0110] In block **712**, the processor may measure at each of the Z different heights, the average value of the output of the sensor output (e.g., the measured quantity) together with the height of the measurement location relative to a reference height. In some embodiments, the reference height may be the level of the patient's heart. In an embodiment, the measured quantity of the artery and elevation may be measured continuously. In an embodiment, measurements at an elevation may be averaged over a period of a few seconds.

[0111] In block **714**, the processor may determine the value of the Z unknown parameters of the expression (c). The processor may use the known effect of the hydrostatic force on the transmural pressure at the different heights of the measurement locations to find the unknown parameters. In an embodiment, the processor may fit the obtained measurements and Z different elevation differentials to expression (c) to obtain a system of Z equations, and solve the equations for the unknown parameters. In some embodiments, one of the unknown parameters may be a bias term. Upon determining the value of the parameters, the processor may begin normal collection of blood pressure readings using the sensor. Obtained sensor outputs (e.g., measured quantities) may be directly related to transmural pressure by fitting the output to expression (c) as modified with the known parameters. In some embodiments, the blood pressure measuring device may be recalibrated to update the value of the unknown parameters and reduce error in blood pressure calculations.

[0112] An embodiment blood pressure measuring device may be configured to transmit data to any of a variety of computing devices. For example, FIG. **8** illustrates a computing device **800** suitable for use in various embodiments. The computing device **800** may exchange data to and/or from the blood pressure measuring devices discussed above, such as blood pressure measuring device **102**, and may perform one or more of the operations of method **700** described above. For example, DBP, PP, SBP, MAP, and/or measured pulses, hydrostatic pressure, distension of an artery, and/or elevation may be sent from the blood pressure measuring device to the computing device **800**.

[0113] In various embodiments, the computing device **800** may include a processor **801** coupled to a touch screen controller **804** and an internal memory **802**. The processor **801** may be one or more multicore ICs designated for general or specific processing tasks. The internal memory **802** may be volatile or non-volatile memory, and may also be secure and/or encrypted memory, or unsecure and/or unencrypted memory, or any combination thereof. The touch screen controller **804** and the processor **801** may also be coupled to a touch screen panel **812**, such as a resistive-sensing touch screen, capacitive-sensing touch screen, infrared sensing touch screen, etc. The computing device **800** may have one or more radio signal transceivers **808** (e.g., Peanut®, Bluetooth®, Zigbee®, Wi-Fi, RF, cellular, etc.) and antennae **810**, for sending and receiving, coupled to each other and/or to the processor **801**. The transceivers **808** and antennae **810** may be used with the above-mentioned circuitry to implement the various wireless transmission protocol stacks and interfaces. The computing device **800** may include a cellular network wireless modem chip **816** that enables communication via a cellular network, such as an eMBMS network, and is coupled to the processor. The computing device **800** may include a peripheral device connection interface **818** coupled to the processor **801**. The peripheral device connection interface **818** may be singularly configured to accept one type of connection, or multiply configured to accept various types of physical and communication connections, common or proprietary, such as USB, FireWire, Thunderbolt, or PCIe. The peripheral device connection interface **818** may also be coupled to a similarly configured peripheral device connection port (not shown). The computing device **800** may also include speakers **814** for providing audio outputs. The computing device **800** may also include a housing **820**, constructed of a plastic, metal, or a combination of materials, for containing all or some of the components discussed herein. The computing device **800** may include a power source **822** coupled to the processor **801**, such as a disposable or rechargeable battery. The rechargeable battery may also be coupled to the peripheral device connection port to receive a charging current from a source external to the computing device **800**.

[0114] Processors of computing devices suitable for use in various embodiments may be any programmable microprocessor, microcomputer or multiple processor chip or chips that can be configured by software instructions (applications) to perform a variety of functions, including the functions of the various embodiments described above. In the various devices, multiple processors may be provided, such as one processor dedicated to wireless communication functions and one processor dedicated to running other applications. Typically, software applications may be stored in internal memory before they are accessed and loaded into the processors. The processors may include internal memory sufficient to store the application software instructions. In many devices, the internal memory may be a volatile or nonvolatile memory, such as flash memory, or a mixture of both. For the purposes of this description, a general reference to memory refers to memory accessible by the processors including internal

memory or removable memory plugged into the various devices and memory within the processors.

[0115] Further, those of skill in the art will appreciate that the foregoing method descriptions and the process flow diagrams are provided merely as illustrative examples and are not intended to require or imply that the operations of the various embodiments must be performed in the order presented. As will be appreciated by one of skill in the art the order of operations in the foregoing embodiments may be performed in any order. Words such as "thereafter," "then," "next," etc. are not intended to limit the order of the operations; these words are simply used to guide the reader through the description of the methods. Further, any reference to claim elements in the singular, for example, using the articles "a," "an" or "the" is not to be construed as limiting the element to the singular.

[0116] The various illustrative logical blocks, modules, circuits, and algorithm operations described in connection with the embodiments disclosed herein may be implemented as electronic hardware, computer software, or combinations of both. To clearly illustrate this interchangeability of hardware and software, various illustrative components, blocks, modules, circuits, and operations have been described above generally in terms of their functionality. Whether such functionality is implemented as hardware or software depends upon the particular application and design constraints imposed on the overall system. Skilled artisans may implement the described functionality in varying ways for each particular application, but such implementation decisions should not be interpreted as causing a departure from the scope embodiments.

[0117] The hardware used to implement the various illustrative logics, logical blocks, modules, and circuits described in connection with the embodiments disclosed herein may be implemented or performed with a general purpose processor, a digital signal processor (DSP), an application specific integrated circuit (ASIC), a field programmable gate array (FPGA) or other programmable logic device, discrete gate or transistor logic, discrete hardware components, or any combination thereof designed to perform the functions described herein. A general-purpose processor may be a microprocessor, but, in the alternative, the processor may be any conventional processor, controller, microcontroller, or state machine A processor may also be implemented as a combination of computing devices, e.g., a combination of a DSP and a microprocessor, a plurality of microprocessors, one or more microprocessors in conjunction with a DSP core, or any other such configuration. Alternatively, some operations or methods may be performed by circuitry that is specific to a given function.

[0118] The functions in the various embodiments may be implemented in hardware, software, firmware, or any combination thereof. If implemented in software, the functions may be stored as one or more processor executable instructions or code on a non-transitory computer readable medium or non-transitory processor readable medium. The operations of a method or algorithm disclosed herein may be embodied in a processor-executable software module that may reside on a non-transitory computer-readable or processor-readable storage medium. Non-transitory computer-readable or processor-readable storage media may be any storage media that may be accessed by a computer or a processor. By way of example but not limitation, such non-transitory computer-readable or processor-readable media may include RAM, ROM, EEPROM, FLASH memory, CD-ROM or other optical disk storage, magnetic disk storage or other magnetic storage devices, or any other medium that may be used to store desired program code in the form of instructions or data structures and that may be accessed by a computer. Disk and disc, as used herein, includes compact disc (CD), laser disc, optical disc, digital versatile disc (DVD), floppy disk, and blu-ray disc where disks usually reproduce data magnetically, while discs reproduce data optically with lasers. Combinations of the above are also included within the scope of non-transitory computer-readable and processor-readable media. Additionally, the operations of a method or algorithm may reside as one or any combination or set of codes and/or instructions on a non-transitory processor-readable medium and/or computer-readable medium, which may be incorporated into a computer program product.

[0119] The preceding description of the disclosed embodiments is provided to enable any person skilled in the art to make or use the claims. Various modifications to these embodiments will be readily apparent to those skilled in the art, and the generic principles defined herein may be applied to other embodiments without departing from the scope of the claims. Thus, the present invention is not intended to be limited to the embodiments shown herein but is to be accorded the widest scope consistent with the following claims and the principles and novel features disclosed herein.

What is claimed is:

1. A method for calibrating a blood pressure measurement device, comprising:

determining, by an elevation sensor, an elevation of the blood pressure measurement device;

determining, by an arterial measurement sensor, distension of an artery;

determining, by a processor of the blood pressure measurement device, a pulse shape;

determining, by the processor, whether a change in distension of an artery and elevation of a measurement device occurred between two observation times;

determining, by the processor, whether a change in pulse rate has occurred between the two observation times in response to determining that a change in distension of an artery and elevation of a measurement device occurred between two observation times;

storing, in a memory, the pulse shape, distension, and elevation in response to determining that the pulse rate is constant;

determining, by the processor, a coefficient fitting an exponentially decaying function representing an exponential decay of a portion of a diastolic phase to diastolic parts of measured pulses; and

determining, by the processor, a calibration of the arterial measurement sensor based at least in part on the exponentially decaying function and an incremental variation between the two observation times.

2. The method of claim **1**, wherein determining, by the processor, a calibration of the arterial measurement sensor based at least in part on the exponentially decaying function and an incremental variation between the two observation times comprises determining an initial calibration of the arterial measurement sensor.

3. The method of claim **2**, wherein determining, by the processor, a calibration of the arterial measurement sensor based at least in part on the exponentially decaying function

and an incremental variation between the two observation times is performed prior to each measurement session.

4. The method of claim **1**, wherein determining distension of an artery comprises measurement one or more of bioimpedance, impedance plethysmography, photoplethsmography, ultrasound, and surface pressure sensing.

5. A blood pressure measurement device comprising:

a non-interfering arterial measurement sensor configured to measure a first change in distension of an artery at a measurement location on a limb of a subject without interference to an arterial pressure at the measurement location during a series of pulses; and

a processor in communication with the non-interfering arterial measurement sensor, wherein the processor is configured with processor executable instructions to perform operations to:

determine an elevation of the blood pressure measurement device;

determine distension of an artery;

determine a pulse shape;

determine whether a change in distension of an artery and elevation of a measurement device occurred between two observation times;

determine whether a change in pulse rate has occurred between the two observation times in response to determining that a change in distension of an artery and elevation of a measurement device occurred between two observation times;

store the pulse shape, distension, and elevation in response to determining that the pulse rate is constant;

determine a coefficient fitting an exponentially decaying function representing an exponential decay of a portion of a diastolic phase to diastolic parts of measured pulses; and

determine a calibration of the arterial measurement sensor based at least in part on the exponentially decaying function and an incremental variation between the two observation times.

6. The blood pressure measurement device of claim **5**, wherein determine a calibration of the arterial measurement sensor based at least in part on the exponentially decaying function and an incremental variation between the two observation times comprises determining an initial calibration of the arterial measurement sensor.

7. The blood pressure measurement device of claim **6**, wherein determine a calibration of the arterial measurement sensor based at least in part on the exponentially decaying function and an incremental variation between the two observation times is performed prior to each measurement session.

8. The blood pressure measurement device of claim **5**, wherein distension of the artery is measured by one or more of bioimpedance, impedance plethysmography, photoplethsmography, ultrasound, and surface pressure sensing.

9. A non-transitory processor-readable storage medium having stored thereon processor-executable instructions to cause a processor to perform operations comprising:

determining an elevation of the blood pressure measurement device;

determining distension of an artery by an arterial measurement sensor;

determining a pulse shape;

determining whether a change in distension of an artery and elevation of a measurement device occurred between two observation times;

determining whether a change in pulse rate has occurred between the two observation times in response to determining that a change in distension of an artery and elevation of a measurement device occurred between two observation times;

storing the pulse shape, distension, and elevation in response to determining that the pulse rate is constant;

determining a coefficient fitting an exponentially decaying function representing an exponential decay of a portion of a diastolic phase to diastolic parts of measured pulses; and

determining a calibration of the arterial measurement sensor based at least in part on the exponentially decaying function and an incremental variation between the two observation times.

10. The non-transitory processor-readable storage medium of claim **9**, wherein the stored processor readable instructions are configured to cause a processor to perform operations such that determining a calibration of the arterial measurement sensor based at least in part on the exponentially decaying function and an incremental variation between the two observation times comprises determining an initial calibration of the arterial measurement sensor.

11. The non-transitory processor-readable storage medium of claim **10**, wherein the stored processor readable instructions are configured to cause a processor to perform operations such that determining a calibration of the arterial measurement sensor based at least in part on the exponentially decaying function and an incremental variation between the two observation times is performed prior to each measurement session.

12. The non-transitory processor-readable storage medium of claim **9**, wherein the stored processor readable instructions are configured to cause a processor to perform operations such that distension of the artery is measured by one or more of bioimpedance, impedance plethysmography, photoplethsmography, ultrasound, and surface pressure sensing.

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