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(54) **CONTINUOUS NON-INVASIVE BLOOD PRESSURE MONITOR**

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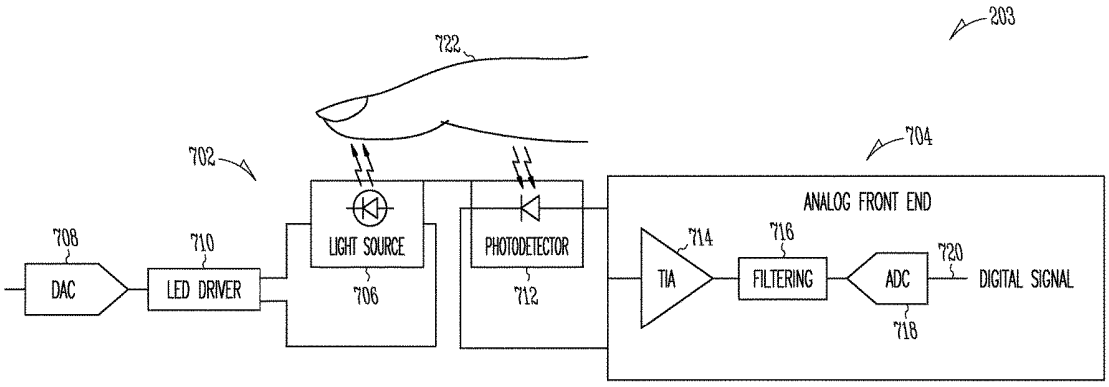
(57) **ABSTRACT**

A blood pressure monitoring system is provided comprising: an impedance monitoring circuit configured to detect an occurrence of a blood pulse wave ejection from the heart; a blood pulse detection circuit detect to an arrival of the blood pulse wave at a body site peripheral to the heart; and a processor configured to compute pulse transit time (PTT) based at least in part upon a difference in a time of occurrence of the blood pulse wave ejection from the heart first signal and a time of occurrence of the arrival of the blood pulse wave at a body site peripheral to the heart.



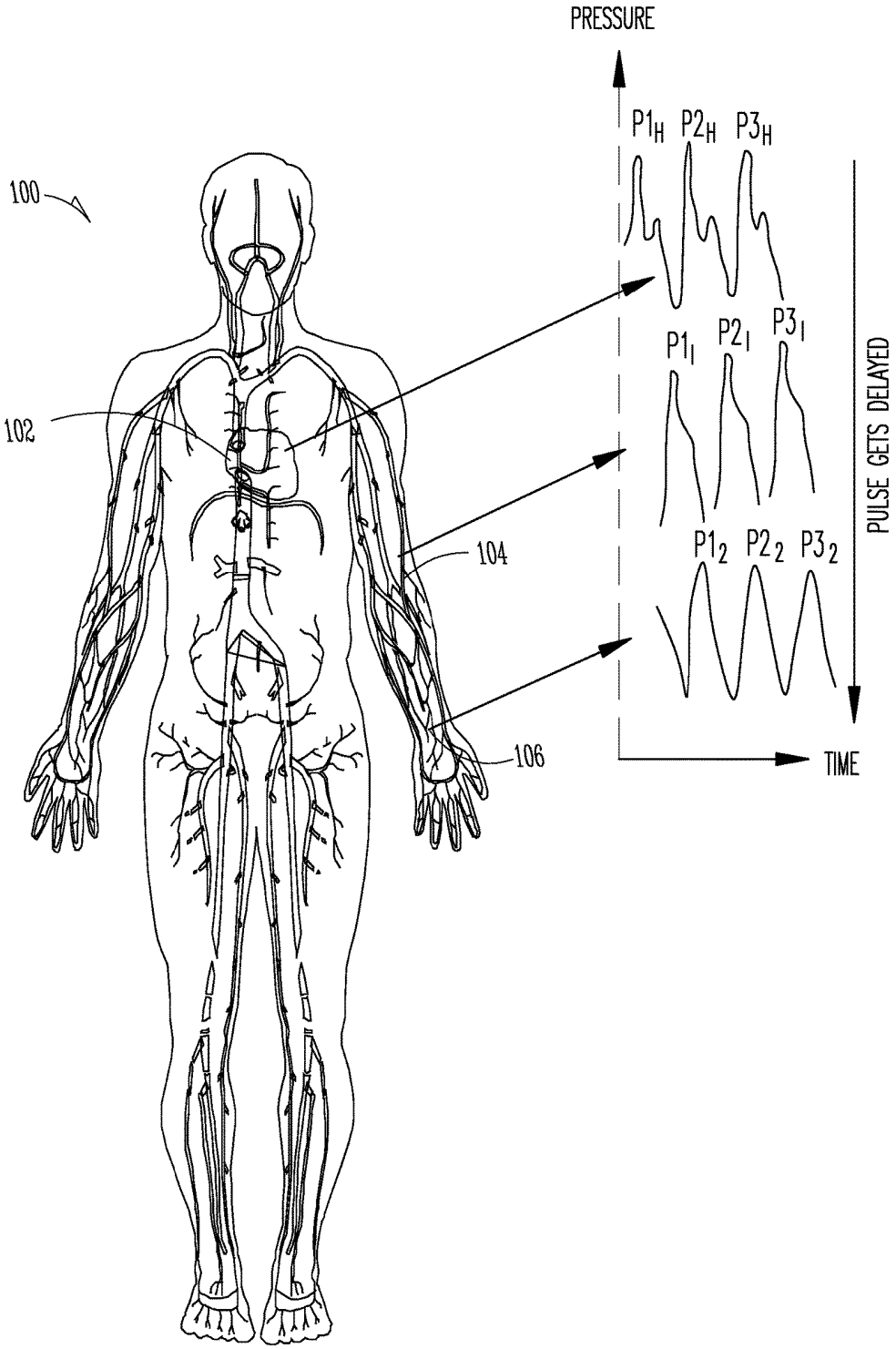

PRESSURE
$P1_H$ $P2_H$ $P3_H$
$P1_I$ $P2_I$ $P3_I$
$P1_2$ $P2_2$ $P3_2$
PULSE GETS DELAYED
TIME
100
102
104
106

Fig. 1

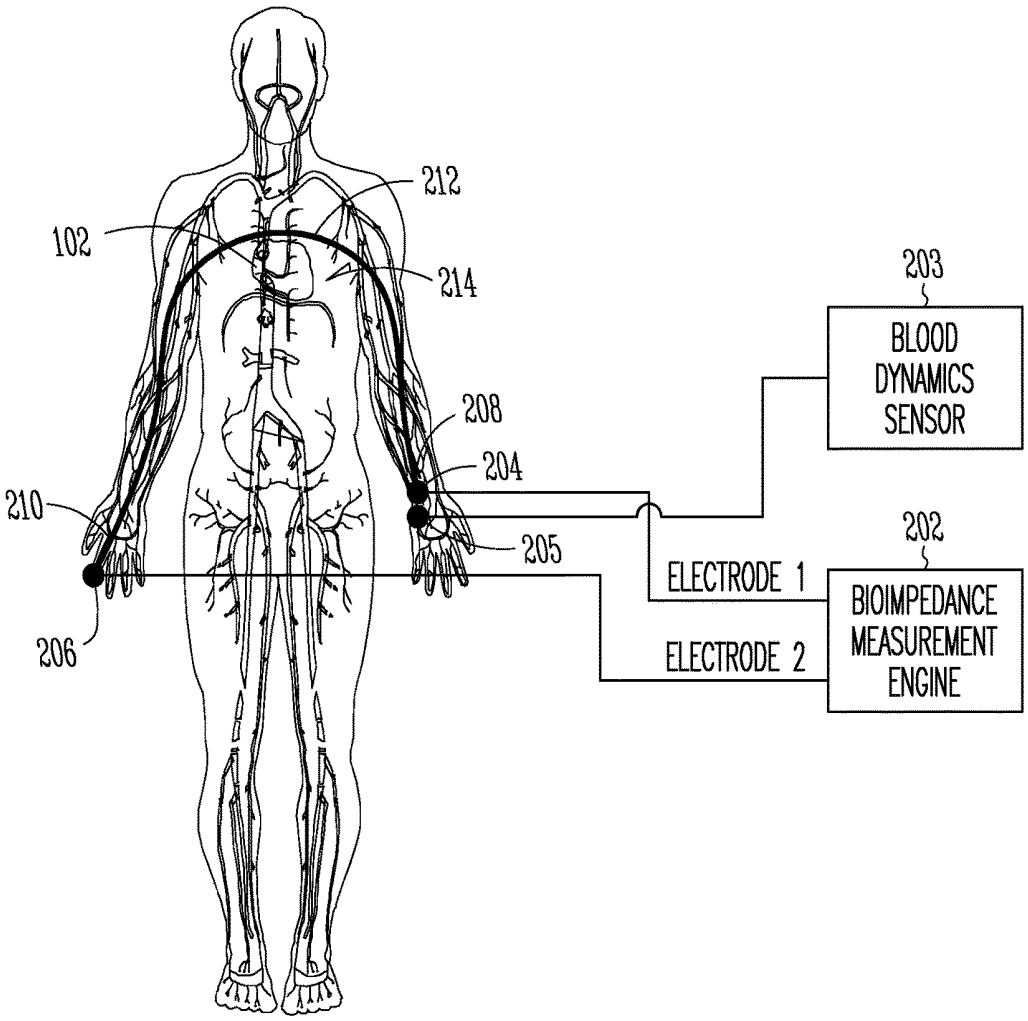

212
102
214
203
BLOOD
DYNAMICS
SENSOR
208
204
210
205
202
ELECTRODE 1
BIOIMPEDANCE
MEASUREMENT
ENGINE
ELECTRODE 2
206

Fig.2

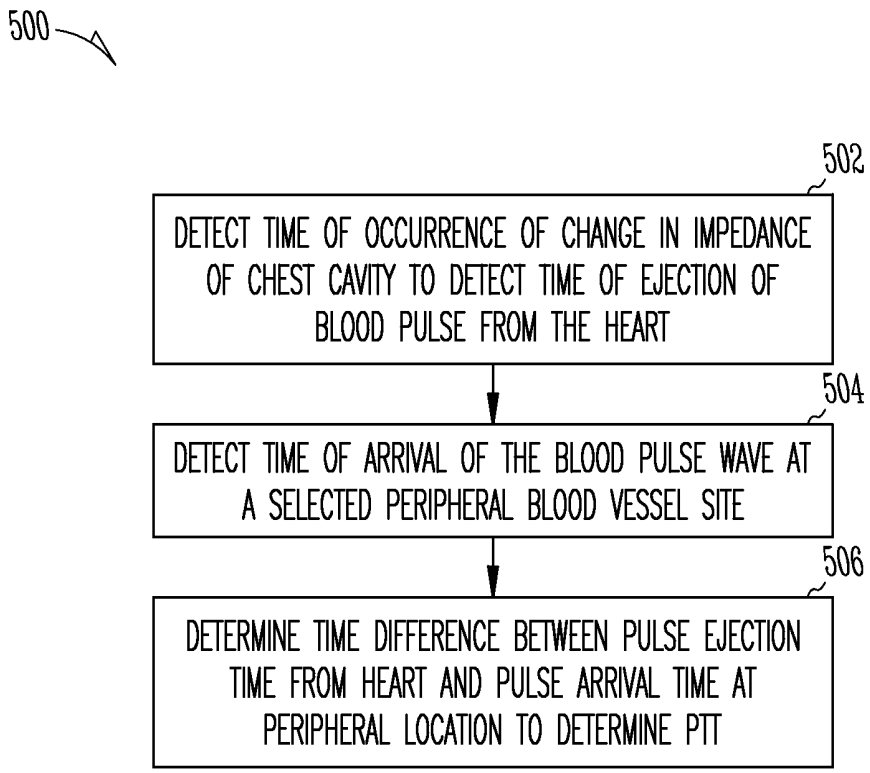

500
502
DETECT TIME OF OCCURRENCE OF CHANGE IN IMPEDANCE OF CHEST CAVITY TO DETECT TIME OF EJECTION OF BLOOD PULSE FROM THE HEART
504
DETECT TIME OF ARRIVAL OF THE BLOOD PULSE WAVE AT A SELECTED PERIPHERAL BLOOD VESSEL SITE
506
DETERMINE TIME DIFFERENCE BETWEEN PULSE EJECTION TIME FROM HEART AND PULSE ARRIVAL TIME AT PERIPHERAL LOCATION TO DETERMINE PTT

Fig. 3

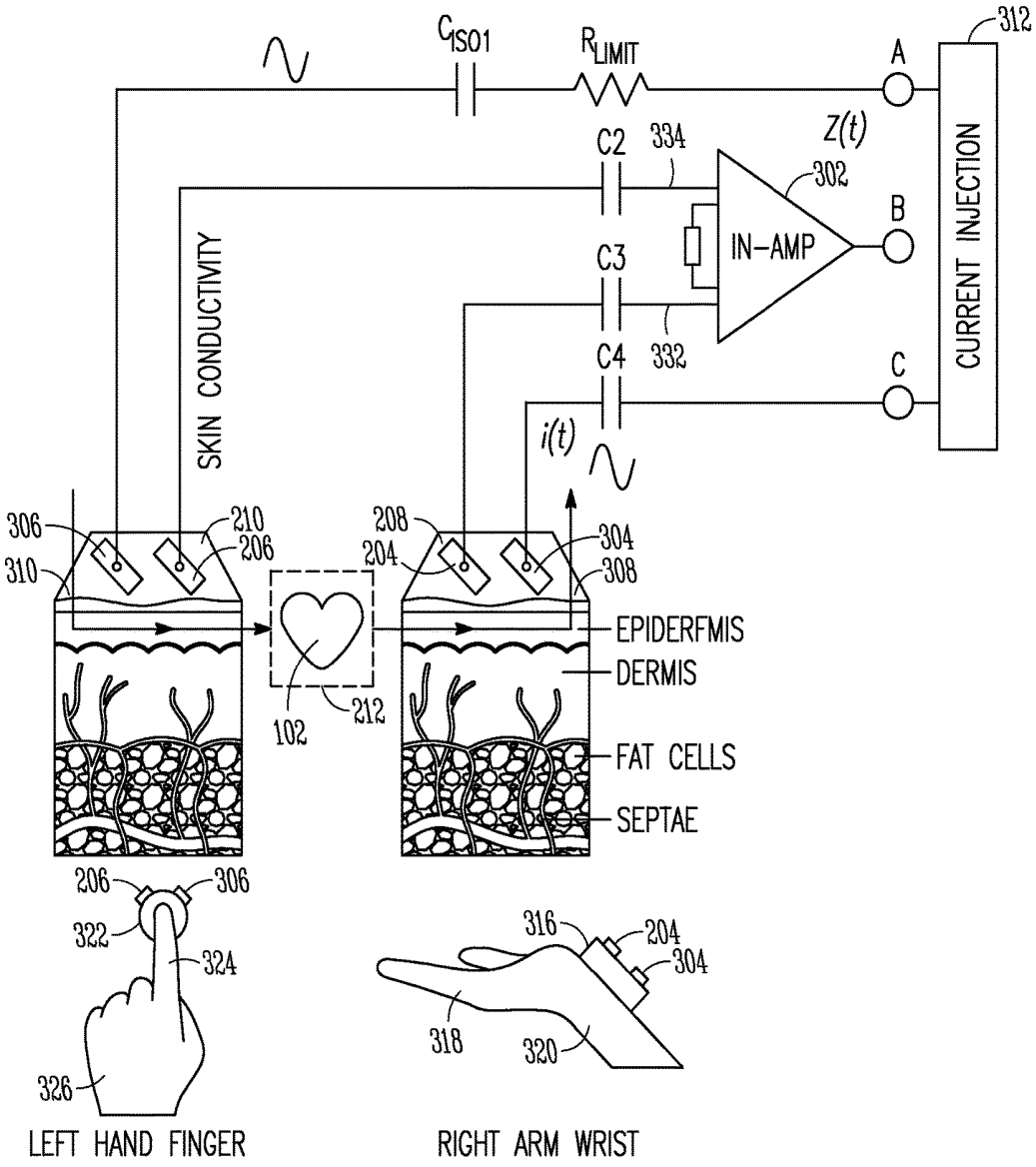

C_{ISO1}
R_{LIMIT}
312
A
Z(t)
C2
334
302
B
IN-AMP
C3
C4
332
C
CURRENT INJECTION
SKIN CONDUCTIVITY
i(t)
306
310
210
206
208
204
304
308
EPIDERFMIS
DERMIS
FAT CELLS
SEPTAE
102
212
206
306
322
324
326
316
204
304
318
320
LEFT HAND FINGER
RIGHT ARM WRIST

Fig. 4

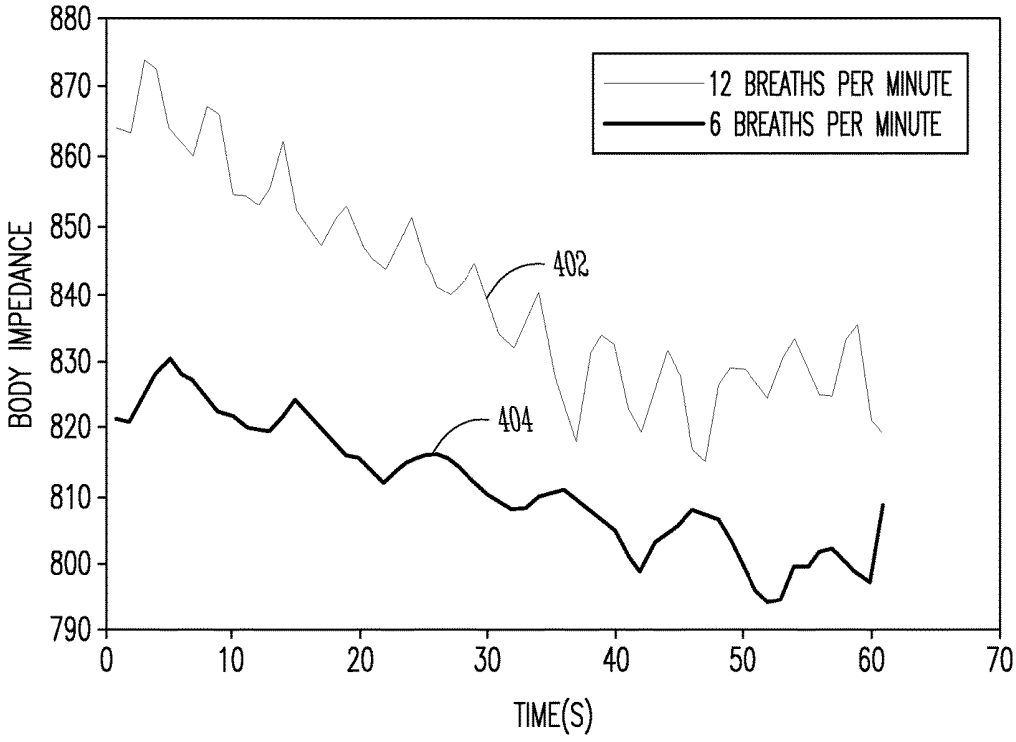

880
870
860
850
840
830
820
810
800
790
BODY IMPEDANCE
0
10
20
30
40
50
60
70
TIME(S)
12 BREATHS PER MINUTE
6 BREATHS PER MINUTE
402
404

Fig. 5

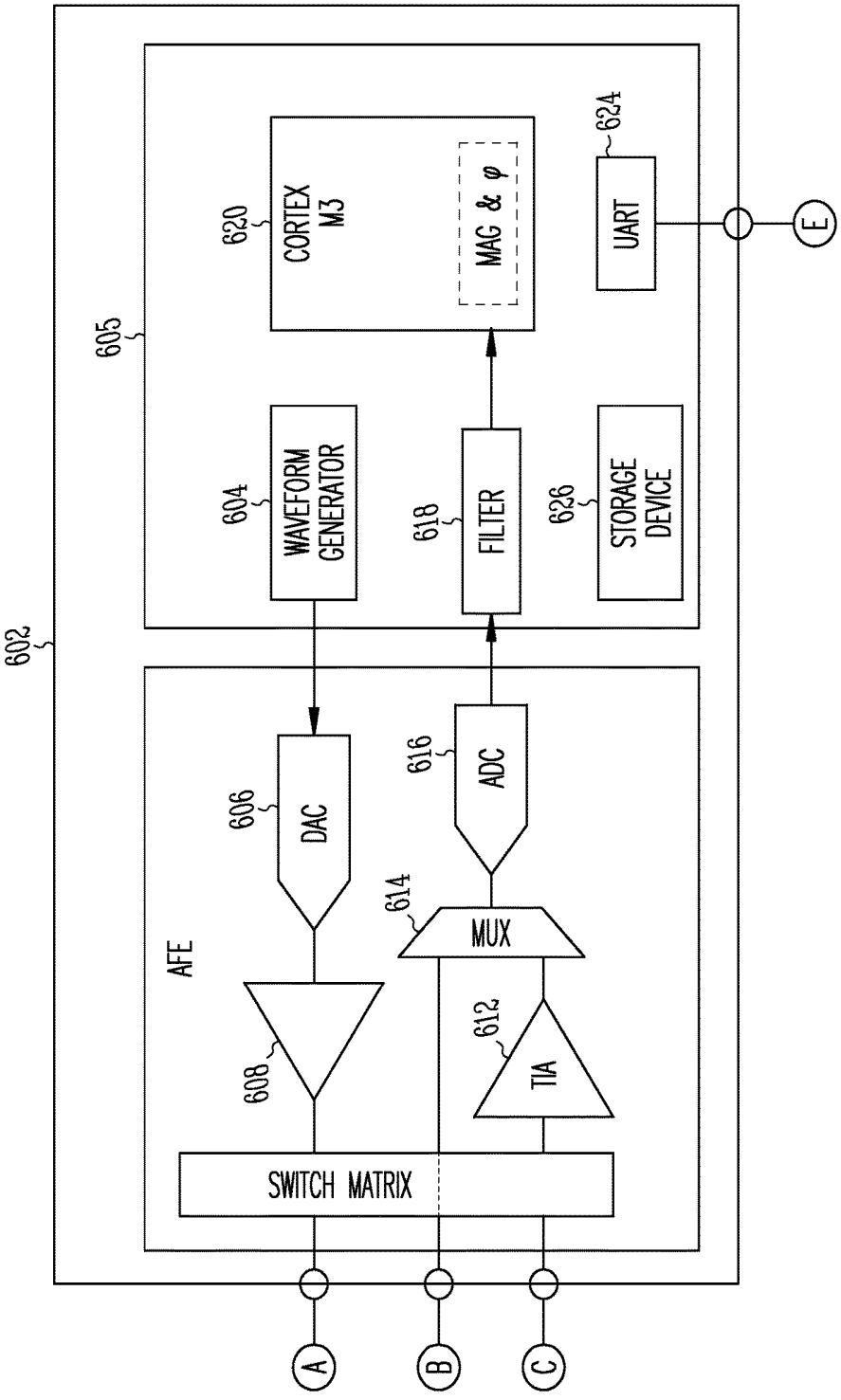

602
605
620
CORTEX M3
MAG & φ
624
UART
E
604
WAVEFORM GENERATOR
618
FILTER
626
STORAGE DEVICE
AFE
606
DAC
616
ADC
614
MUX
608
612
TIA
SWITCH MATRIX
A
B
C

Fig. 6

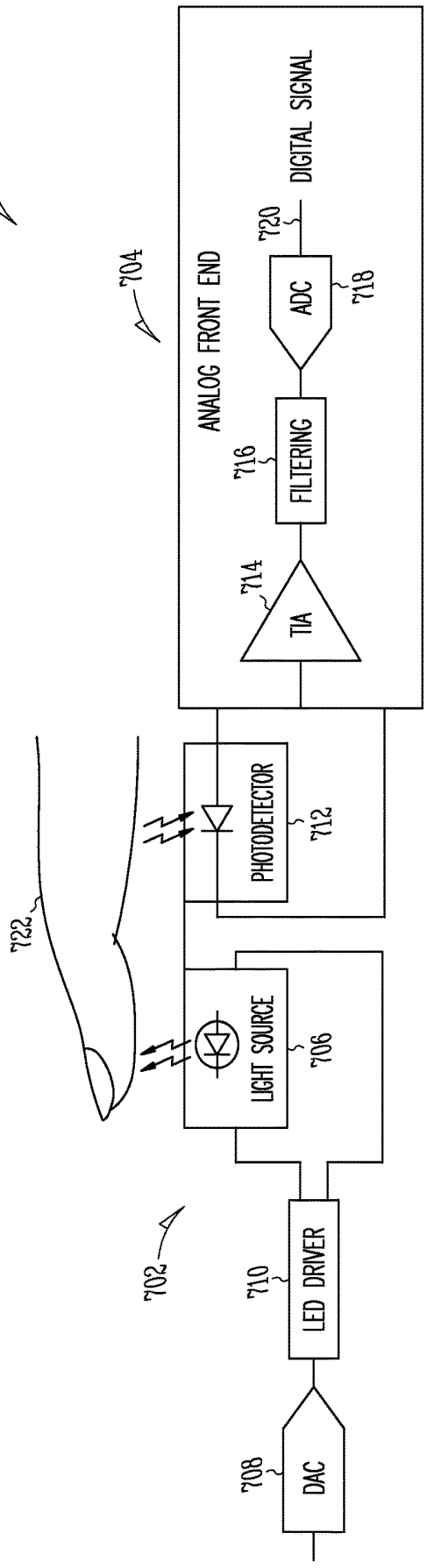

203
704
ANALOG FRONT END
DIGITAL SIGNAL
720
ADC
718
716
FILTERING
714
TIA
PHOTODETECTOR
712
722
LIGHT SOURCE
706
702
710
LED DRIVER
708
DAC

Fig. 7

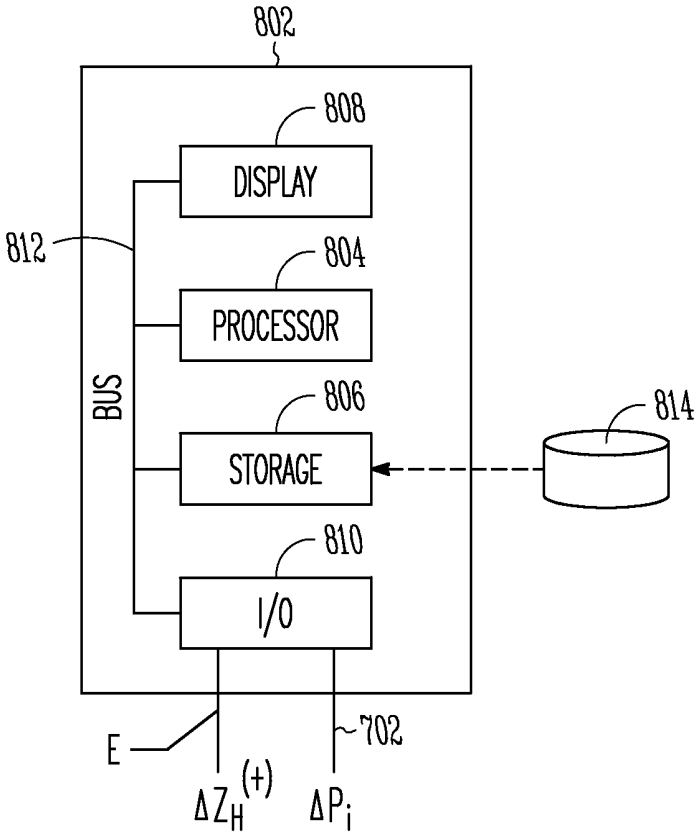

802
808
DISPLAY
812
804
PROCESSOR
BUS
806
814
STORAGE
810
I/O
E
702
ΔZH(+)
ΔPi

Fig. 8

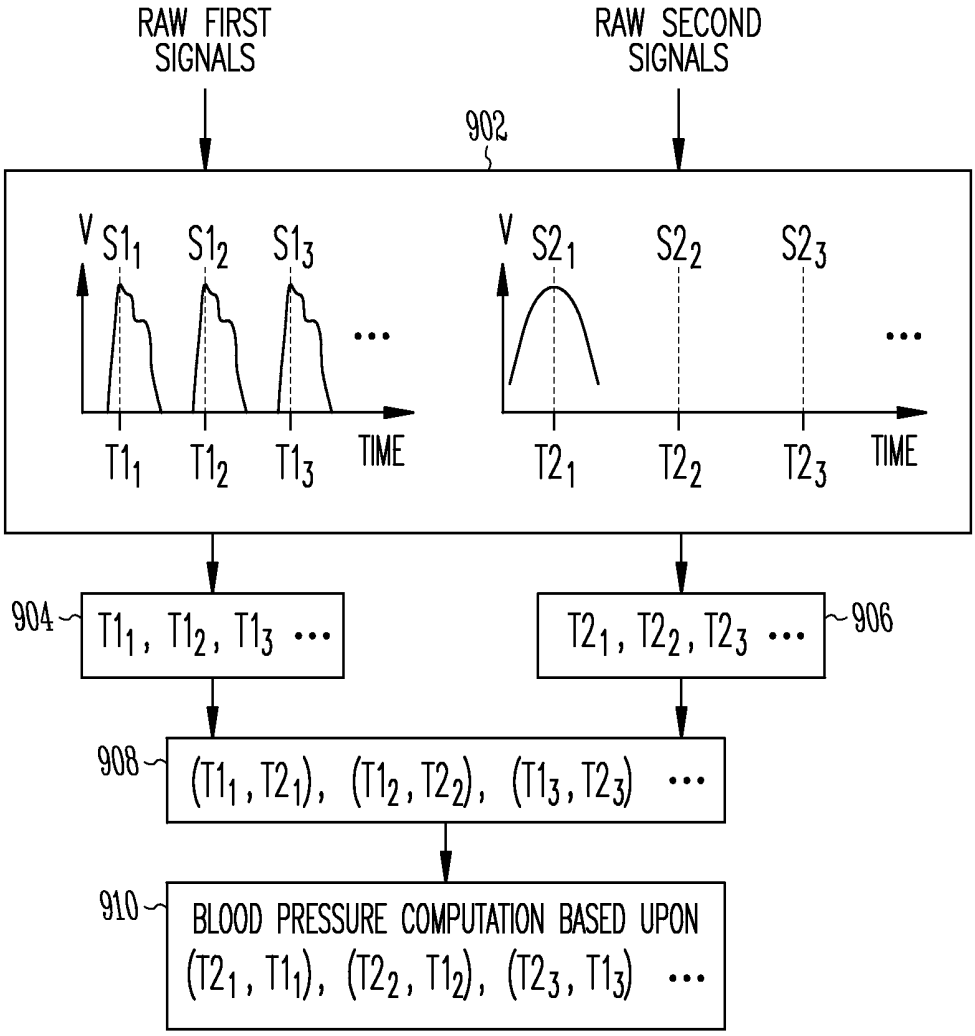

RAW FIRST SIGNALS
RAW SECOND SIGNALS
902
V
S1 1
S1 2
S1 3
T1 1
T1 2
T1 3
TIME
V
S2 1
S2 2
S2 3
T2 1
T2 2
T2 3
TIME
904
T1 1, T1 2, T1 3 ...
T2 1, T2 2, T2 3 ...
906
908
(T1 1, T2 1), (T1 2, T2 2), (T1 3, T2 3) ...
910
BLOOD PRESSURE COMPUTATION BASED UPON
(T2 1, T1 1), (T2 2, T1 2), (T2 3, T1 3) ...

Fig. 9

CONTINUOUS NON-INVASIVE BLOOD PRESSURE MONITOR

BACKGROUND

[0001] Blood pressure (BP) is the pressure exerted by the circulating blood on the blood vessel walls of the circulatory system. Each beat of the heart pumps a blood pressure pulse wave out from the heart into the blood vessels. The blood pressure pulse waves propagate throughout the circulatory system causing pulses of blood to course through the blood vessels and to reach peripheral parts of the body. Each blood pressure pulse wave exerts a pressure wave upon the blood vessel walls as it surges through. The pulse wave velocity (PWV) is the speed of a blood pressure pulse propagating along the blood vessel walls. The PWV can be calculated based upon pulse transit time (PTT), which is the time required for a blood pressure pulse wave to propagate on the same cardiac cycle from a blood vessel site closer to the heart to a blood vessel site more distant from the heart. The relationship between PWV and PTT can be expressed as follows,

$$PWV = \frac{x}{PTT}, \tag{1}$$

The parameter x represents a distance between two blood vessel sites between which a blood pressure pulse wave propagates, such as a distance between the heart and a specified blood vessel site that is peripheral to the heart. PTT has been shown to be quasi-linear to low blood pressure values, but to increase exponentially at higher pressures.

[0002] The velocity of a longitudinal blood pressure wave is related to arterial pressure and the intrinsic elastic properties of the arterial wall. The Moens-Korteweg equation expresses the relationship as follows,

$$PWV = \sqrt{\frac{gEh}{\rho d}} \tag{2}$$

The parameter g is the acceleration of gravity, E is the elastic modulus of the blood vessel walls, h is the thickness of the vessel walls, p is the density of blood, and d is the blood vessel diameter. See, Gesche, H. et al., Continuous blood pressure measurement by using the pulse transit time: comparison to a cuff-based method, *Eur. J. Appl. Physiol.*, April 2011.

[0003] The elastic modulus of the blood vessels has an exponential relationship to BP:

$$E=E_0e^{\gamma \cdot BP} \tag{3}$$

The parameter E0 is the elastic modulus at zero pressure and γ is a coefficient of vascular characterization.

[0004] The following relationship between change in blood pressure and change in PTT has been determined based upon the above relationships:

$$dBP = \frac{2}{\gamma T} dPTT \tag{4}$$

This relationship signifies that if the blood vessel elasticity remains unchanged, then changes in BP are proportional to changes in PTT. Thus the changes in BP can be identified by identifying changes in PTT. See, Sheng, H. et al., A wireless wearable body sensor network for continuous noninvasive blood pressure monitoring using multiple parameters, *Recent Researches in Circuits, Systems, Communications and Computers*, ISBN: 978-1-61804-056-5, pages 308-314, at **310**.

[0005] Various techniques have been used to measure PTT. For example, Chen et al. Continuous and noninvasive blood pressure measurement: a novel modeling methodology of the relationship between blood pressure and pulse wave velocity, *Ann. Biomed. Eng*, Vol. 40, No. 4, April 2012 pages 871-882, teach photoplethysmography (PPG) measurements at ear and toe to determine PTT. Myint, C Z. et al., Blood Pressure Measurement from Photo-plethysmography to Pulse Transit Time, 2014 *IEEE Conference on Biomedical Engineering and Sciences,* 8-10 Dec. 2014, Miri, Sarawak, Malaysia, pages 496-501, teach PPG measurements at wrist and finger to determine PTT. Also, for example, Sheng et al. teach a combination of an ECG signal and a PPG signal to determine PTT.

[0006] Moreover, various mathematical relationships have been found between BP and PTT and PWV. For example, Chen et al. proposed the following relationship,

$$BP = be^{-\frac{k}{PWV}} \tag{5}$$

The parameters k and b are calibration parameters that depend on the age and gender of the user.

[0007] Also, for example, Shriram et al. proposed the following relationship,

$$BP = \frac{1}{\alpha}\left[\ln\left(\frac{x^2 rBP}{E_0 h}\right) - 2\ln(PTT)\right] \tag{6}$$

The parameter r is the inner radius of the artery, and the other parameters of equation (6) are the same as corresponding parameters defined above. See, Shriram, R. et al., Continuous cuffless BP monitoring based on PTT, *Bioinformatics and Biomedical Technology* (*ICBBT*), 2010 *International Conference*, Chengdu, China, April 2010.

SUMMARY

[0008] In one aspect, a blood pressure monitoring system is provided that includes an impedance measurement circuit configured to detect a change in impedance indicative of an occurrence of a blood pulse wave ejection from the heart. The system includes a blood pulse detection sensor to detect arrival of the blood pulse wave at a body site peripheral to the heart. A non-transitory computer readable storage device is provided that includes computer program code to configure a processor to compute pulse transit time (PTT) based at least in part upon a difference in a time of occurrence of the blood pulse wave ejection from the heart first signal and a time of occurrence of the arrival of the blood pulse wave at a body site peripheral to the heart.

[0009] In another aspect, a method is provided to monitor blood pressure. The method includes monitoring electrical

impedance at first and second body skin tissue sites and monitoring blood pressure at a third skin tissue site. A PTT is determined based at least in part upon a difference in a time of occurrence of a monitored change in impedance at the first skin tissue site and a monitored change in blood pressure at the second skin tissue site.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] FIG. **1** is an illustrative drawing representing a human circulatory system and showing illustrative blood pressure pulse waveforms that propagate from the heart throughout the circulatory system.

[0011] FIG. **2** is an illustrative an impedance measurement system and a blood pulse detection sensor operatively coupled to detect blood pulses in the human circulatory system, in accordance with some embodiments.

[0012] FIG. **3** is an illustrative flow diagram representing a process to measure PTT in accordance with some embodiments.

[0013] FIG. **4** is an illustrative drawing showing certain details of the impedance measurement system of FIG. **2** in accordance with some embodiments.

[0014] FIG. **5** is an illustrative graph showing an experimental result of impedance measurement across the chest cavity versus time for two different respiration rates.

[0015] FIG. **6** is an illustrative block diagram showing certain other details of the impedance measurement system of FIG. **2** in accordance with some embodiments.

[0016] FIG. **7** is an illustrative schematic block diagram showing certain details of a blood dynamics sensor in accordance with some embodiments.

[0017] FIG. **8** is an illustrative drawing showing a computer system coupled to process PTT related information in accordance with some embodiments.

[0018] FIG. **9** is an illustrative flow diagram representing configuration of the processor of FIG. **8** to determine PTT values in accordance with some embodiments.

DESCRIPTION OF EMBODIMENTS

[0019] The following description is presented to enable any person skilled in the art to create and use a continuous non-invasive blood pressure monitor. Various modifications to the embodiments will be readily apparent to those skilled in the art, and the generic principles defined herein may be applied to other embodiments and applications without departing from the spirit and scope of the invention. Moreover, in the following description, numerous details are set forth for the purpose of explanation. However, one of ordinary skill in the art will realize that the invention might be practiced without the use of these specific details. In other instances, well-known processes are shown in block diagram form in order not to obscure the description of the invention with unnecessary detail. Identical reference numerals may be used to represent different views of the same or similar item in different drawings. Flow diagrams in drawings referenced below are used to represent processes. Thus, the present invention is not intended to be limited to the embodiments shown, but is to be accorded the widest scope consistent with the principles and features disclosed herein.

[0020] FIG. **1** is an illustrative drawing representing a human circulatory system **100** showing illustrative blood pressure pulse waveforms that propagate from the heart **102** throughout the circulatory system. A sequence of blood pulse waveforms P**1**, P**2**, P**3**, each characterized by a an increase in blood pressure ΔP_i upon the arrival of a blood pressure wave, are shown as they propagate from the heart **102** to a first blood vessel site **104** and then to a second blood vessel site **106**. A first pulse P**1** is ejected followed in sequence by a second pulse P**2** and a third pulse P**3**. The waveform $P1_H$ represents the first pulse at the heart site **102**. The waveform $P1_1$ represents the first pulse at the first peripheral blood vessel site **104**. The waveform $P1_2$ represents the first pulse at the second peripheral blood vessel site **106**, which is more distant from the heart **102** than is the first site **104**. Similarly, waveforms $P2_H$, $P2_1$ and $P2_2$ represent the second pulse at the heart and at the first and second blood vessel sites, respectively. Likewise, the waveforms $P3_H$, $P3_1$ and $P3_2$ represent the third pulse at the heart and at the first and second blood vessel sites, respectively. It can be seen that the blood pressure pulse waveforms change as they propagate farther from the heart. The change in the pressure pulses is represented by the changes in the shape of the curves representing the pulses at each site.

[0021] FIG. **2** is an illustrative an impedance measurement circuit **202** and a blood pulse detection sensor **203** operatively coupled to detect occurrence of blood pulses in the human circulatory system **100**, in accordance with some embodiments. A change in blood dynamics at a selected location within the circulatory system caused by an arrival of a blood pulse at the location in the circulatory system can involve one or more of a change in blood pressure, a change in blood volume and a change in blood flow, for example, at the selected location The impedance measurement circuit **202** includes first and second electrodes **204**, **206** that are suited for monitoring physiological electrical signals produced at body skin tissue sites. In accordance with some embodiments, the first and second electrodes **204**, **206** include wet contact, dry contact or noncontactelectrodes. See, Yu Mike Chi et al. Dry-Contact and Noncontact Biopotential Electrodes: Methodological Review, IEEE Reviews in Biomedical Engineering, Vol. 3, pages 106-119, 2010 for a review of the various types of electrodes for biopotential signals. The impedance measurement circuit **202** is used to measure impedance of an electrical signal path between its electrodes. When the electrodes **204**, **206** are to monitor physiological electrical signals at different sites on the human body, an impedance measurement system **202** can measure impedance of an electrical signal path comprising body tissue disposed between the different sites. In the illustrative drawing of FIG. **2**, the first electrode **204** is electrically coupled to monitor a first site **208** disposed at the left wrist, and the second electrode **206** is electrically coupled to monitor a second site **210** at a finger of the right hand. It can be seen that a body tissue electrical path **212** between the illustrative first site **208** and the illustrative second site **210** crosses the chest cavity **214**, which contains the heart **212**. Therefore, with the first and second electrodes **204**, **206** electrically coupled to monitor the first and second skin sites **208**, **210**, the impedance measurement circuit **202** can detect changes in impedance of the chest cavity and the heart. The pulse detection sensor **203** detects arrival of a blood pulse wave at a selected site **205** on the body peripheral to the heart **102**.

[0022] FIG. **3** is an illustrative flow diagram representing a process to measure PTT in accordance with some embodiments. In step **502**, a time of occurrence of a change of

impedance across the chest cavity **214** is detected to detect the time of ejection of a blood pulse wave from the heart. In some embodiments, the impedance measurement circuit **202** performs this step by monitoring a voltage drop across the chest cavity **214** while conducting a current across the chest cavity, through body tissue. Certain changes in the voltage drop across the chest cavity are indicative of ejection of a blood pulse wave from the heart. In step **504**, the time of arrival of the blood pulse wave is detected at a selected peripheral blood vessel site **205**. In step **506**, PTT is calculated based upon a time difference between the time of blood pulse wave ejection from the heart and the time arrival time of the blood pulse wave at the selected peripheral site **205**.

[0023] An advantage of using bioimpedance monitoring rather than an ECG monitoring to determine a time of ejection of a blood pulse from the heart is that time of occurrence of ECG signal components such as R-wave and Q-wave often do not coincide precisely with time of occurrence of blood pulse ejection from the heart and the relationship can vary. The difference between the two time points (ECG and blood ejection from the heart) is often referred to as the pre-ejection period. The use of bioimpedance monitoring advantageously does not depend upon identification of ECG waveform components. Rather, bioimpedance monitoring more directly detects time of occurrence of blood pulse ejection based upon changes in impedance that correspond directly to changes in physical shapes of anatomical structures in the course of blood pulse ejection from the heart.

[0024] Referring again to FIG. **1** and to waveforms P**1**, P**2** and P**3**, measurement of PTT involves detecting the arrival time of a pulse at at least two different blood vessel locations that are spaced apart from each other at different distances from the heart **102** within the circulatory system **100**. Values measured for PTT may vary from one pulse to the next. Assume, for example, that the first pulse $P1_H$ is ejected from the heart at time t_1, and that $P1_1$ arrives at the first blood vessel site **104** at time $t_1+\Delta1_{t1}$, and that $P1_2$ arrives at the second blood vessel site **106** at time $t_1+\Delta2_{t1}$. Then, for the first pulse, the PTT between the occurrence of Phi at the heart **102** and the occurrence of $P1_1$ at the first blood vessel site **104** is $\Delta1_{t1}$, the PTT between the occurrence of $P1_H$ at the heart **102** and the occurrence of $P1_2$ at the second blood vessel site **104** is $t_1+\Delta2_{t1}$, and the PTT between the occurrence of $P1_1$ at the first blood vessel site **104** and the occurrence of $P1_2$ at the second blood vessel site **106** is $\Delta2_{t1}-\Delta1_{t1}$. Similarly, assuming that the second pulse $P2_H$ is ejected from the heart at time t_2, and that $P2_1$ arrives at the first blood vessel site **104** at time $t_2+\Delta1_{t2}$, and that $P2_2$ arrives at the second blood vessel site **106** at time $t_2+\Delta1_{t2}$. Then, for the second pulse, the PTT between the occurrence of $P2_H$ at the heart **102** and the occurrence of $P2_2$ at the first blood vessel site **104** is $\Delta1_{t2}$, the PTT between the occurrence of $P2_2$ at the heart **102** and the occurrence of $P2_2$ at the second blood vessel site **104** is $t_2+\Delta1_{t2}$, and the PTT between the occurrence of $P2_1$ at the first blood vessel site **104** and the occurrence of $P2_2$ at the second blood vessel site **106** is $\Delta2_{t2}-\Delta1_{t2}$. Likewise, assuming that the third pulse $P3_H$ is ejected from the heart at time t_3, and that $P3_1$ arrives at the first blood vessel site **104** at time $t_3+\Delta1_{t3}$, and that $P3_2$ arrives at the second blood vessel site **106** at time $t_3+\Delta1_{t3}$. Then, for the third pulse, the PTT between the occurrence of $P3_H$ at the heart **102** and the occurrence of $P3_1$ at the first blood vessel site **104** is $\Delta1_{t3}$, the PTT between the occurrence of $P3_H$ at the heart **102** and the occurrence of $P3_2$ at the second blood vessel site **104** is $t_3+\Delta1_{t3}$, and the PTT between the occurrence of $P3_1$ at the first blood vessel site **104** and the occurrence of $P3_2$ at the second blood vessel site **106** is $\Delta2_{t3}-\Delta1_{t3}$.

[0025] In accordance with some embodiments, the impedance measurement system **102** can be used to make a first PTT measurement that detects the time of ejection of a blood pulse wave from the heart, and the pulse detection sensor **203** makes a second PTT measurement that detects time of arrival of the same blood pulse wave at a peripheral blood vessel site. Thus, continuing with the above example, for the first pulse, the first PTT would be $\Delta1_{t1}$, if the first blood vessel site **104** is used for the second PTT measurement and would be $\Delta2_{t1}$, if the second blood vessel site **106** is used for the second PTT measurement, for example. Similarly, for the second pulse, the second PTT would be $\Delta1_{t2}$, if the first blood vessel site **104** is used for the second PTT measurement and would be $\Delta1_{t2}$, if the second blood vessel site **106** is used for the second PTT measurement. Likewise, for the third pulse, the second PTT would be $\Delta1_{t3}$ or $\Delta1_{t3}$, depending upon the first or second blood vessel site **104** or **106** is used.

[0026] Each waveform represents a heartbeat cycle in which the heart **102** pumps oxygenated blood to the body and deoxygenated blood to the lungs. In a normal healthy person, the resting heartbeat rate is about seventy-two beats per minute. The heart **102** rests momentarily between beats. The heart includes a right atrium in the upper chamber of the right side of the heart. The blood that is returned to the right atrium is deoxygenated (poor in oxygen) and is passed into the right ventricle to be pumped through the pulmonary artery to the lungs for re-oxygenation and removal of carbon dioxide. The heart includes a left atrium that receives newly oxygenated blood from the lungs as well as the pulmonary vein which is passed into the strong left ventricle to be pumped through the aorta to the different organs of the body. The shape and blood fluid content of the heart **102** changes during a heartbeat as the heart pumps blood through its four chambers. The shape and blood fluid content of the heart **102** during a heartbeat is different from its shape and blood fluid content while at rest between beats. The first and second electrodes **202**, **204** are disposed to monitor physiological electrical signals at first and second sites **208**, **210** on a person's skin such that electrical impedance of an electrical path that includes body tissue disposed between them is different during occurrence of a heartbeat than it is between heartbeats. In accordance with some embodiments, a blood pulse ejection from the heart is defined as an ejection from the left ventricle to the aorta/body. However, other alternative pulse ejection time points can be used for various reasons such as, for example, simplicity or better signal quality.

[0027] FIG. **4** is an illustrative drawing showing certain details of the impedance sensor circuit **202** of FIG. **2**, in accordance with some embodiments. The impedance measurement circuit **202** includes voltage signal measurement circuit **302** and a current injection circuit **303**. The voltage signal measurement circuit **302** produces an electrical signal that represents voltage drop across the first and second electrodes **204**/**304**, which represents voltage drop across a body tissue circuit path **212** comprising human body tissue disposed between a first skin surface site **208**/**308** that is monitored using the first electrode **206**/**306** and the second

skin surface site **310** that is monitored using the second electrode **208/308**. The current injection circuit **303** includes a third electrode **304** suited monitoring a third skin site **308** and includes a fourth electrode suited for monitoring a fourth skin site. The current injection circuit **303** is operable to inject current flow through the body tissue circuit path **212**, which is disposed between the third and fourth electrodes **308**, **310**.

[0028] The third and fourth electrodes **304**, **306** are disposed to physiologically monitor third and fourth body tissue sites **308**, **310** on the skin surface so as to define an electrical path between them that is substantially the same as the body tissue electrical path **212** between the first and second electrodes **204**, **206**. In accordance with some embodiments, the first and third electrodes **204**, **304** are disposed to physiologically monitor tissue sites **208**, **308** that are close enough together and the second and fourth electrodes **206**, **306** are disposed to physiologically monitor tissue sites **210**, **310** that also are close enough together, such that a voltage difference between the first and second electrodes **204**, **206** is indicative of an impedance of the body tissue within the body tissue circuit path **212** to a current flowing between the third and fourth electrodes **304**, **306**.

[0029] A measure of voltage drop across first and second electrodes **204**, **206** together with a measure of the current waveform signal conducted through the third and fourth electrodes **308**, **306** is used to determine an impedance measurement signal Z(t) across the body tissue signal path **212** according to the following relationship:

$$Z(t)=\Delta v(t)/i(t) \tag{7}$$

where,

$$\Delta v(t)=v1(t)-v2(t) \tag{8}$$

The parameter i(t) represents a current waveform signal conducted through a body tissue electrical path **212** between the first and second electrodes **204**, **206**. The parameter v1(t) represents a first voltage waveform signal v1(t) at the first electrode **204**, and the parameter v1(t) represents a second voltage waveform signal v2(t) at the second electrode **206**.

[0030] In operation the current injection circuit **303** injects a current waveform signal i(t) that flows via the fourth electrode **306** to the fourth tissue surface site **310**, though human body tissue, which includes at least a portion of the chest cavity **214** and the heart **102**, to the third tissue surface site **308**, and from there to the third electrode **304**. In some embodiments, the current waveform i(t) is a steady state waveform. During the flow of current i(t), the voltage signal measurement circuit **302** produces the Δv(t) representing the voltage drop across the body tissue signal path **212**. Changes in the difference between v1(t) and v2(t) in the course of the flow of the current waveform i(t) are indicative of changes in the impedance of the body tissue electrical path **212** between the first and second tissue sites **208**, **210**, which can be caused by the occurrence of blood pulse waves ejected from the heart **102**. It will be appreciated, however, that there are other causes of changes in the impedance of the body tissue that can show up in the impedance measure, such as changes due to breathing/movement of the lungs. The impedance effects of these other changes are separated out through signal processing.

[0031] In accordance with some embodiments, the voltage signal measurement circuit **302** includes a voltage difference amplifier, and the signal Δv(t) represents an amplifier output signal having a waveform that is indicative of the difference between v1(t) and v2(t). In some embodiments the, the voltage signal measurement circuit **302** can be implemented using a differential amplifier. A change in the shape and blood fluid content of the heart **102** during a heartbeat results in a change in the impedance of the body tissue circuit path **212**, which in turn, results in a change in the Δv(t) waveform signal during current flow i(t). The voltage signal measurement circuit **302** monitors the voltage difference between the voltage signals on the first and second electrodes **204/304**, **206/306** and produces the Δv(t) signal, which has a waveform indicative of the voltage difference, which is indicative of impedance of the body tissue circuit path **212**. The beating of the heart results in changes in the impedance of the chest cavity, which causes changes in the Δv(t) waveform indicative of those changes in impedance.

[0032] Capacitor C_{ISO1} and Resistor R_{LIMIT} are electrically coupled between a node A, which is coupled to the current injection circuit **312**, and the fourth electrode **306** to provide electrical protection and isolation. The voltage signal measurement circuit **302** provides a voltage difference measurement (v1(t)−v2(t)) as an output signal on a node B. A capacitor C_4 is electrically coupled between a node C, which is coupled to the current injection circuit **312**, and the third electrode **304** to provide electrical protection and isolation.

[0033] The impedance voltage signal measurement circuit **302** includes a first voltage signal input node **332** electrically coupled to monitor the first electrode **204** and includes a second voltage signal input node **334** electrically coupled to motor the second electrode **206**. A capacitor C_2 is electrically coupled between the first voltage signal input node **332** and the first electrode **304**, and capacitor C_3 is electrically coupled between the second voltage signal input node **334** and the second electrode **206** to provide electrical protection and isolation.

[0034] In an alternative embodiment, the current waveform i(t) may be injected through the same electrodes used to measure voltage drop across the body tissue circuit path **212**. However, the four electrode embodiment described above with separate electrical paths for the current injection and for impedance measurement removes some signal artifacts that may arise in an alternate two electrode implementation and generally provides more accurate results.

[0035] Still referring to FIG. **4**, in accordance with some embodiments, the first and third electrodes **204**, **304** are located in band mount structure **316** suited to be secured to a hand **318** and/or wrist **320**, and the second, and fourth electrodes **206**, **306** are located in a finger mount structure **322** suited to be secured to a finger **324** of the other hand **326**. Thus, changes in impedance across the left and right hands **318**, **326** can be used to measure changes in shape and blood fluid content of the chest cavity **214**. In some embodiments, the hand and wrist electrodes can be located in the same band with the wrist electrodes on the bottom side of the band making contact with the hand/wrist while the finger electrodes are located on one of the outer surfaces of the band allowing the user to make contact with them when needed.

[0036] FIG. **5** is an illustrative graph showing an experimental result of impedance measurement across the chest cavity versus respiration rate for two different respiration rates. A first curve **402** indicates impedance measurements during a 60 second time frame during which the breathing

rate was twelve breaths per minute. The twelve peaks in the first curve indicate a distinct change in impedance for each of the twelve breaths. The impedance rises and falls twelve times in the course of the twelve breaths in which the lung volume changes twelve times. A second curve **404** indicates impedance measurements during a 60 second time frame during which the breathing rate was six breaths per minute. The six peaks in the second curve indicate a distinct change in impedance for each of the six breaths. The impedance rises and falls six times in the course of the six breaths in which the lung volume changes six times. Thus, the example demonstrates that a change in lung volume results in a change in body tissue current path that crosses the chest cavity. The principles of measurement of impedance changes due to breaths during respiration illustrated in the experimental results of FIG. **5** are similarly applicable to measurement of impedance changes due to heartbeat.

[0037] FIG. **6** is an illustrative block diagram showing certain other details of the voltage signal measurement circuit **302** in accordance with some embodiments. In particular, the signal measurement circuit **302** includes a signal processor **602** configured to perform certain functions. To implement the current injection system **312** component of the voltage measurement system **302**, a waveform generator **604** produces a digital representation of the current waveform signal i(t). A DAC **606** converts the digital waveform to an analog representation. An amplifier circuit **608** provides an amplified version of the analog representation. A switch matrix **610** is electrically coupled to monitor nodes A and C. The switch matrix **610** provides the amplified version of the analog representation the signal i(t) to node A for injection to the body tissue the second electrode **306**.

[0038] To compute a Z(t) waveform signal, the switch matrix **610** is electrically coupled to receive the voltage difference measurement signal Δv(t) provided on node B. The multiplexer circuit **614** selects the signal Δv(t) and provides it to ADC **616**, which converts it to a digital representation. The switch matrix **610** receives at node C a return version of the signal i(t) conducted out from the body tissue via the first electrode **304**. A transconductance amplifier **612** amplifies the return version of the i(t) signal received on node C. The multiplexer circuit **614** selects the return version of the current signal i(t) and provides it to ADC **616**, which converts it to a digital representation.

[0039] A signal processing module **618** produces the Z(t) signal based upon the Δv(t) signal received on node B and the i(t) signal received on node C. In accordance with some embodiments, the signal frequency filter module **618** filters the received signals so as to separate signal components indicative of changes in impedance due to ejection of blood wave pulses from the heart from signal components indicative of changes in impedance due to other events. It will be appreciated that certain changes in the value of impedance Z(t) are indicative of occurrence of the heart ejecting blood pulses to peripheral regions of the circulatory system. Other changes in the value of Z(t) are indicative other events such as respiration or of other physical movements by the human subject. For example, at rest, the rate in respiration for an adult typically is at frequencies less than 0.33 Hz. At rest, the rate of heartbeat typically for an adult is greater than 0.5 Hz. Consequently, high pass frequency signal filtering can be used to separate impedance changes due to heartbeat from impedance changes due to respiration. In some embodiments, the signal frequency filter module **618** uses a Discrete Fourier Transform (DFT) algorithm to filter the received signals. Thus, the signal processing module **618** produces a blood pulse wave ejection signal $\Delta Z_H(t)$, also referred to herein as a first signal, that is indicative of times at which a change in impedance of the chest cavity indicates an occurrence of ejection of a blood pulse to the circulatory system. The cortex M3 module **620** is used to control the different blocks of the sensor, perform low level digital signal processing, and communicate the data to other devices through the Universal Asynchronous Receiver Transmitter (UART) interface **624**. In addition, the Cortex M3 optionally receives commands from other devices (not shown) through interface **624** as well. The cortex M3 can be replaced with higher end processors if more on-chip processing is required. A storage device **626**, such as DRAM, ROM, Flash or Disc, is included to store computer readable instructions and/or data to configure the processor **602**.

[0040] An I/O interface at node E is coupled to a UART interface **624** to send and receive signals to and from an outside source. In accordance with some embodiments the blood pulse wave ejection signal is provided as an output signal at node E.

[0041] FIG. **7** is an illustrative schematic block diagram showing certain details of the blood pulse detection sensor **203** of FIG. **2**, in accordance with some embodiments. The sensor **203** includes a light source **702** and a photodetector **704**. The light source **702** includes a light emitting diode (LED) **706**. A DAC circuit **708** provides a signal to an LED driver circuit **710**, which drives the LED **706**. The photodetector **704** includes a photodetector diode **712**. An amplifier circuit **714** amplifies a signal produced by the photodetector **704**. A filtering circuit **716** filters the amplified signal. An ADC circuit **718** converts the amplified and filtered representation of the photodetector output signal from an analog to a digital representation and provides the digital version of the photodetector output signal, also referred to herein as a second signal, on line **720**.

[0042] In operation, the light source **706** and the photodetector **712** are placed in close proximity to a body site peripheral to the heart at which the arrival times of blood pulses are to be detected. The example show in the drawing shows them disposed close to a finger **722**, although they can be placed in close proximity to other body sites such as wrist, ear lobe, ear cavity, etc. More particularly, in accordance with some embodiments, the light source **706** and the photodetector **712** are position relative to a body site so as to be suitable for photoplethysmography (PPG) measurements in which the output signal on line **720** is indicative of local blood volume changes ΔV_i that occur upon the arrival of a blood pulse wave at a body site where the optical sensor is sensing. A PPG sensor detects blood pressure change by detecting a change in the reflectivity of light through the skin surface, which is indicative of the arrival of a blood pulse wave.

[0043] Thus, it will be understood that the blood pulse detection sensor **203** detects arrival of a blood pulse through detection of changes in blood dynamics such as changes in blood density, changes in blood pressure or changes blood flow, for example. As explained above, in some embodiments the blood pulse detection sensor **203** includes a PPG sensor that detects arrival of a blood pulse based upon a change in blood volume. In alternative embodiments, the blood pulse detection sensor **203** can be implemented to detect arrival of a blood pulse based upon a change in blood

pressure or to detect arrival of a blood pulse based upon a change in blood flow, for example.

[0044] FIG. **8** is an illustrative drawing showing a computer system **802** coupled to process PTT related information in accordance with some embodiments. The computer system **802** includes a processor **804**, non-transitory storage **806**, such as disc, RAM, ROM disc and/or Flash, a graphic display monitor **808**, I/O **810** and a bus circuit **812** providing a communication path among the components. The computer system **802** is electrically coupled to receive impedance change signal information via node E of the signal processor **602** and is coupled to receive blood pressure change signal information via output line **702** of the blood pulse detection sensor **203**. Both node E and the output line **702** can be wired or wireless. The computer system **802** is configured to compute PTT information by determining a time difference between times of occurrence of a change in impedance signal value indicative of a blood pulse ejected from the heart left ventricle to the aorta, detected using the impedance measurement circuit **202**/**302**, and time of arrival of that same blood pulse, detected using the blood pulse detection sensor **203**, at a location peripheral to the heart. More particularly, the computer system **802** is coupled to receive the blood pulse wave ejection signal $\Delta Z_H(t)$ provided on node E and to receive the blood pressure change signal ΔP_i on line **720**. The storage device **806** includes computer program code to configure the computer system to determine PTT based upon impedance change measurements and peripheral site blood pressure change measurements.

[0045] FIG. **9** is an illustrative flow diagram representing configuration of the processor **804** of the computer system of FIG. **8** to determine PTT values in accordance with some embodiments. Computer readable computer program code that includes instructions stored in a storage device **806** can be used to configure the processor to determine PTT values. Module **902** configures the processor to receive from the impedance sensor circuit **202** of FIG. **4**, raw first signals $S1_1$, $S1_2$, $S1_3$, etc., indicative times of occurrences of changes of impedance and receives from the blood pulse detection sensor **203** of FIG. **7**, raw second signals $S2_1$, $S2_2$, $S2_3$, etc., indicative of change changes in blood pressure. Module **902** filters and conditions the received impedance change signal and blood pressure change signals to remove interferers and artifacts (such as motion) are removed from the sensors raw data. Module **904** configures the processor to determine a sequence of impedance change time reference signals $T1_1$, $T1_2$, $T1_3$, etc., that indicate each time of occurrence of a first signal. It will be appreciated that a sequence of occurrences of a blood pulse wave ejections results in the sequence of first signal occurrences $S1_1$, $S1_2$, $S1_3$, etc., corresponding to the ejections. Thus, a first sequence of reference time signals $T1_1$, $T1_2$, $T1_3$, etc., is produced that corresponds to the sequence of first signal occurrences $S1_1$, $S1_2$, $S1_3$, etc. Module **906** configures the processor to determine a sequence of blood pressure change time reference signals $T2_1$, $T2_2$, $T2_3$, etc., that indicate each time of occurrence of a second signal. It will be appreciated that each occurrence of a blood pulse wave ejection wave results in an occurrence (after a PTT delay) of a second signal corresponding to occurrence of an arrival of that pulse wave at a body location monitored by the blood pulse detection sensor **203**. Thus, a second sequence occurrence reference time signals $T2_1$, $T2_2$, $T2_3$, etc., is produced that corresponds to the sequence of second signal occurrences $S2_1$, $S2_2$, $S2_3$, etc. For each of the first and second signals, reference times can be determined based upon a local maximum, local minimum, zero crossing, or other defined feature of a measured impedance change waveform or pressure change waveform to determine its time of occurrence. The fourth module **908** configures the processor to associate first and second time reference signals that correspond to the same cardiac cycle, e.g., ($T1_1$, $T2_1$), ($T1_2$, $T2_2$), ($T1_3$, $T2_3$), etc. Module **910** configures the processor to use the associated first and second signal time of occurrence reference points to compute a time delay between them (PTT), e.g. ($T2_1$–$T1_1$), ($T2_2$–$T1_2$), ($T2_3$–$T1_3$), etc., and to convert the time delay to a blood pressure measurement. In accordance with some embodiments, one or more of relationships expressed in formulas (1)-(6), or other suitable formulations, can be used to convert PTT to a blood pressure determination or to a blood pressure change determination.

[0046] In accordance with some embodiments, a non-transitory storage device **808** external to the computer system **802**, can be used to deliver the computer program code. The external storage device **808** may include a thumb drive or may include remote storage accessible over a network (not shown) such as the internet, for example.

[0047] The foregoing description and drawings of embodiments in accordance with the present invention are merely illustrative of the principles of the invention. For example, the storage device **626** can store computer readable code instructions to configure processor **602** to perform the process of FIG. **9**. Also, for example, a ballistocardiogram (BCG) measurement can be used instead of an impedance measurement to detect the time of occurrence of ejection of a blood pulse. As another alternative, an electrocardiogram (ECG) measurement can be used instead of an impedance measurement to detect the time of occurrence of ejection of a blood pulse. Moreover, an impedance plethysmography (IPG) sensor can be used instead of a PPG sensor. Therefore, it will be understood that various modifications can be made to the embodiments by those skilled in the art without departing from the spirit and scope of the invention, which is defined in the appended claims.

1. A blood pressure monitoring system comprising:

an impedance measurement circuit configured to detect a change in impedance indicative of an occurrence of a blood pulse wave ejection from the heart;

a blood pulse detection circuit configured to detect arrival of the blood pulse wave at a body site peripheral to the heart; and

a non-transitory computer readable storage device that includes computer program code to configure a processor to compute pulse transit time (PTT) based at least in part upon a difference in a time of occurrence of the blood pulse wave ejection from the heart first signal and a time of occurrence of the arrival of the blood pulse wave at a body site peripheral to the heart.

2. The system of claim **1** further including:

a first electrode;

a second electrode;

a third electrode;

a fourth electrode;

a current injection circuit; and

a voltage difference measurement circuit,

wherein the current waveform generator is coupled to inject a current between the first and second electrodes; and

wherein the voltage difference measurement circuit is coupled to monitor a voltage difference between the third and fourth electrodes.

3. The system of claim **2**,

wherein the first and third electrodes are secured to a first mount structure suited for mounting to a first anatomical location; and

wherein the second and fourth electrodes are secured to a second mount structure suited for contact to a second anatomical location.

4. The system of claim **2**,

wherein the current injection circuit includes a current waveform generator.

5. The system of claim **1** further including:

a first electrode;

a second electrode;

a current injection circuit; and

a voltage difference measurement circuit,

wherein the current injection circuit is coupled to inject a current between the first and second electrodes; and

wherein the voltage difference measurement circuit is coupled to monitor a voltage difference between the first second electrodes.

6. The system of claim **5**,

wherein the first electrode is secured to a first mount structure suited for mounting to a first anatomical location; and

wherein the second electrode is secured to a second mount structure suited for mounting to a second anatomical location;

7. The system of claim **5**,

wherein the current injection circuit includes a current waveform generator.

8. The system of claim **1** further including;

a frequency filter circuit configured to identify signal components within a voltage difference measurement signal produced using the voltage difference measurement circuit that are indicative of changes in impedance due to ejection of blood wave pulses from the heart.

9. The system of claim **1**,

wherein the blood pressure measurement circuit includes a light source and a photodetector.

10. The blood pressure monitoring system of claim **1**,

wherein the impedance measurement circuit is configured to produce a first signal indicative of a change in impedance indicative of an occurrence of a blood pulse wave ejection from the heart; and

wherein the blood pulse detection circuit is configured to produce a second signal indicative of an occurrence of an arrival of the blood pulse wave at a body site peripheral to the heart; and

wherein the non-transitory computer readable storage device that includes computer program code to configure a processor to compute pulse transit time (PTT) based at least in part upon a difference in a time of occurrence of the first signal and a time of occurrence of the second signal.

11. The system of claim **10**,

wherein the computer program code includes code to configure a processor to determine a reference time of occurrence associated with the first signal and to determine a reference time of occurrence associated with the second signal and to compute a pulse transit time (PTT) based at least in part upon a difference in the determined reference time of occurrence associated with the first signal and the determined reference time of occurrence associated with the second signal.

12. The system of claim **10**,

wherein the impedance measurement circuit is configured to produce a sequence of first signals indicative of a sequence of changes in impedance indicative of each occurrence of a blood pulse wave ejection from the heart for a sequence of cardiac cycles; and

wherein the blood pressure measurement circuit is configured to produce a sequence of second signals indicative of a sequence of occurrences of changes in blood pressure upon arrival of the blood pulse wave at a body site peripheral to the heart for the sequence of cardiac cycles.

13. The system of claim **10**,

wherein the impedance measurement circuit is configured to produce a sequence of first signals indicative of a sequence of changes in impedance indicative of each occurrence of a blood pulse wave ejection from the heart for a sequence of cardiac cycles;

wherein the blood pressure measurement circuit is configured to produce a sequence of second signals indicative of a sequence of occurrences of changes in blood pressure upon arrival of the blood pulse wave at a body site peripheral to the heart for the sequence of cardiac cycles; and

wherein the computer program code includes code to configure a processor to determine a sequence of reference times of occurrence associated with the sequence of first signals and to determine a sequence of reference times of occurrence associated with the sequence of second signals and to compute a sequence of pulse transit times (PTT) based at least in part upon differences in the determined reference times of occurrence associated with corresponding first and second signals.

14. The system of claim **10**,

wherein the impedance measurement circuit is configured to produce a sequence of first signals indicative of a sequence of changes in impedance indicative of each occurrence of a blood pulse wave ejection from the heart for a sequence of cardiac cycles;

wherein the blood pressure measurement circuit is configured to produce a sequence of second signals indicative of a sequence of occurrences of changes in blood pressure upon arrival of the blood pulse wave at a body site peripheral to the heart for the sequence of cardiac cycles; and

wherein the computer program code includes code to configure a processor to determine a sequence of reference times of occurrence associated with the sequence of first signals and to determine a sequence of reference times of occurrence associated with the sequence of second signals and to associate, with each other, determined reference times of occurrence that correspond to the same cardiac cycle and to compute a sequence of pulse transit times (PTT) based at least in part upon differences in the determined reference times of occurrence associated with corresponding first and second signals.

15. A blood pressure monitoring system including:

an impedance measurement circuit configured to detect a change in impedance indicative of an occurrence of a blood pulse wave ejection from the heart;

a blood pressure measurement circuit configured to detect an occurrence of a change in blood dynamics upon arrival of the blood pulse wave at a body site peripheral to the heart; and

a processor configured to compute pulse transit time (PTT) based at least in part upon a difference in a time of occurrence of the blood pulse wave ejection from the heart first signal and a time of occurrence of the arrival of the blood pulse wave at a body site peripheral to the heart.

16. A method to monitor blood pressure comprising:

monitoring electrical impedance at first and second body skin tissue sites;

monitoring blood pressure at a third skin tissue site; and

determining a pulse transit time (PTT) based at least in part upon a difference in a time of occurrence of a monitored change in impedance at the first skin tissue site and a monitored change in blood pressure at the second skin tissue site.

17. The method of claim **16**,

wherein the first and second skin tissue sites are disposed such that the heart is located between them.

18. The method of claim **16**,

wherein the first and second skin tissue sites are disposed such that a blood pulse wave ejection from the heart produces a change in impedance of a body tissue electrical path between the first and second skin sites.

19. The method of claim **16**,

wherein monitoring electrical impedance at first and second body skin tissue sites includes monitoring a voltage difference between the first and second body skin tissue sites.

20. The method of claim **16**,

wherein monitoring blood pressure at the third skin tissue site includes monitoring blood volume at the third skin site.

21. The method of claim **16**,

wherein monitoring electrical impedance at the first and second body skin tissue sites includes producing a voltage difference measurement signal indicative of a voltage difference between voltage at the first skin tissue site and a voltage at the second skin tissue site; and further including:

filtering the voltage difference signal to identify signal components within the voltage difference measurement signal that are indicative of changes in impedance due to ejection of blood wave pulses from the heart.

22. The method of claim **16**,

wherein monitoring electrical impedance at the first and second body skin tissue sites includes producing a sequence of first signals indicative of a sequence of changes in impedance indicative of each occurrence of a blood pulse wave ejection from the heart for a sequence of cardiac cycles;

wherein monitoring blood pressure at a third skin tissue site includes producing a sequence of second signals indicative of a sequence of occurrences of changes in blood pressure upon arrival of the blood pulse wave at a body site peripheral to the heart for the sequence of cardiac cycles; and

wherein determining a PTT includes determining a sequence of reference times of occurrence associated with the sequence of first signals and determining a sequence of reference times of occurrence associated with the sequence of second signals and computing a sequence of PTTs based at least in part upon differences in the determined reference times of occurrence associated with corresponding first and second signals.

* * * * *

专利名称(译)	连续无创血压计		
公开(公告)号	US20170105637A1	公开(公告)日	2017-04-20
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申请(专利权)人(译)	奥克兰，TONY JOSEPH Errico，PAUL V.		
当前申请(专利权)人(译)	奥克兰，TONY JOSEPH Errico，PAUL V.		
[标]发明人	AKL TONY JOSEPH ERRICO PAUL V		
发明人	AKL, TONY JOSEPH ERRICO, PAUL V.		
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摘要(译)

提供一种血压监测系统，包括：阻抗监测电路，被配置为检测从心脏发射的脉搏波的发生;血脉冲检测电路检测血脉波到达心脏周围的身体部位;处理器，被配置为至少部分地基于从心脏第一信号发生的脉波波发生的时间与血脉冲波到达的发生时间的差异来计算脉搏传导时间（PTT）。心脏周围的身体部位。