McCALLUM, RADEMEYER & FREIMOND
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Classified By: McCALLUM, RADEMEYER & FREIMOND

Full Name(s) of Applicant(s)

71	ULTRASIS INTERNATIONAL (1993) LTD.

Full Name(s) of Inventor(s)

72	SHUSTERMAN, Vladimir; ROYTVARF, Alex; ORBACH, Tuvi

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Title of Invention

54	METHOD AND DEVICE FOR CONTINUOUS ANALYSIS OF CARDIOVASCULAR ACTIVITY OF A SUBJECT

57	Abstract (not more than 150 words)

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ABSTRACT

A method for obtaining continuously and non–invasively one or more parameters relating to the cardiovascular system of a subject. The parameters obtainable by the method are systolic blood pressure, diastolic blood pressure, young modulus of an artery, cardiac output, relative changes in vascular resistance, and relative changes in vascular compliance. In accordance with the method, the ratio, κ of the subject's blood flow velocity to the propagation speed of the subject's pulse wave is obtained continuously and non–invasively. κ is then processed so as to obtain the instantaneous values of the desired parameters.

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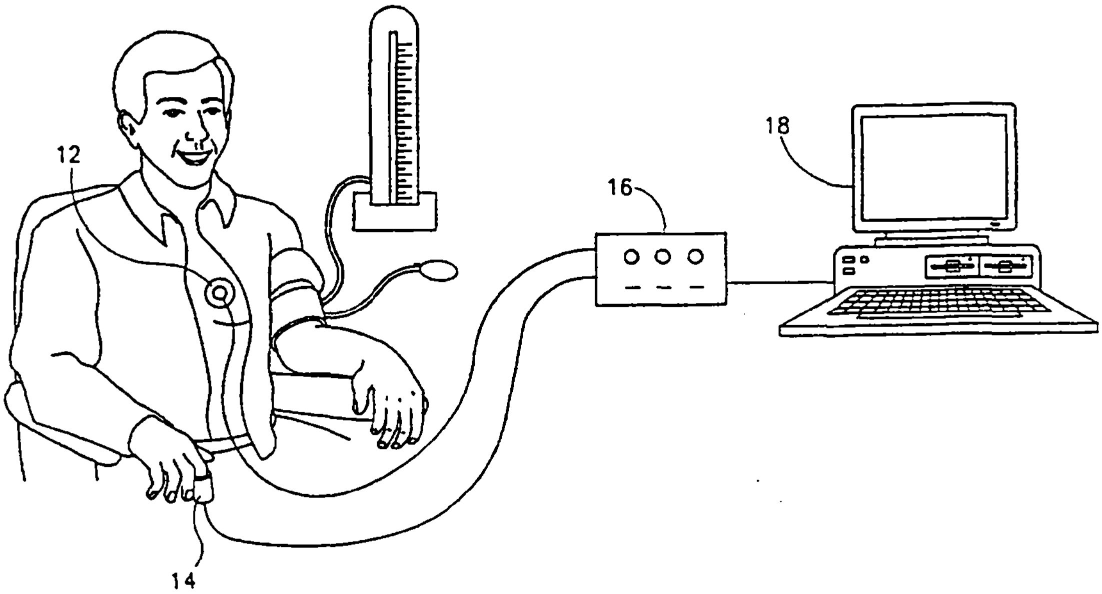
ADVERTISEMENT DRAWING



METHOD AND DEVICE FOR CONTINUOUS ANALYSIS OF CARDIOVASCULAR ACTIVITY OF A SUBJECT

FIELD OF THE INVENTION

The invention is in the field of medical diagnostic devices and more specifically devices for analyzing cardiovascular activity of a subject.

GLOSSARY

There follows a glossary of terms used herein, some of which are standard, others having been coined, together with their abbreviations.

Plethysmograph (PG) - An instrument for measuring blood flow.

Pulse Transit Time (PTT) – The elapsed time between the arrival of a pulse pressure peak at two points in the arterial system, or the elapsed time between a particular point in the ECG signal and the arrival of the consequent pulse wave at a particular point in the arterial system.

Cardiac output (CO) - The blood volume pumped into the aorta by the heart per minute.

Vascular compliance (VCL) - The ratio of the change in the blood vessel volume to the change in pressure.

AREA - The area under the peak of a plethysmograph signal.

Peak Amplitude (PA) - The amplitude of the peak of a plethysmograph signal.

Systolic Pressure (SP) - The blood pressure during the contraction phase of the cardiac cycle.

Diastolic Pressure (DP) - The blood pressure during the relaxation period of the cardiac cycle.

BACKGROUND OF THE INVENTION

Continuous, non-invasive monitoring of blood pressure and vascular parameters is important, for example, in people for whom abnormally high or low blood pressure poses a major threat to their health. Several approaches have been developed for noninvasive, continuous, blood pressure monitoring. For example, U.S. Patent 4,475,554 discloses a device which determines blood pressure from oscillometric measurements. These devices utilize an inflatable cuff that can be placed on an arm above the elbow or on a finger. The cuff is inflated to equilibrate with the internal pressure in the underlying digital vessels. As the blood pressure in the digital arteries fluctuates, the cuff pressure is adjusted by a feedback control mechanism so as to balance the blood pressure. The blood pressure at any moment is considered to be proportional to the cuff pressure. This assumes that the elasticity and tone of the digital arteries remains constant over time while in fact it is extremely variable. For this reason, these devices are not practical for prolonged blood pressure monitoring. Moreover, the constant cuff pressure makes these cuffs uncomfortable for the patient and often causes problems in the peripheral blood circulation. These oscillometric devices are therefore rarely used for continuous blood pressure monitoring.

Several studies have attempted to estimate systolic and diastolic pressure by analyzing only the plethysmograph (PG) signal. These methods, however, employ high order derivatives and therefore require a signal with extremely low noise that is practically unattainable due to the subject's movements. Moreover, these methods cannot be used for real time blood pressure measurements since the data must be averaged over several minutes.

US patents 4,869,262 to Orr, 4,807,638 to Sramek, and 5,709,212 to Sugo, disclose devices that calculate blood pressure only from pulse transient time (PTT). The reliability and reproducibility of blood pressure measurements determined solely from PTT, however, is not great enough to allow accurate blood pressure measurements.

Another approach to non-invasive monitoring of blood pressure is disclosed in European Patent Application EP 0 443 267 A1 of Smith. This method uses both the PG signal and a PTT for the calculation of the systolic and diastolic pressures. The PG signal must first be normalized in each cardiac cycle by dividing the AC signal by the DC signal assuming that the variation in vascular tone and elasticity is slower than that in the heart rate. This normalization procedure is empirical and inaccurate. Moreover, the equations used for calculating the systolic and diastolic pressures are also empirical and thus inaccurate in many cases.

It has long been known that changes in cardiac output and other vascular characteristics (compliance, resistance, and Young modulus) affect blood pressure. Different physiological processes govern blood pressure changes of different origins and a different medical treatment is required for the same change in blood pressure when it arises from different origins. Determining the cause of a change in blood pressure is therefore crucial for successful treatment. However none of the prior-art devices and methods discloses means for the non-invasive monitoring of these factors. Moreover, all of the prior-art devices and methods ignore the effects of these factors on blood pressure.

There is accordingly a need in the art for a method and device for the non-invasive, continuous monitoring of blood pressure, cardiac output, and other vascular characteristics in which the disadvantages of the aforementioned prior-art methods are substantially reduced or eliminated.

REFERENCES

US Patents

US 4,475,554	10/1984	Hyndman
US 4,807,638	2/1989	Sramek
US 4,869,262	9/1989	Orr
US 5,709,212	1/98	Sugo

European Patent Application

EP 0 443 267 A1 (Corresponding to US 484687) 2/1990 Smith

SUMMARY OF THE INVENTION

In the context of the present invention, two explicitly described, calculable or measurable variables are considered equivalent to each other when the two variables are proportional to each other.

In the following description and set of claims, κ will be used to denote the ratio of the blood flow velocity to the propagation speed of the pressure pulse wave in an individual.

The invention is based on the novel and non-obvious finding that diastolic and systolic blood pressures determined from calculations involving κ are more accurate than those obtained by prior art methods where κ is not used.

The invention thus comprises a method and a device for the continuous and non-invasive measurement of κ. In a preferred embodiment of the invention, κ is obtained from a PG signal and PTT of a subject. In a most preferred embodiment κ is obtained from a PG signal and PTT of a subject according to the theory of waves of strong discontinuities as described for example in Landau L.D. and Lifshitz E.M., *Statistical Physics,* Pergamon Press, 1979; Landau L.D., and Lifshitz E.M., *Fluid Mechanics,* Pergamon Press, 1987; and Landau L.D., Lifshitz E.M., *Theory of Elasticity,* Pergamon Press, 1986, and Kaplan D. and Glass, *Understanding Non-Linear Dynamics,* Springer-Verlag, N.Y., 1995, which are hereby incorporated in their entirety by reference. In a yet more preferred embodiment, κ is given by:

$$\kappa = 1/(1/(PEAK \cdot v) + 1),$$

where v is the propagation speed of the pulse wave (the pulse wave velocity) which is inversely proportional to PTT, and

$$PEAK = k_1 \cdot PTT\ \ PA + k_2 \cdot AREA,$$

where PA and AREA are respectively the amplitude and area of the pulse wave obtained from the PG signal, and k_1 and k_2 are two empirically obtained constants.

In another preferred embodiment κ is given by: $\kappa = \frac{1}{\left(\left(\frac{1}{PA}\right)+1\right)}$

Slow (0.01-0.05 Hz) fluctuations in vascular radius (vasomotor tone) can optionally be filtered out from the PG signal in order to increase the accuracy of the κ measurement. This can be carried out, for example, by replacing PEAK in the definition of κ with PEAK/(slow component of PEAK)^2. The slow component of PEAK can be obtained, for example, by low-pass filtering of the pulse wave. Other methods for obtaining κ continuously and non-invasively are also contemplated within the scope of the invention.

Means for obtaining the PG signal of a subject continuously and non-invasively is known in the art and may, for example, be a photo-PG sensor. Other methods for measuring pressure waves in a blood vessel are also contemplated within the scope of the invention. This includes, but is not limited to, use of several photo PG devices, impedance PG devices, piezoelectric, ultrasound, laser, or other types of sensors.

Means for the continuous and non-invasive determination of PTT is known in the art and may comprise, for example, an electrocardiograph monitor and a PG sensor. The PTT in this case is the time lapse between a particular point in the ECG wave, for example the R peak, and the arrival of the corresponding pressure wave at the PG sensor. Other means for measuring PTT comprise, for example, a pair of PG sensors that are attached to the skin along the same arterial vessel and separated from one another. In this case, the PPT is the time lapse between the arrival of a pressure wave at the two locations.

The invention thus further provides for a device for processing κ in real time so as to obtain a continuous and non-invasive measurement of systolic and diastolic blood pressures.

Still further, the invention provides for a device for processing κ in real time so as to obtain a continuous and non-invasive measurement of Young modulus, vascular resistance, cardiac output, and vascular compliance. The prior art does not disclose methods for obtaining these parameters.

The measurements provided by the invention of the diastolic and systolic blood pressures, Young modulus, vascular resistance, cardiac output, and vascular compliance are more robust and less sensitive to external noises, changes in body position, and sensor placement than measurements provided by prior art devices.

The invention further provides for a device for processing κ in real time so as to continuously and non-invasively obtain indices for indicating a change in the blood pressure in a subject due to a change in cardiac output or a change in vascular compliance. Since different physiological processes govern blood pressure changes of different origins and a different medical treatment is required for the same change in blood pressure when it arises from different origins, the present invention provides means for determining the appropriate treatment.

In a preferred embodiment, κ is processed in real time so as to obtain the aforementioned parameters according to the theory of waves of strong discontinuities. In a most preferred embodiment, the aforementioned parameters are obtained using the following algorithmic expressions:

Systolic Pressure (SP)

Method 1

$$SP = \rho v^2 \Phi(\kappa, \gamma),$$

where ρ is the blood density, γ is the thermodynamic Poisson exponent of the blood, and

$$\Phi = \frac{\sqrt{2\kappa(\gamma-1)^2 + 4\cdot(\gamma-1)+1} - 1}{2(\gamma-1)}$$

Method 2

$$SP = (\log v^2)/\alpha + 2\rho\, v^2\kappa/3 + \lambda,$$

where $\lambda = (\log(2\rho R/E_0 h))/\alpha$, where R is the radius of the artery, h is the thickness of the arterial wall, E_0 is Young modulus referred to zero pressure, and α is an empirically obtained constant.

Method 3

$$SP = (\log v^2/(1 - \varepsilon H^2))/\alpha + 2\rho v^2\kappa/3 + \lambda,$$

where ε is an empirically obtained constant and H is the heart rate.

Method 4

$$SP = [(\log v^2)/\alpha + \lambda]/(1 - \kappa).$$

Method 5

$$SP = [(\log v^2/(1 - \varepsilon H^2))/\alpha + \lambda]/(1 - \kappa).$$

Diastolic Pressure (DP)

$$DP = SP - \rho v^2 \kappa,$$

Young Modulus

Method 1

$$E = (2R/h)\,(SP\text{-}DP)/\kappa$$

Method 2

$$E = (2R/h)\,SP/\Phi\,(\kappa,\gamma)$$

Method 3

$$E = (2R/h)\,\rho\,\exp[(-\lambda+MP)\alpha]$$

where MP is the mean pressure, $MP = (SP + 2\cdot DP)/3$, where SP or DP is obtained using an algorithmic expression involving κ.

Method 4

$$E = (2R/h)\cdot\rho\cdot\exp\,((-\lambda+SP\cdot(1\text{-}\kappa))\alpha)$$

Cardiac Output (CO)

$$CO = PEAK \cdot \{ v \cdot [1 + SP/(2\rho\cdot v^2)]\}^2$$

where SP is obtained using an algorithmic expression involving κ, and the slow component of PEAK has been filtered out as described above.

Vascular Resistance (VR)

$$VR = (SP - DP)/CO.$$

where any one or more of SP, DP, and CO are obtained using an algorithmic expression involving κ.

Vascular Compliance (VC)

$$VC = PEAK/(SP - DP).$$

where any one or more of SP, and DP are obtained from a calculation involving κ. Other methods for obtaining vascular compliance from κ are also contemplated within the scope of the invention.

The Effect of VC, VR and CO on Blood Pressure

The relative contribution of CO to an observed change in SP is given by a parameter INDEX1 defined by

$$INDEX1 = \partial SP/\partial CO - \partial SP/\partial VC$$

where any one or more of the parameters SP, CO, and VC are obtained from a calculation involving κ. An increase in INDEX1 over time is indicative of a change in SP primarily due to changes in cardiac output (CO). A decrease in INDEX1 over time is indicative of a changes in SP primarily due to a change in vascular compliance (VC).

The relative contribution of VR and CO to an observed change in SP is given by a parameter INDEX2 defined by

$$INDEX2 = \partial SP/\partial CO - \partial SP/\partial VR$$

where any one or more of the parameters SP, CO, and VR are obtained from a calculation involving κ. An increase in INDEX2 over time is indicative of a change in SP primarily due to changes in cardiac output (CO). A decrease in INDEX2 over time is indicative of a change in SP and DP primarily due to a change in vascular resistance (VR).

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will now be described by way of example only with reference to the accompanying non-limiting drawings in which:

Fig. 1. shows one embodiment using a device of the invention; and

Fig. 2 shows a generalized flow chart of the processing steps according to one embodiment of the invention.

DETAILED DESCRIPTION OF A PREFERRED EMBODIMENT

Fig. 1 shows a subject **10** being monitored by a device according to a preferred embodiment of the invention. ECG electrodes **12** have been affixed to the subject's chest for continuously and non-invasively monitoring his/her electrocardiograph. A PG sensor **14** has been attached to the subject's finger for continuously and non-invasively monitoring his/her pulse wave. Signals from the ECG electrodes and the PG sensor are continuously fed into a processor **16**. The processor **16** includes an interface, an A/D converter, amplifiers and a cable to a serial port of a PC computer **18**. Preliminary blood pressure measurements are carried out for calibration purposes in order to obtain any empirically defined constants using a commercially available sphygmomanometer **20**.

A generalized flow chart of the processing carried out by processor **16** is shown in Fig 2. The ECG and PG signals are first processed in real time so as to obtain instantaneous values of κ. κ is then processed in real time so as to obtain the instantaneous values of the desired parameters. The calculated values of the desired parameters are transferred in real time to PC **18** for storage and display.

Example

The invention will now be demonstrated by way of a non-limiting example.

Methods

The blood pressure of a group of eleven subjects, 7 males and 4 females ranging in age from 21-44, was examined using the invention. Of the 11 subjects, 10 were known to have normal blood pressure, while one had borderline hypertension. Each subject was examined at least twice. Each examination lasted approximately one hour and included measurements in the following positions: supine (15 min), sitting (15 min), and standing (10 min). In 7 subjects measurements were also made in a sitting position after 10 min of controlled physical exercise on a bicycle or during a Valsalva test. The data were processed separately for each subject and for each position.

Reference blood pressure measurements were obtained from each subject using one or both of the following devices:

1. A commercially available blood pressure measurement device (A Dynapulse 200M™ comprising a cuff-manometer connected to a PC computer).
2. Continuous oscillometric blood pressure measurement from the finger arteries (Finapress™, Ohmeda) combined with a device (Ultramind) for the transmission of the output to a PC computer.

When the Finapress™ device was used as a reference, blood pressure was measured continuously and saved in real time. When the Dynapulse™ device was used, discrete blood pressure measurements were made 3 - 4 times during the examination. The reference blood pressure measurements at the beginning of each examination were used to obtain the constant parameters k_1, k_2

ECG and PG signals were obtained from each subject and processed by custom software in real time. Processing included the following successive operations:

1. Smoothing (filtering and high-frequency noise).
2. Baseline drift correlation of the PG signal (high pass filtering using a cut-off frequency of 1.0-2.0 Hz).

3. Performing a peak recognition procedure on the ECG and PG signals.
4. Obtaining PA as the height of the PG peak.
5. Calculating PTT as the time interval between an ECG peak and the corresponding PG peak.
6. Calculating AREA by integration of the PG signal over the time interval from the ECG peak to the PG peak.
7. Calculating the heart rate.
8. Calculating the constant parameters k_1, k_2, α and ε using a chi-square test in accordance with the maximal likelihood principle.

SP and DP were then obtained for each subject as follows:

ECG and PG signals were obtained from each subject and processed by custom software in real time. Processing included the following successive operations:

1. Smoothing (filtering and high-frequency noise).
2. Baseline drift correlation of the PG signal (high pass filtering using a cut-off frequency of 1.0-2.0 Hz).
3. Performing a peak recognition procedure on the ECG and PG signals.
4. Obtaining PA as the height of the PG peak.
5. Calculating PTT as the time interval between an ECG peak and the corresponding PG peak.
6. Calculating AREA by integration of the PG signal over the time interval from the ECG peak to the PG peak.
7. Calculating the heart rate.
8. Calculating SP and DP according to the methods of the invention.
9. Calculating SP and DP according to the method of European Patent Application EPO 443267A1 of Smith.

The constant parameters were adjusted from time to time during the examination as required.

The results were compared with those obtained by the following methods.

The output consisted of the following two parts:

1. SP and DP time series obtained according to the invention and according to the method of Smith.
2 The mean error and the root-mean-square error between the SP and DP time series and the reference blood pressure measurements.

Results

The blood pressure measurements obtained according to the invention on subjects at rest, and those calculated by the empirical formulas of European Patent Application EPO 443267A1 of Smith (Table 1) were compared with those obtained by the reference devices. SP and DP determinations obtained according to the present invention are more stable than those obtained by the method of Smith. In particular, the mean error and standard deviations of SP measurements obtained after stress according to Methods 3 and 5 of the present invention were 2 and 5 times smaller, respectively, than those obtained by the method of Smith. In all 26 subjects, when SP measurements were obtained according to Method 3 and 5 the mean error was 1.6 times smaller than that obtained by the method of Smith (p=0.023).

Table 2 shows the results of blood pressure measurements obtained on subjects while supine or sitting after exercise. The five methods of the invention and the method of European patent Application EPO 443267A1 of Smith were compared with measurements obtained by Finapress™ and a Dynapulse 200M™. In particular, the mean error between SP measurements obtained according to Methods 3 and 5 in all 26 subjects was 54% of the error obtained of Smith (p=0.023).

Table 1

Subject's position		Method 1	Methods 2, 4	Methods 3, 5	Smith
Dynapulse™ (n=12)	SP	18±13	13±8	10±8	20±37
	DP	11±8	7±5	6±4	8±4
Finapress™ (n=14)	SP	12±5	9±4	8±4	9±4
	DP	7±3	6±3	8±4	6±3

Table 1. Mean error ± standard deviation (mm Hg) between the blood pressure measurements obtained by the five methods of the present invention, and the

method of Smith compared with measurements obtained using a Finapress™ or Dynapulse™.

Table 2

Subject's position		**Method 1**	**Methods 2, 4**	**Methods 3, 5**	**Smith**
Supine, (n=19)	SP	11±5	9±4	7±4	8±4
	DP	7±4	6±4	7±4	6±3
Sitting, following exercise (n=7+)	SP	23±14	17±8	14±9	30±47
	DP	14±8	7±4	7±4	8±4
Total (n=26)	SP	15±10	11±6	9±6	14±26
	DP	9±6	6±4	7±4	7±3

Table 2. Mean error ± standard deviation (mm Hg) obtained by the five methods of the present invention and the method of Eurpean Patent Application EPO 443267A1 of Smith compared with measurements obtained using a Finapress™ and a Dynapulse 200M™. The measurements were made while the subject was either supine with no prior exercise or sitting following exercise.

The present invention has been described with a certain degree of particularity, but it should be understood that various notifications and alterations may be made without departing from the scope or spirit of the invention as defined by the following claims:

CLAIMS

1. A method for obtaining continuously and non-invasively one or more of the parameters of a subject from the list comprising:

i. systolic blood pressure,

ii. diastolic blood pressure,

iii. Young modulus of an artery,

iv. cardiac output,

v. relative changes in vascular resistance, and

vi. relative changes in vascular compliance;

said method comprising:

(a) substantially obtaining continuously and non-invasively the ratio, κ, of the subject's blood flow velocity to the propagation speed of the subject's pulse wave; and

(b) processing κ substantially in real time so as to obtain the instantaneous values of the desired parameters.

2. The method according to Claim 1 wherein κ is obtained by processing a PG signal and a PTT continuously and non-invasively obtained from the subject.

3. The method of Claim 2 wherein κ is obtained according to the following algorithmic expression:

$$\kappa = 1/(1/(\mathrm{PEAK}\cdot v) + 1),$$

where v is the pulse velocity, and

$$\mathrm{PEAK} = k_1 \cdot \mathrm{PTT} \cdot \mathrm{PA} + k_2 \cdot \mathrm{AREA},$$

where PA and AREA are respectively the amplitude and area of the pulse wave obtained from the PG signal, and k_1 and k_2 are obtained empirically.

4. The method of Claim 2. wherein κ is obtained according to the following algorithm expression:

$$\kappa = \frac{1}{\left(\left(\frac{1}{PA}\right)+1\right)}$$

where PA is the amplitude of the pulse wave obtained from the PG signal.

5. The method of Claims 3 and 4 further comprising filtering out slow fluctuations in the pulse wave.

6. The method of Claim 5 wherein slow fluctuations in PEAK are filtered out by replacing PEAK in Claim 3 with PEAK/(slow component of PEAK)^2

7. The method of Claim 1, wherein the processing stipulated in step (a) for the calculation of the subject's systolic blood pressure includes the algorithmic expression

$$SP = \rho v^2 \Phi(\kappa, \gamma),$$

where ρ is the blood density, γ is the thermodynamic Poisson exponent of the blood, v is the pulse wave velocity and

$$\Phi = \frac{\sqrt{2\kappa(\gamma-1)^2 + 4\cdot(\gamma-1)+1}-1}{2(\gamma-1)}$$

8. The method of Claim 1, wherein the processing stipulated in step (a) for the calculation of the subject's systolic blood pressure includes the algorithmic expression

$$SP = (\log v^2)/\alpha + 2\rho\, v^2\kappa/3 + \lambda,$$

where ρ is the blood density, v is the pulse wave velocity, and $\lambda = (\log(2\rho R/E_0 h))/\alpha$, where R is the radius of the artery, E_0 is Young modulus referred to zero pressure, h is the thickness of the arterial wall and α is obtained empirically.

9. The method of Claim 1. wherein the processing stipulated in step (a) for the calculation of the subject's systolic blood pressure includes the algorithmic expression

$$SP = [(\log v^2)/\alpha + \lambda]/(1 - \kappa)$$

where v is the pulse wave velocity and $\lambda = (\log (2\rho R/E_0 h))/\alpha$, where R is the radius of the artery, E_0 is Young modulus referred to zero pressure, ρ is the blood density. h is the thickness of the arterial wall and α is obtained empirically.

10. The method of Claim 1, wherein the processing stipulated in step (a) for the calculation of the subject's systolic blood pressure includes the algorithmic expression

$$SP = (\log v^2/(1 - \varepsilon H^2))/\alpha + 2\rho v^2 \kappa/3 + \lambda$$

where ρ is the blood density, v is the pulse wave velocity, H is the heart rate, $\lambda = (\log (2\rho R/E_0 h))/\alpha$, where R is the radius of the artery, E_0 is Young modulus referred to zero pressure, h is the thickness of the arterial wall and ε and α are obtained empirically.

11. The method of Claim 1, wherein the processing stipulated in step (a) for the calculation of the subject's systolic blood pressure includes the algorithmic expression

$$SP = [(\log v^2/(1 - \varepsilon H^2))/\alpha + \lambda]/(1 - \kappa),$$

where, v is the pulse wave velocity, H is the heart rate, $\lambda = (\log (2\rho R/E_0 h))/\alpha$, where R is the radius of the artery, E_0 is Young modulus referred to zero pressure, h is the thickness of the arterial wall, ρ is the blood density, and ε and α are obtained empirically.

12. The method of Claim 1, wherein the processing stipulated in step (a) for the calculation of the subject's diastolic blood pressure includes the algorithmic expression

$$DP = SP - \rho v^2 \kappa,$$

where SP is the systolic pressure, ρ is the blood density, and v is the pulse wave velocity.

13. The method of Claim 1, wherein the processing stipulated in step (a) for the calculation of Young modulus of an artery of the subject includes the algorithmic expression

$$E = (2R/h)\,(SP-DP)/\kappa$$

where R is the radius of the artery, h is the thickness of the arterial wall, SP is the systolic pressure and DP is the diastolic pressure.

14. The method of Claim 1, wherein the processing stipulated in step (a) for the calculation of Young modulus of an artery of the subject includes the algorithmic expression

$$E = (2R/h)\,SP/\Phi\,(\kappa,\gamma)$$

where R is the radius of the artery, h is the thickness of the arterial wall, SP is the systolic pressure, γ is the thermodynamic Poisson exponent of the blood and

$$\Phi = \frac{\sqrt{2\kappa(\gamma-1)^2 + 4\cdot(\gamma-1)+1}-1}{2(\gamma-1)}$$

15. The method of Claim 1, wherein the processing stipulated in step (a) for the calculation of Young modulus of an artery of the subject includes the algorithmic expression

$$E = (2R/h)\cdot\rho\cdot\exp\,(-\lambda + MP)\alpha$$

where R is the radius of the artery, h is the thickness of the arterial wall, ρ is the blood density, $MP = (SP + 2\cdot DP)/3$ where SP is the systolic pressure, DP is the diastolic pressure wherein at least one of the systolic pressure or the diastolic pressure is obtained using an algorithmic expression involving κ, and $\lambda = (\log\,(2\rho R/E_0 h))/\alpha$ where E_0 is Young modulus referred to zero pressure and α is an empirically obtained constant.

16. The method of Claim 1, wherein the processing stipulated in step (a) for the calculation of Young modulus of an artery of the subject includes the algorithmic expression

$$E = (2R/h) \cdot \rho \cdot \exp((-\lambda + SP \cdot (1-\kappa))\alpha)$$

where R is the radius of the artery, h is the thickness of the artery wall, ρ is the blood density, SP is the systolic pressure and $\lambda = (\log(2\rho R/E_0 h))/\alpha$, wherein E_0 is Young Modulus referred to zero pressure and α is an empirically obtained constant.

17. The method of Claim 1, wherein the processing stipulated in step (a) for the calculation of the relative change in the cardiac output of a subject includes the algorithmic expression

$$CO = PEAK \cdot \{v \cdot [1 + SP/(2\rho \cdot v^2)]\}^2$$

where SP is a systolic pressure obtained using an algorithmic expression involving κ, ρ is the blood density, and v is the pulse wave velocity and

$$PEAK = k_1 \cdot PTT \cdot PA + k_2 \cdot AREA,$$

where PA and AREA are respectively the amplitude and area of the pulse wave peak obtained from a PG signal, and k_1 and k_2 are obtained empirically.

18. The method of Claim 14 further comprising filtering out slow fluctuations in the pulse wave.

19. The method of Claim 1, wherein the processing stipulated in step (a) for the calculation of the subject's cardiac resistance includes the algorithmic expression

$$VR = (SP - DP)/CO.$$

where any one or more of SP, DP, and CO are obtained from a calculation involving κ.

20. The method of Claim 1, wherein the processing stipulated in step (a) for the calculation of the relative change in the vascular compliance of a subject includes the algorithmic expression

$$VC = PEAK/(SP - DP),$$

Where

$$PEAK = k_1 \cdot PTT \cdot PA + k_2 \cdot AREA,$$

where PA and AREA are respectively the amplitude and area of the pulse wave obtained from the PG signal, and k_1 and k_2 are obtained empirically.

21. A method for determining continuously and non-invasively whether a change in a subject's blood pressure is due to a change in cardiac output or vascular compliance, comprising:

(a) substantially obtaining continuously and non-invasively the ratio, κ of the subject's blood flow velocity to the propagation speed of the subject's pulse wave;

(b) processing κ substantially in real time so as to obtain the instantaneous values of the subject's SP, CO and VC; and

(c) processing the subject's SP, CO, and VC in real time so as to obtain the instantaneous values of the algorithmic expression:

$$INDEX1 = \partial SP/\partial CO - \partial SP/\partial VC,$$

an increase in INDEX1 over time indicating a change in the subject's blood pressure due to a change in cardiac output, otherwise the change in the subject's blood pressure is due to a change in vascular compliance.

22. A method for determining continuously and non-invasively whether a change in a subject's blood pressure is due to a change in the subject's cardiac output or vascular resistance, comprising:

(a) substantially obtaining continuously and non-invasively the ratio, κ of the subject's blood flow velocity to the propagation speed of the subject's pulse wave;

(b) processing κ substantially in real time so as to obtain the instantaneous values of the subject's SP, CO and VR; and

(c) processing the subject's SP, CO, and VR in real time so as to obtain the instantaneous values of the algorithmic expression:

$$INDEX2 = \partial SP/\partial CO - \partial SP/\partial VR$$

an increase in INDEX2 over time indicating a change in the subject's blood pressure due to a change in cardiac output, otherwise the change in the subject's blood pressure is due to a change in vascular resistance.

23. A device for obtaining continuously and non-invasively one or more of the vascular parameters of a subject from the list comprising:

i. systolic blood pressure,

ii. diastolic blood pressure,

iii. Young's modulus of an artery,

iv. relative change in cardiac output,

v. relative change in vascular resistance, and

vi. relative changes in vascular compliance;

said device comprising:

(a) a device substantially obtaining continuously and non-invasively the ratio, κ of the subject's blood flow velocity to the propagation speed of the subject's pulse wave; and

(b) a device processing κ substantially in real time so as to obtain the instantaneous values of the desired parameters.

24. The device according to Claim 23 wherein κ is obtained by processing a PG signal and a PTT continuously and non-invasively obtained from the subject.

25. The device of Claim 24 wherein κ is obtained according to the following algorithmic expression:

$$\kappa = 1/(1/(PEAK \cdot v) + 1),$$

where v is inversely proportional to PTT, and

$$PEAK = k_1 \cdot PTT \cdot PA + k_2 \cdot AREA,$$

where PA and AREA are respectively the amplitude and area of the pulse wave obtained from the PG signal, and k_1 and k_2 are obtained empirically.

26. The device according to Claim 23, wherein κ is obtained according to the following algorithmic expression

$$\kappa = 1/((1/PA) + 1)$$

where PA is the amplitude of the pulse wave obtained from the PG signal.

27. The device of Claim 25 capable of filtering out slow fluctuations in the pulse wave.

28. The device of Claim 27 wherein slow fluctuations in the pulse wave are filtered out by replacing PEAK in Claim 22 with PEAK/(slow component of PEAK)^2

29. The device of Claim 23, wherein the processing stipulated in step (a) for the calculation of the subject's systolic blood pressure includes the algorithmic expression

$$SP = \rho v^2 \Phi(\kappa, \gamma),$$

where ρ is the blood density, γ is the thermodynamic Poisson exponent of the blood, v is the pulse wave velocity and

$$\Phi = \frac{\sqrt{2\kappa(\gamma-1)^2 + 4\cdot(\gamma-1)+1} - 1}{2(\gamma-1)}$$

30. The device of Claim 23, wherein the processing stipulated in step (a) for the calculation of the subject's systolic blood pressure includes the algorithmic expression

$$SP = (\log v^2)/\alpha + 2\rho\, v^2\kappa/3 + \lambda,$$

where ρ is the blood density, and $\lambda = (\log 2\rho R/E_0 h)/\alpha$, where R is the radius of the artery, E_0 is Young modulus referred to zero pressure, h is the thickness of the arterial wall and α is obtained empirically.

31. The device of Claim 23, wherein the processing stipulated in step (a) for the calculation of the subject's systolic blood pressure includes the algorithmic expression

$$SP = [(\log v^2)/\alpha + \lambda]/(1 - \kappa)$$

where v is the pulse wave velocity and $\lambda = (\log (2\rho R/E_0 h))/\alpha$, where R is the radius of the artery, E_0 is Young modulus referred to zero pressure, ρ is the blood density, h is the thickness of the arterial wall and α is obtained empirically.

32. The device of Claim 23, wherein the processing stipulated in step (a) for the calculation of the subject's systolic blood pressure includes the algorithmic expression

$$SP = (\log v^2/(1 - \varepsilon H^2))/\alpha + 2\rho v^2\kappa/3 + \lambda$$

where ρ is the blood density, v is the pulse wave velocity, H is the heart rate, $\lambda = (\log (2\rho R/E_0 h))/\alpha$, where R is the radius of the artery, E_0 is Young modulus referred to zero pressure, h is the thickness of the arterial wall and ε and α are obtained empirically.

33. The device of Claim 23, wherein the processing stipulated in step (a) for the calculation of the subject's systolic blood pressure includes the algorithmic expression

$$SP = [(\log v^2/(1 - \varepsilon H^2))/\alpha + \lambda]/(1 - \kappa),$$

where, v is the pulse wave velocity, H is the heart rate, $\lambda = (\log (2\rho R/E_0 h))/\alpha$, where R is the radius of the artery, E_0 is Young modulus referred to zero pressure, h is the thickness of the arterial wall, ρ is the blood density, and ε and α are obtained empirically.

34. The device of Claim 23, wherein the processing stipulated in step (a) for the calculation of the subject's diastolic blood pressure includes the algorithmic expression

$$DP = SP - \rho v^2\kappa,$$

where SP is the systolic pressure ρ is the blood density, and v is the pulse wave velocity.

35. The device of Claim 23, wherein the processing stipulated in step (a) for the calculation of Young modulus of an artery of the subject includes the algorithmic expression

$$E = (2R/h)\,(SP-DP)/\kappa$$

where R is the radius of the artery. h is the thickness of the arterial wall, SP is the systolic pressure and DP is the diastolic pressure.

36. The device of Claim 23, wherein the processing stipulated in step (a) for the calculation of Young modulus of an artery of the subject includes the algorithmic expression

$$E = (2R/h)\ SP/\Phi\ (\kappa,\gamma)$$

where R is the radius of the artery, h is the thickness of the arterial wall, SP is the systolic pressure, γ is the thermodynamic Poisson exponent of the blood and

$$\Phi = \frac{\sqrt{2\kappa(\gamma-1)^2 + 4\cdot(\gamma-1)+1} - 1}{2(\gamma-1)}$$

37. The device of Claim 23, wherein the processing stipulated in step (a) for the calculation of Young modulus of an artery of the subject includes the algorithmic expression

$$E = (2R/h)\cdot\rho\cdot\exp\ (-\lambda+MP)\alpha$$

where R is the radius of the artery, h is the thickness of the arterial wall, ρ is the blood density, MP = (SP+ 2·DP)/3 where SP is the systolic pressure, DP is the diastolic pressure wherein at least one of the systolic pressure or the diastolic pressure is obtained using an algorithmic expression involving κ, and $\lambda = (\log(2\rho R/E_0 h))/\alpha$ where E_0 is Young modulus referred to zero pressure and α is an empirically obtained constant.

38. The device of Claim 35, wherein the processing stipulated in step (a) for the calculation of Young modulus of an artery of the subject includes the algorithmic expression

$$E = (2R/h)\cdot\rho\cdot\exp\ ((-\lambda+SP\cdot(1-\kappa))\alpha$$

where R is the radius of the artery, h is the thickness of the artery wall, ρ is the blood density, SP is the systolic pressure and $\lambda = (\log(2\rho R/E_0 h))/\alpha$, wherein E_0 is Young Modulus referred to zero pressure and α is an empirically obtained constant.

39. The device of Claim 23, wherein the processing stipulated in step (a) for the calculation of the relative change in the cardiac output of a subject includes the algorithmic expression

$$CO = PEAK \cdot \{v \cdot [1 + SP/(2\rho \cdot v^2)]\}^2$$

where SP is a systolic pressure obtained using an algorithmic expression involving κ and

$$PEAK = k_1 \cdot PTT \cdot PA + k_2 \cdot AREA,$$

where PA and AREA are respectively the amplitude and area of the pulse wave obtained from a PG signal, and k_1 and k_2 are obtained empirically.

40. The device of Claim 23, wherein the processing stipulated in step (a) for the calculation of the subject's cardiac resistance includes the algorithmic expression

$$VR = (SP - DP)/CO.$$

where any one or more of SP, DP, and CO are obtained from a calculation involving κ.

41. A device determining continuously and non-invasively whether a change in a subject's blood pressure is due to a change in cardiac output or vascular compliance, comprising:

(a) a device substantially obtaining continuously and non-invasively the ratio, κ of the subject's blood flow velocity to the propagation speed of the subject's pulse wave;

(b) a device processing κ substantially in real time so as to obtain the instantaneous values of the subject's SP, CO and VC; and

(c) a device processing the subject's SP, CO, and VC in real time so as to obtain the instantaneous values of the algorithmic expression:

$$INDEX1 = \partial SP/\partial CO - \partial SP/\partial VC,$$

an increase in INDEX1 over time indicating a change in the subject's blood pressure due to a change in cardiac output, otherwise the change in the subject's blood pressure is due to a change in vascular compliance.

42. A device determining continuously and non-invasively whether a change in a subject's blood pressure is due to a change in the subject's vascular resistance comprising:

(a) a device substantially obtaining continuously and non-invasively the ratio, κ of the subject's blood flow velocity to the propagation speed of the subject's pulse wave;

(b) a device processing κ substantially in real time so as to obtain the instantaneous values of the subject's SP, CO and VR; and

(c) a device processing the subject's SP, CO, and VR in real time so as to obtain the instantaneous values of the algorithmic expression:

$$INDEX2 = \partial SP/\partial CO - \partial SP/\partial VR,$$

an increase in INDEX2 over time indicating a change in the subject's blood pressure due to a change in cardiac output, otherwise the change in the subject's blood pressure is due to a change in vascular resistance.

DATED this 23rd day of JULY 2001

McCALLUM, RADEMEYER & FREIMOND
Patent Agents for the Applicant

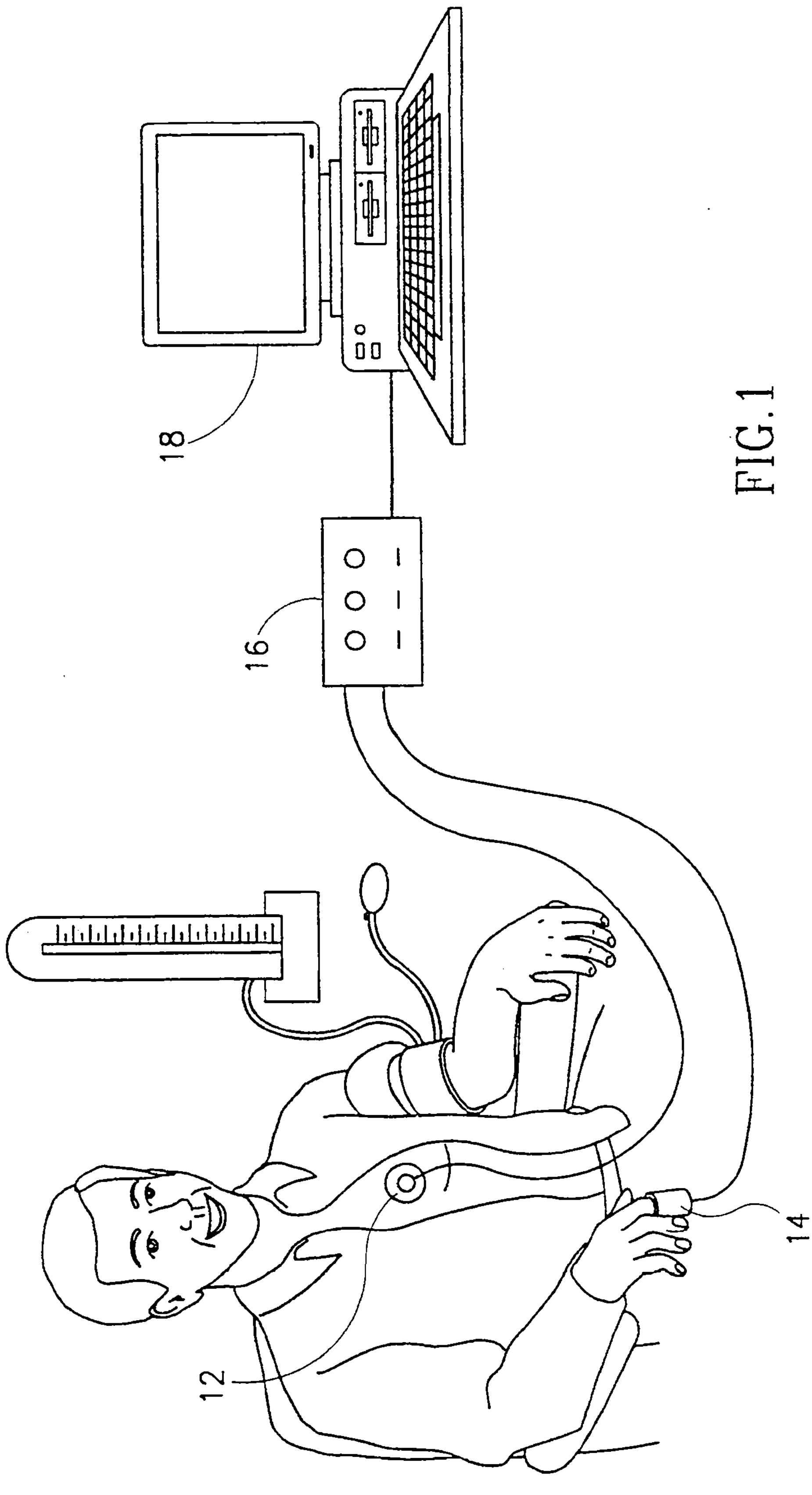
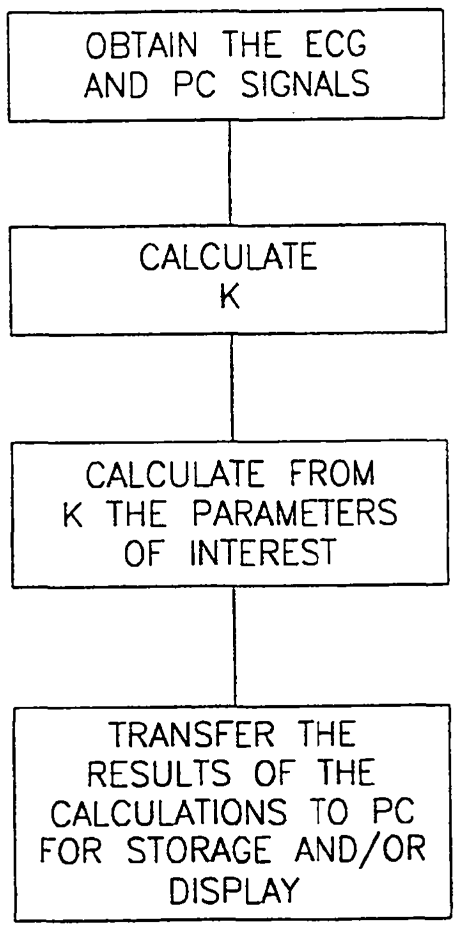


FIG.1


OBTAIN THE ECG
AND PC SIGNALS
CALCULATE
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CALCULATE FROM
K THE PARAMETERS
OF INTEREST
TRANSFER THE
RESULTS OF THE
CALCULATIONS TO PC
FOR STORAGE AND/OR
DISPLAY

FIG.2