(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
15 November 2012 (15.11.2012)

WIPO | PCT

(10) International Publication Number
WO 2012/155133 A2

(51) International Patent Classification:
A61B 5/02 (2006.01) *A61B 5/08* (2006.01)
A61B 5/0285 (2006.01)

(21) International Application Number:
PCT/US2012/037771

(22) International Filing Date:
14 May 2012 (14.05.2012)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/485,334 12 May 2011 (12.05.2011) US

(71) Applicant *(for all designated States except US)*: **THE JOHNS HOPKINS UNIVERSITY** [US/US]; 3400 North Charles Street, Baltimore, Maryland 21218 (US).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **SILBER, Harry A.** [US/US]; 1651 Bullock Circle, Owings Mills, Maryland 21117 (US).

(74) Agent: **RYAN, Louisa T.**; 100 N. Charles Street, 5th Floor, Baltimore, Maryland 21201 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

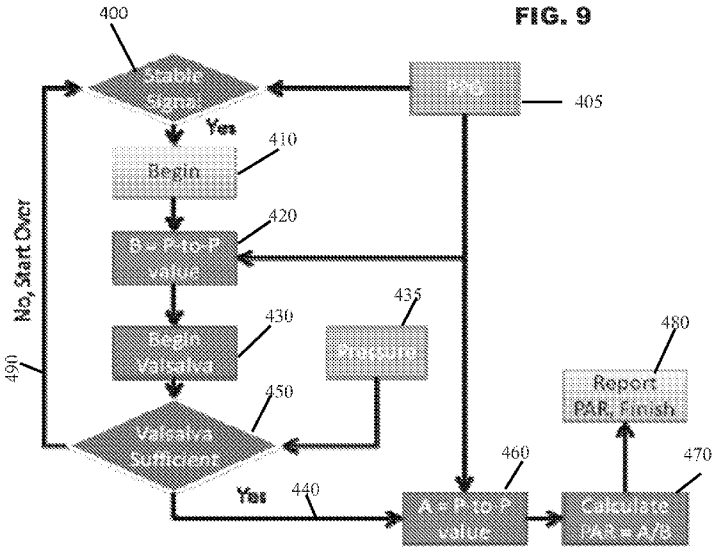
(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

(54) **Title**: AUTOMATED PROCESS FOR ASSESSING CARDIAC FILLING PRESSURE NON-INVASIVELY

FIG. 9



(57) **Abstract**: An embodiment in accordance with the present invention provides an automated device and method for determining cardiac filling pressure non-invasively. The device includes a computer readable medium programmed to analyze a photoplethysmography signal having a pulse amplitude. The analysis is done to determine a point in time that the pulse amplitude of the photoplethysmography signal does not vary by a predetermined amount over a first predetermined time period. The method also includes displaying instructions for the user to prepare for and begin an expiratory effort. The expiratory effort of the user is compared to a predetermined goal range for expiratory effort, and an indicator of the user's expiratory effort relative to the predetermined goal range is displayed on the user interface.

WO 2012/155133 A2

AUTOMATED PROCESS FOR ASSESSING CARDIAC FILLING PRESSURE NON-INVASIVELY

CROSS REFERENCE TO RELATED APPLICATION

This application claims the benefit of U.S. Provisional Patent Application No. 61/485,334 filed May 12, 2011, which is incorporated by reference herein, in its entirety.

FIELD OF THE INVENTION

The present invention relates generally to cardiac care. More particularly, the present invention relates to a method for assessing cardiac filling pressure.

BACKGROUND OF THE INVENTION

Heart failure is a prevalent diagnosis and is increasing at an annual growth rate of 10.5%. Additionally, more than 1 million hospital discharges per year have a primary diagnosis of heart failure, the most common discharge diagnosis. Patients admitted to the hospital with Congestive Heart Failure (CHF) symptoms from severe fluid overload usually have had fluid build-up without symptoms for days or weeks prior to admission. Detection of elevated fluid prior to symptoms could prevent admissions for "acute" decompensated heart failure. Also, many patients with CHF are inadequately diuresed at discharge (i.e., not enough fluid has been removed prior to discharge). This, typically leads to re-admission of the patient for CHF. The rate of rehospitalization for heart failure is very high; about 20% at 30 days after discharge, and about 30% at 60-90 days after discharge.

As is known to those skilled in the art, measurement of left ventricular filing pressure (LVFP) allows detection of CHF and helps assessment of the efficacy of therapy for CHF. Left ventricular pressure can be measured directly by placing a catheter in the left ventricle to obtain the end diastolic pressure (LVDEP) or indirectly by placing a catheter in the pulmonary artery to measure the pulmonary capillary wedge pressure (PCWP). It should be noted that measuring LV filing pressure using a catheter is generally considered the gold

standard. The pulmonary artery catheterization (PAC) technique that is used to measure either LVFP or PCWP is considered an invasive surgical procedure. Thus, there are attendants risks and costs associated with such a technique and the reported complications include catheter migration, arrhythmias, pulmonary artery rupture, thrombosis, infection, bleeding and pneumothorax.

Physical examination of a patient has poor sensitivity for detecting elevated cardiac filing pressure, especially in patients with chronic heart failure. Some common aids use to help in the diagnosis of elevated LVFP include chest X-ray, serum biomarkers (BNP, pro_BNP) and echocardiography. These techniques have important practical limitations. Also, clinical and radiographic methods of detecting CHF are generally insensitive to alterations in LVFP.

There have been attempts made to develop a non-invasive method and system for estimating LVFP to allow for early detection and treatment of CHF, which has been shown to reduce the rate of hospitalization and mortality. A non-invasive method of assessing PCWP has been reported that uses the strain phase of the Valsalva maneuver. In a Valsalva maneuver, the subjects or patients perform a forced expiration into a closed tube or strain against a closed glottis. This results in a unique, well-described cardiovascular response, involving both a rise and fall in arterial pressure and a momentary opposite-direction change in right and left heart stroke volume. The effect of the Valsalva maneuver on blood pressure for a normal heart and a heart diagnosed with heart failure is shown in FIG. 1.

In this method a non-invasive pulmonary tonometer and a digital pulmonary monitor is used to continuously acquire arterial and expiratory pressure signals during a Valsalva maneuver. A software program also is used to analyze the arterial pressure signals and derive a LVEDP using a predictive algorithm. The tonomter is not easy to use and is located on the wrist or finger. While this system is not yet commercially available it is expected to cost in

the tens of thousands of dollars. The tonometer also is not as widely used a technology as compared to some other medical devices.

Another reported non-invasive technique is referred to as impedance cardiography (ICG). In the ICG technique, four electrodes are placed around the neck and lower thorax and four electrodes are placed on the lateral surface of the abdomen. In this arrangement the outer sensors transmit current and the inner sensors measure impedance. The impedance being measured across the chest is related to fluid volume; thus it can be used to measure changes in fluid volume. However, such measurements do not reflect absolute measurements of LVEDP. The cost for such a device also is in the tens of thousands.

Thus, there is a continuing need to develop non-invasive systems and methods for assessing cardiac filing pressure, more specifically LV filing pressure. It also would be desirable to provide such a device that provides similar useful clinical information as prior art systems and methods. Such systems preferably would be less costly than prior art systems, would use a robust transducer and such methods would not involve or require a greater skill set than that required for user of prior art methods. Moreover, it would be desirable to provide a device or system whose operation is automated and therefore simple enough for a patient or the like to use at home.

SUMMARY OF THE INVENTION

The foregoing needs are met, to a great extent, by the present invention, wherein in one aspect a method for automating a process for determining cardiac filling pressure non-invasively includes analyzing a photoplethysmography signal having a pulse amplitude. The analysis is done to determine a point in time that the pulse amplitude of the photoplethysmography signal does not vary by a predetermined amount over a first predetermined time period. The method also includes displaying an instruction on a user

interface to inform a user that an instruction to initiate an expiratory effort will be displayed. An instruction is displayed on the user interface informing the user to begin an expiratory effort. The expiratory effort of the user is compared to a predetermined goal range for expiratory effort, and an indicator of the user's expiratory effort relative to the predetermined goal range is displayed on the user interface.

In accordance with another embodiment of the present invention a method for automating a process for determining cardiac filling pressure non-invasively includes programming a computer readable medium to execute steps for the method. These steps include analyzing a photoplethysmography signal having a pulse amplitude. The analysis is done to determine a point in time that the pulse amplitude of the photoplethysmography signal does not vary by a predetermined amount over a first predetermined time period. Another step includes transmitting a first instruction to be displayed on a user interface, said instruction informing a user that an instruction to initiate an expiratory effort will be displayed. The method also includes transmitting a second instruction to be displayed on the user interface, said instruction informing the user to begin an expiratory effort. The expiratory effort of the user is compared to a predetermined goal range for expiratory effort. Additionally, a third instruction is transmitted to be displayed on the user interface, said instruction indicating the user's expiratory effort relative to the predetermined goal range on the user interface.

In accordance with yet another aspect of the present invention, the method further includes instructing the user to sustain the expiratory effort for a second predetermined period of time. The method can also include displaying an elapsed time for the expiratory effort as well as a time remaining in the second predetermined period of time.

It is indicated to the user that the data acquisition sequence is invalid, when the expiratory effort does not meet the predetermined goal range within a third predetermined period of

time. It can also be indicated to the user that the data acquisition sequence is invalid when the expiratory effort exceeds the predetermined range for expiratory effort. After the predetermined amount of time has elapsed it is displayed that the user can cease the expiratory effort. A first average of the pulse amplitude of the photoplethysmography signal can be calculated for a fourth predetermined period of time before the user ceases the expiratory effort. A second average of the pulse amplitude of the photoplethysmograpy signal can also be calculated for a fifth period of time before an initiation of the expiratory effort. Additionally, a pulse amplitude ratio of the first average of the pulse amplitude to the second average of the pulse amplitude can be calculated. These steps can also be programmed into the computer, computer readable medium or any other device for executing the steps known to one of skill in the art.

In accordance with another aspect of the present invention, an apparatus for automating a process for determining cardiac filling pressure non-invasively, includes a device including a housing, said device having a user interface disposed within said housing. The device also includes an expiratory effort reception apparatus being coupled to said housing. A photoplethysmograph is also coupled to the housing. A computer readable medium is also included and is programmed to execute steps to determine cardiac filling pressure. The computer readable medium is programmed to analyze a signal from the photoplethysmograph. The signal has a pulse amplitude, and the analysis is done to determine a point in time that the pulse amplitude of the signal does not vary by a predetermined amount over a first predetermined time period. The computer readable medium is also programmed to transmit a first instruction to be displayed on a user interface, said instruction informing a user that an instruction to initiate an expiratory effort will be displayed. A second instruction is transmitted to be displayed on the user interface, said instruction informing the user to begin an expiratory effort. The expiratory effort of the user

to a predetermined goal range for expiratory effort is calculated. Additionally, a third instruction is transmitted to be displayed on the user interface, said instruction indicates the user's expiratory effort relative to the predetermined goal range on the user interface.

BRIEF DESCRIPTION OF THE DRAWINGS

The accompanying drawings provide visual representations which will be used to more fully describe the representative embodiments disclosed herein and can be used by those skilled in the art to better understand them and their inherent advantages. In these drawings, like reference numerals identify corresponding elements and:

FIG. 1 illustrates a graphical view illustrating the effect of the Valsalva maneuver on blood pressure for a normal heart and a heart with heart failure.

FIG. 2 illustrates a high level flow diagram of a methodology for assessing cardiac filing pressure non-invasively according to the present invention.

FIG. 3A illustrates a block diagram of an exemplary system for assessing cardiac filing pressure non-invasively according to the present invention.

FIG. 3B illustrates a block diagram of another exemplary system for assessing cardiac filing pressure non-invasively according to the present invention.

FIG. 3C illustrates a block diagram of yet another exemplary system for assessing cardiac filing pressure non-invasively according to the present invention.

FIG. 3D illustrates a block diagram of yet another exemplary system for assessing cardiac filing pressure non-invasively according to the present invention.

FIGS. 3E-H illustrate various block diagrams illustrating a device according to the present invention used in various communication environments.

FIG. 4 illustrates graphical view of a photoplethysmography signal and of invasively measured blood pressure during the Valsava maneuver.

FIG. 5 illustrates a graphical view of a photoplethysmography waveform and the

expiratory pressure waveform for a heart with a normal filing pressure using the system of the present invention.

FIG. 6 illustrates a graphical view of a photoplethysmography waveform and the expiratory pressure waveform for a heart with an elevated filing pressure using the system of the present invention.

FIG. 7 illustrates a graphical view of a photoplethysmography waveform and the expiratory pressure waveform for a heart of a patient that had been initially diagnosed as being fluid overloaded, but which it was later determined that the heart had a normal filing pressure using the system of the present invention.

FIG. 8 illustrates a graphical view of LVEDP by catheter versus Average Pulse Amplitude Ratio for a patient study, where the pulse amplitude ratios were determined using the system of the present invention.

FIG. 9 illustrates a flow chart of a method of automation for determining cardiac filling pressure non-invasively, according to an embodiment of the invention.

FIG. 10 illustrates a diagram of a method of automation for determining cardiac filling pressure non-invasively, according to an embodiment of the invention.

DETAILED DESCRIPTION

The presently disclosed subject matter now will be described more fully hereinafter with reference to the accompanying Drawings, in which some, but not all embodiments of the inventions are shown. Like numbers refer to like elements throughout. The presently disclosed subject matter may be embodied in many different forms and should not be construed as limited to the embodiments set forth herein; rather, these embodiments are provided so that this disclosure will satisfy applicable legal requirements. Indeed, many modifications and other embodiments of the presently disclosed subject matter set forth

herein will come to mind to one skilled in the art to which the presently disclosed subject matter pertains having the benefit of the teachings presented in the foregoing descriptions and the associated Drawings. Therefore, it is to be understood that the presently disclosed subject matter is not to be limited to the specific embodiments disclosed and that modifications and other embodiments are intended to be included within the scope of the appended claims.

An embodiment in accordance with the present invention provides an automated device and method for determining cardiac filling pressure non-invasively. The device includes a computer readable medium programmed to analyze a photoplethysmography signal having a pulse amplitude. The analysis is done to determine a point in time that the pulse amplitude of the photoplethysmography signal does not vary by a predetermined amount over a first predetermined time period. The method also includes displaying instructions for the user to prepare for and begin an expiratory effort. The expiratory effort of the user is compared to a predetermined goal range for expiratory effort, and an indicator of the user's expiratory effort relative to the predetermined goal range is displayed on the user interface.

FIG. 2 illustrates a high level flow diagram of a methodology for assessing cardiac filing pressure non-invasively according to the present invention. Reference also should be made to FIGS. 3A-D which illustrate various block diagrams of systems **200***a-d* for assessing cardiac filing pressure non-invasively according to the present invention that can include details and features not shown in FIG. 2. Reference also should be made to FIGS. 3E-H which are various block diagrams illustrating various ways in which a system **200** or a device embodying such a system (whole or in part) along with one of a number of communication techniques whereby the system or device can transmit or communicate information to for example, the practitioner or a monitoring service. Before describing the methodology, the

illustrative composition of such each system **200***a-d* of the present invention is first described.

FIG. 3A illustrates a block diagram of a device **200***a* according to an embodiment of the invention. The device **200***a* includes an optical pulse volume sensing device **210** and a pressure transducer **220**. A means for determining a pulse amplitude ratio uses the pulse amplitude as determined from output signals from the optical pulse volume sensing device. The measure of the pulse amplitude is taken near the end of the expiratory effort as determined from the outputs from the pressure transducer and a baseline pulse amplitude as determined from output signals from the optical pulse volume sensing device. The device also includes a means for assessing the determined pulse amplitude ratio so as to determine a filing pressure condition for the heart of the patient.

Also as illustrated in FIG. 3A, the optical pulse volume sensing device **210** is configured and arranged so it can be located on, and removably secured to, a finger **2** or digit of a patient or subject and so that the optical pulse volume sensing device senses a change in volume cause by the pressure pulse. The pressure transducer **220** is configured and arranged to be fluidly coupled to a mouth **4** of the patient, such that the pressure transducer measures expiratory pressure of the a patient. Preferably, the optical pulse volume sensing device **210** is a photoplethysmography (PPG) transducer and the pressure transducer **220** is any one of a number of devices known to those skilled in the art and appropriate for the intended use.

The pressure transducer **210**, illustrated in FIG. 3A, is operably coupled to a mouth piece **212** and/or tubing **214**, so that the pressure transducer is remote from the patient's mouth **4**. One end of the mouth piece **212** or the tubing **214** is fluidly coupled to the mouth. Preferably, one end of the mouth piece **212** is removably, fluidly coupled to the mouth using any of a number of techniques known to those skilled in the art, and the other end of the

mouth piece and an end of the tubing are fluidly coupled or joined to each other to form a unitary structure.

As illustrated in FIG. 3B, there is shown another system **200***b* according to the present invention that is configured and arranged so as to include a positive pressure delivery device **280** that is selectively fluidly coupled to the tubing **214** and operably and/or communicatively coupled to the microprocessor **230**. The microprocessor **230** controls the positive pressure delivery device **280**, so that a pressurized breathing gas mixture (e.g., air) is delivered to the patient via the tubing **214** for a predetermined period of time. Suggested times for the expiratory effort are described herein. The microprocessor **230** controls the positive pressure delivery device **280**, so that a pressurized breathing gas mixture of different pressures is delivered to the patient. The a positive pressure delivery device **280** includes a source of the breathing mixture (e.g., tank, or connection to a delivery system) and a valve that is interposed between the breathing mixture source and the tubing **214**. The valve is operably coupled to the microprocessor **230**, whereby the microprocessor controls the valve for selectively delivering the breathing mixture to the patient. In further embodiments, the valve also is of the type that is controllable so as to deliver gas mixtures at different pressures.

FIGS. 3C, D illustrate exemplary systems **200***b-c* that further include a device **285***a,b* that allows the acquisition of information that the clinician can use to assess or determine the arterial stiffness or central arterial stiffness (e.g., the pulse wave velocity, PWV) of the patient. Some studies have shown that central arterial stiffness can affect the Pulse Amplitude Ratio. Thus, taking into account central arterial stiffness can improve the accuracy of the device for evaluating cardiac filling pressure. The device can take the form of another photoplethysmography (PPG) transducer **285***a*, as illustrated in FIG. 3C, that is located on or attached to a toe of the patient, but any suitable device for the purpose could be used. An ECG signal lead **285***b*, as illustrated in FIG. 3D, is attached to one finger of each hand. Either

of these two provided outputs can be used in combination with any of a number of techniques known to those skilled in the art to provide a mechanism by which the clinician can ascertain the central arterial stiffness of the patient.

The means for determining a pulse amplitude ratio and the means for assessing the determined pulse amplitude ratio are embodied in a microprocessor **230** that is communicatively coupled to each of the pressure transducer **220** and the optical pulse volume sensing device **210**. The functionalities are coupled by cables **236**, as is known to those skilled in the art and appropriate for the intended use (e.g., electrical cables, optical cables). Such a microprocessor **230** includes random access memory, cache and other functionalities (not shown) that allow the microprocessor to function in the intended manner. The microprocessor **230** is embodied in any of a number of computers, as are known to those skilled in the art.

An applications program for execution on the microprocessor **230** is provided, as well. The applications program controls operation of the system and the microprocessor. It is within the skill of those knowledgeable in the computer or software arts to develop such an applications program based on the disclosure herein, including the following discussion regarding the methodology of the present invention. In particular, the applications program includes program or code segments and instructions and criteria for determining the pulse amplitude ratio from the output signals from the pressure transducer and the optical pulse volume sensing device.

One or more storage devices **232** are operably coupled to the microprocessor **230** for storage of, for example, the applications program, the operating system and any data or input information as directed by the user and/or the applications program. Such a storage device is any of a number of devices known to those skilled in the art and includes magnetic hard drives, and flash storage devices that embody flash or non-volatile flash memory. Also

operably coupled to the microprocessor **230** is/are one or more input devices **234** such as a keyboard and/or mouse that allow the user to control operation of the microprocessor.

In the case where the microprocessor **230** is not embodied in a computer, the microprocessor **230** is further configured and arranged so it can be operably coupled to a computer **270**, for example via removable cables **237** (e.g., USB cables). In this way, information temporarily stored in the storage device **232** can be uploaded to the computer for further analysis and/or long term storage or to allow communication of data and information to another via a network, an external communication system or via a recording medium (e.g., optical disk, magnetic recording medium).

In further embodiments, the microprocessor **230** also is operably coupled to an output display **250** and a printing device **240**. The output display **250** can take the form of any of a number of display devices as are known to those skilled in the art or hereinafter developed that are appropriate for inter connection with a microprocessor and for displaying information thereon that is communicated from the microprocessor. The printing device **240** can take the form of any of a number of devices known to those skilled in the art or hereinafter developed that are appropriate for inter connection with a microprocessor and for printing information there from and communicated from the microprocessor.

In embodiments or aspects of the present invention, the microprocessor **230** and other functionalities of the systems **200***a-d* are intended to be disposed within any of a number of enclosures known to those skilled in the art to form a device that can be configured to have varying degrees of portability, for example, from being located on a rolling cart to being put in the coat of the medical personnel using the device. As such, the output display **250** and/or printing device **240** also can be any of a number of devices that can be co-located in such an enclosure with the microprocessor **230** and other functionalities of the system **200***a-d*. Preferably, to increase portability for home and patient use, the enclosure and display are

integrated and are portable in size. There are a number of devices or existing platforms known to those skilled (e.g., Wellch Allyyn Spot Vital Signs Model 42NOB-E1) that can be configured to acquire patient data and are operably couplable to an optical pulse volume sensing device. Thus, it also is contemplated and thus within the scope of the present invention to adapt such existing platforms or devices so as to carry out any functions described herein for the systems **200***a-d* of the present invention.

The system of the present invention also are configurable so that it is free-standing, on a rolling cart, or portable. Such a system is also configurable so that it can be used in an outpatient clinic, an emergency department, a medical ward, an intensive care unit, skilled care facilities, assisted living facilities, or home or used by home services such as for example a visiting nursing service.

The system **200***a-d* further includes a pressure display **260** that is operably coupled to the pressure transducer **220** to provide a local display of the expiratory pressure/pressurized inspiratory pressure. Such a display is used by the medical personnel and/or the patient to determine that the expiratory pressure of the patient is at the value desired for a given measurement process. Thus, the pressure display **260** is any of a number of digital or analog displays or pressure measurement devices that are appropriate for the intended use and anticipated pressures or pressure ranges. In more particular embodiments, the pressure display **260** is configurable to further provide a display of elapsed time.

The device can include an enclosure configured to from a portable device, where the device is further configured and arranged so as to be in a form that is usable by a patient or other persons that do not have specific medical training outside a clinical setting (e.g., the home of a patient) and without the aid or guidance of a clinical practitioner or other medical personnel, or the device is usable by medical personnel (e.g., visiting nurse or nursing aid) outside the clinical setting (e.g., patient's home). For example, the device is preferably

configured to execute the method described below, such that the device provides a simple automated method of assessing cardiac filling pressure non-invasively.

The device is configured and arranged with one or more communication interfaces **310**, illustrated in FIGS. 3E-3H, so that the user of the device (e.g., patient, practitioner, visiting nurse, technician, clinical personnel) can easily transmit or communicate the data acquired and/or determined using the device (i.e., acquired information), directly or ultimately to the practitioner who should receive such clinical information. For example, the information being transmitted can be communicated directly to a computer or storage device under the control of the practitioner or to a monitoring service that subsequently transmits the acquired information to the practitioner also using any of a number of techniques known to those skilled in the art. In another example, data can be acquired by a monitoring service in a clinical setting or from patient's home and then communicated to the practitioner or their office.

FIGS. 3E-H also illustrate that the one or more communication interfaces **310***a-d* provide a mechanism by which the device **300***a-d* can be communicatively coupled to any of a number of communication systems known or hereinafter created so that the acquired information can be transmitted or communicated over such a communication system.

More particularly, FIG. 3E illustrates one exemplary device **300***a* according to the present invention that includes an interface **310***a*, such as a modem or equivalent, which is operably coupled to the microprocessor **230** and to a telephone phone system **10** via a hard land line **302** (e.g., copper, optical). As is known to those skilled in the art, such an interface **310** is configured and arranged so that the microprocessor can communicate information over the telephone system **10** to another device that is similarly operably coupled to the telephone system. In this way, the clinical information obtained using the device **300***a* can be communicated to one or both of the practitioner **320** or a monitoring service **330** via the

telephone system. As illustrated in FIG. 3E, the monitoring service is communicatively coupled to the practitioner using any of a number of communication techniques know to those skilled in the art.

FIG. 3F illustrates a second exemplary device **300***b* that includes an interface **310***b*, as is known to those skilled in the telephone arts for wirelessly (e.g., using RF transmissions) coupling the second exemplary device **300***b* to a wireless telephone system **20**. As is known to those skilled in the art, such a wireless telephone system **20** includes an antenna **22** or tower that receives the signals from a wireless device and also can be coupled to a wired telephone system or another wireless telephone system so as to allow a communication link between the second exemplary device **300***b* and another device. Such an interface **310***b* is operably coupled to the microprocessor **230** and generally includes an antenna so that wireless (RF) signals pass between the wireless telephone phone system **20** and the exemplary second device **300***b*.

Such a wireless interface **310***b* allows the microprocessor **230** to communicate information via RF transmission to/from the telephone system **20** and thus onto another device that is similarly operably coupled to the telephone system. In this way, the clinical information obtained using the device **300***b* can be communicated to one or both of the practitioner **320** or a monitoring service **330** or monitoring apparatus via the telephone system. As illustrated in FIG. 3F, the monitoring service is communicatively coupled to the practitioner using any of a number of communication techniques know to those skilled in the art.

FIG. 3G illustrates a third exemplary device **300***c* that includes an interface **310***c* for communicatively coupling the third exemplary device to a network **30** (e.g., WAN, LAN), which in turn can be communicatively coupled to the internet **40**. In the illustrated embodiment, the interface **310***c* is any of a number of devices as is known to those skilled in

the art so that the device can be communicatively coupled via a hard line **304** (e.g., optical, copper, shielded cable).

FIG. 3H illustrates a a fourth exemplary device **300***d* including an interface **310***d* that is configured and arranged to communicate with a wireless hub or router **52** so as to thereby create a wireless network **50**. In further embodiments, the wireless network **50** is a part of a larger network **60**. In yet further embodiments, a plurality of devices **300***c* can be coupled to either network **30**, **50**, **60** at any time. Interfaces **310** *c,d* are configured and arranged so that the microprocessor **230** can communicate information over a complimentary network **30**, **50**, **60** to another device that is similarly operably coupled to the network. In this way, the clinical information obtained using either of the devices **300** *c,d* can be communicated to one or both of the practitioners **320** or a monitoring service **330** via the network **30**, **50**, **60**.

As illustrated in FIGS. 3G, H, the monitoring service **330** or monitoring apparatus is communicatively coupled to the practitioner **320** using any of a number of communication techniques know to those skilled in the art. For example, the monitoring apparatus can communicate directly with the practitioner, through the network **30**, **50**, **60** and/or through the internet **40**.

The network can be operably coupled to the internet **40**, so that information from the third or fourth exemplary device **310***c,d* is communicated via the network **30**, **50**, **60** and internet **40** to the monitoring service **330** or the practitioner **320**. In the case where the provided device **300***c,d* is in a non-clinical setting, for example, the communication interface and device are configurable so that the user can couple the device to the patient's internet connection. The user can be the patient, a person who has no specific medical training or it can be a medically trained person such a visiting nurse or aid. Thus, the acquired information can be transmitted or communicated via that connection to the monitoring service or practitioner.

The foregoing is illustrative of a number of communication techniques; however the foregoing shall not be considered limiting. It is well within the scope of the present invention for those skilled in the communication arts to adapt known or hereinafter developed communication systems and interfaces so that acquired information can be communicated from the device **300** or systems **200***a-d* according to the present invention to a practitioner or monitoring service or monitoring station.

As indicated above, the methodology of the present invention is illustrated in the flow diagram shown in FIG. 2. In the following discussion, the reference to a system **200** shall be understood to mean a reference to any of the systems described herein. When the clinician intends to assess the cardiac filing pressure of a patient non-invasively using the system **200** of the present invention, the clinician, technician, medical personnel, or patient provides and arranges the optical pulse volume sensing device **210** on a finger **2** or digit of a patient or subject. The optical pulse volume sensing device senses a change in volume caused by the pressure pulse, Step **100**. The medical professional or patient also provides and fluidly couples a pressure transducer **220** to the patient's mouth **4**, so that the pressure transducer thereafter measures expiratory pressure or inspiratory pressure, Step **102**. It should be recognized that these steps can be done in any order.

When so arranged, the optical pulse volume sensing device **210** such as a PPG, senses a change in volume caused by the pressure pulse by illuminating the skin with light from an LED and then measuring the amount of light either transmitted or reflected to a photodiode. The optical pulse volume sensing device **210** provides an output of a pulse pressure signal of cardiac circulatory flow. As also indicated herein, providing and fluidly coupling of the pressure transducer **220** can further include providing a mouth piece and/or tubing, one end of which is fluidly coupled to the patient's mouth. In such a case, the pressure transducer also

is disposed in either the mouth piece or tubing so the pressure transducer is remote from the mouth.

After so providing, arranging and coupling the optical pulse volume sensing device **210** and the pressure transducer **220**, pressure data as a function of time or measurements of the patient's pulse amplitude is acquired using the optical pulse volume sensing device **210**, Step **104**. In accordance with the specific directions of the medical procedure controlling the assessment process, the patient is directed to breathe through the mouth piece and/or tubing **212**,**214** so as to maintain a desired expiratory pressure for a desired period of time, Step **106**. Alternatively, the positive pressure delivery device **280** is controlled so a desired inspiratory pressure is delivered for a predetermined period of time. As indicated herein, a pressure display **260** is provided to assist the patient in maintaining the desired expiratory pressure. While such expiration or positive pressure inspiration is occurring, the expiratory/inspiratory pressure is measured or pressure data is acquired as a function of time using the pressure transducer **220**, Step **108**.

The expiratory or positive pressure inspiratory pressure condition (e.g., desired expiratory pressure) is maintained for a period of 10 or more seconds or 10 or less seconds, or about 10 seconds or in the range of from about 8 to about 12 seconds. The expiratory or positive pressure inspiratory pressure condition is maintained at about 20 mmHg, or at least 20 mmHg, or in the range of from about 20 mmHg to about 35 mmHg, or in the range of from about 10 mmHg to about 50 mmHg. In the case where a plurality of pulse amplitude ratios are to be obtained, (as discussed further herein in connection with Step **110**) and where at least one of the plurality of pulse amplitude ratios is determined under a different expiratory pressure or a different positive pressure inspiratory pressure; each of the different expiratory/positive pressure inspiratory pressures is in the range of from about 10 mmHg to about 50 mmHg. As indicated herein, the pressure display **260** also can include a display of

time or elapsed time so that the patient can maintain the desired expiratory pressure for the specified time period.

It is within the scope of the present invention to obtain one or more, a plurality or a multiplicity of pressure amplitude ratios under the same expiratory or positive pressure inspiratory pressure conditions or where the expiratory or positive pressure inspiratory pressure conditions differ at least for one of the pulse volume amplitude ratios or per a desired pattern of expiratory pressure conditions. Thus, the specific directions of the medical procedure controlling the assessment process are reviewed initially to determine if more than one pressure amplitude ratio is to be obtained or not. Thus, after the expiratory pressure or positive pressure inspiratory pressure and pulse pressure information or data is acquired, the status of the assessment process is evaluated and a determination is made as to whether the data acquisition process for the intended assessment process is complete, Step **110**. If data acquisition is not complete (No, Step **110**), then the process continues to repeat Steps **104**-**108**.

If the data acquisition is complete (Yes, Step **110**) then the process proceeds to step **112**, and the calculation or determination of the pulse amplitude ratio is undertaken, where a pulse amplitude ratio is determined for each of the pressure data acquisitions that were made. The pulse amplitude ratio is determined using the pulse amplitude near the end of the expiratory effort and a baseline pulse amplitude for each of the acquired data sets.

The pulse volume of the photoplethysmography waveform, which is the width of the signal from minimum to maximum during one cardiac cycle, from the optical pulse volume sensing device **210** is measured. Also, a comparison is made of the pulse volume near the end of the expiratory effort to the pulse volume at baseline before the expiratory or positive pressure inspiratory effort begins. The ratio of the pulse volume near the end of the expiratory or positive pressure inspiratory effort to the pulse volume before the beginning of the

expiratory or positive pressure inspiratory effort, which is called the pulse amplitude ratio, is used.

After determining the pulse amplitude ratio(s), an assessment is made to determine if the corresponding cardiac filing pressure is representative of a normal filing pressure, an elevated filing pressure (generally indicative of a problem) or is in a range which does not provide a reliable indication by itself of an elevated filing pressure condition.

The determined information can be displayed on the output display **250** or via a printing device **240**, Step **116**. The information being displayed includes but is not limited to the photoplethysmography waveform, the expiratory effort waveform and level, and the pulse amplitude ratio number, as well as words or any combination thereof.

Information that relates to central arterial stiffness can be obtained and assessed. Such methods further include, factoring such arterial stiffness information along with the assessment of the pulse amplitude ratio. A microprocessor or a computer can also be provided. The microprocessor can be communicatively coupled to each of the pressure transducer and the optical pulse volume sensing device (e.g., PPG). The provided microprocessor determines the pulse amplitude ratio from the signals from the pressure transducer and the optical pulse volume sensing device (e.g., PPG).

An applications program including program or code segments and instructions and criteria for carrying out the methods of the present invention, including determining the pulse amplitude ratio on demand, automatically and/or periodically can also be provided. Such an applications program includes program segments and instructions and criteria for causing the periodically determined pulse amplitude ratios as well as any other data such as the pulse amplitude near the end of the expiratory effort, the baseline pulse amplitude and measured expiratory pressures, to be stored in a storage device.

The method further include providing a device including an enclosure, the microprocessor and storage device, where the microprocessor and storage device are disposed within the enclosure so that the device is one of free-standing, on a rolling cart or portable so as for example, the device can be carried in the pocket of a jacket worn by the clinician, technician or medical personnel. The device is arranged so as to include one of a display or a printing device, so that determined information is displayed to the user or printed. This displaying or printing is done one of automatically or in response to an input from the user. The device also can include a means for communicatively coupling the device microprocessor to each of the optical pulse pressuring sensing device and the pressure transducer.

A means for communicatively coupling the device to a communication system (e.g., telephone system, network, internet) for communication the acquired information to the practitioner or a service for monitoring for such communications can also be provided. Such monitoring services include storing the acquired information and/or for re-transmitting such information onto the practitioner. Information can be acquired using the provided device in clinical and non-clinical settings and transmitting the acquired information via a communication system to the practitioner and/or monitoring service. In more particular embodiments, such methods further include having a person not having medical training (e.g., patient) use the device to acquiring information, couple the device to a communication system and transmit the so acquired information via the communication system to the practitioner and/or monitoring service.

FIG. 9 illustrates a flow diagram representing the automation of the system for non-invasively assessing cardiac filling pressure. Initially the device determines that the PPG signal is stable, step **400**. This ensures that the patient isn't moving around and that the results will not be affected by external factors. This is done by determining whether the baseline is

within some standard deviation of its mean for a given time (described below). Once the device detects a stable PPG from input **405**, it informs the patient that the procedure can begin, step **410**. Next, it calculates the baseline peak to peak amplitude, B, step **420**. Once the baseline amplitude (B) is detected, it instructs the patient to perform the Valsalva maneuver, step **430** using input **435**. As long as the patient holds a proper Valsalva for approximately 10 seconds, condition **440**, as determined by the pressure sensor input, the device obtains the second peak to peak value, A, after Valsalva completion, step **460**. However, it should be noted that the amount of time for holding the Valsalva maneuver can be any length of time known to one of skill in the art. PAR is then calculated, step **470**, and reported as the ratio of A/B, step **480**, and LVEDP is predicted from a predefined model.

During Valsalva the software is constantly checking that the patient is performing the maneuver properly. Should the pressure overshoot, fail to reach the goal pressure or otherwise deviate from the boundaries, the device will restart the procedure, condition **490**. The particulars of each of these steps are described below.

The central function of the software is to automate the entire procedure including accurate retrieval of the incoming data from the sensors and peak-to-peak detection for the PAR calculation. We implemented a robust serial data detection algorithm in order to handle receiving two sources of input from both the PPG and pressure sensors through the same serial port. Instead of alternating values from the PPG and pressure sensors, two PPG values were followed by two pressure values. The algorithm verifies that the two consecutive values are equal before it considers it a valid datum. This redundancy helps reduce noise and error in the signal.

For peak detection, the function iterates through the array of values that is the PPG signal. When it finds the next value that is less than the previous value, it assumes that the previous value was a local maximum. Similarly, if it finds that the next value is greater than

the previous value, this corresponds to a local minimum. There is a heuristically determined 'delta' parameter used to help discriminate between insignificant local extrema.

The software also implements a careful flow control to insure that little involvement on the part of the patient and physician are required. As described above with respect to FIG. 9, the algorithm will continuously read in data from both the PPG and pressure signals after the Start button is pushed. When the Measure button is pushed, it initiates the sequence of automatically detecting the PPG peak-to-peak average to determine if a baseline is reached. If it detects a valid baseline, then it will let the patient know to begin the Valsalva maneuver for 10 seconds. If the Valsalva is done incorrectly or the Restart or Reset buttons are pushed, the entire procedure starts over and detects a new baseline value. After a successful completion of the Valsalva maneuver, the PAR is calculated and displayed. Algorithms were implemented in MATLAB™ and compiled down to stand alone executable for use on the device.

The graphical user interface of the automated device can include two parts: a physician view and a patient view. The physician view displays the PPG signal, the pressure signal, the PAR, and the LVEDP status. Since observing the PPG signal may negatively affect readings, it is hidden on the patient view. The patient sees only two bars: a time progress bar that tells a patient how much longer he must hold the Valsalva maneuver and a pressure status bar that indicates the real-time pressure the patient is exerting. The patient merely has to exert enough pressure to keep the pressure indicator within the desired range, as represented in the visual display for the user. Once the patient completes the procedure, the physician has the option to view the recorded PPG signal. The touch screen allows for an intuitive interface with large buttons and flexible menus that allow the doctor to select various procedure parameters. The fonts are large and easy to read.

In addition, a brief tutorial video explaining how to use the device is included under the help button. The mouthpiece that the patient breathes into is disposable, cheap, and has a one way valve. Its form factor is appropriate for this application and is the same as the kind used in flow meters.

By way of example, patient testing was done using the automated device. The protocol described below for this testing is merely exemplary, and any suitable protocol known to one of skill in the art could be used. The patient testing protocol involved asking hospital patients scheduled for catheterizations (for reasons unrelated to the device) simply to use the device a number of times according to the protocol. In this manner, the PAR values over multiple runs could be compared against the highly accurate catheter LVEDP. Initial results were very favorable. From the data gathered, the device has commendable precision, with small standard deviations for patients A and B over multiple trials. Furthermore, among all of the patients, no PAR values greater than 0.8 were detected. Which is consistent with the fact that from the catheter, no instances of elevated LVEDP (>25 mmHg) were detected. Although more data is necessary, low PAR values seem to correspond to nonelevated LVEDP, as predicted.

There were also several interesting qualitative observations. The patients had very little trouble using the device; by the second or third try they were using the device and performing the Valsalva maneuver properly. One of the patients had chronic obstructive pulmonary disease and he had no trouble holding 20 mmHg for 10 seconds. As designed, individual trials were very fast, 20 to 30 seconds per; in a procedure averaging over multiple trials, the entire process would take under 5 minutes. Lastly, using the doctor's view (where the patient can see his own PPG) didn't affect the outcomes of the results as compared with the patient's view.

FIG. 10 illustrates a diagram of a method of automating the process of assessing cardiac filling pressure non-invasively. The following method steps can be programmed into a computer readable medium, computer or any other device or system for executing the steps known to one of skill in the art. A method **500** for automating a process for determining cardiac filling pressure non-invasively includes step **510** of analyzing a photoplethysmography signal having a pulse amplitude. The analysis of step **510** is done to determine a point in time that the pulse amplitude of the photoplethysmography signal does not vary by a predetermined amount over a first predetermined time period. Step **520** includes displaying an instruction on a user interface to inform a user that an instruction to initiate an expiratory effort will be displayed, and step **530** includes displaying an instruction on the user interface informing the user to begin an expiratory effort. In step **540**, the expiratory effort of the user is compared to a predetermined goal range for expiratory effort. Additionally, in step **550**, an indicator of the user's expiratory effort relative to the predetermined goal range is displayed on the user interface.

The method **500** illustrated in FIG. 10 can also include instructing the user to sustain the expiratory effort for a second predetermined period of time. instructing the user to sustain the expiratory effort for a second predetermined period of time. The method can also include displaying an elapsed time for the expiratory effort as well as a time remaining in the second predetermined period of time. It is indicated to the user that the data acquisition sequence is invalid, when the expiratory effort does not meet the predetermined goal range within a third predetermined period of time. It can also be indicated to the user that the data acquisition sequence is invalid when the expiratory effort exceeds the predetermined range for expiratory effort. After the predetermined amount of time has elapsed it is displayed that the user can cease the expiratory effort. A first average of the pulse amplitude of the photoplethysmography signal can be calculated for a fourth predetermined period of time

before the user ceases the expiratory effort. A second average of the pulse amplitude of the photoplethysmograpy signal can also be calculated for a fifth period of time before an initiation of the expiratory effort. Additionally, a pulse amplitude ratio of the first average of the pulse amplitude to the second average of the pulse amplitude can be calculated. These steps can also be programmed into the computer, computer readable medium or any other device for executing the steps known to one of skill in the art.

FIG. 4 illustrates a graphical view of a photoplethysmography signal and of invasive blood pressure during the Valsava maneuver.

FIG. 5 illustrates a graphical view of a photoplethysmography waveform and the expiratory pressure waveform for a heart with a normal filing pressure. As shown therein, using the methods and systems of the present invention, the determined pulse amplitude ratio equals 0.2 and the LVEDP equals 7.

FIG. 6 illustrates a graphical view of a photoplethysmography waveform and the expiratory pressure waveform for a heart with an elevated filing pressure using the system of the present invention. As shown therein, using the methods and systems of the present invention, the determined pulse amplitude ratio equals 1.0 and the LVEDP equals 37.

FIG. 7 illustrates a graphical view of a photoplethysmography waveform and the expiratory pressure waveform for the heart of a patient that had been initially diagnosed as being fluid overloaded, but which was later determined that the heart had a normal filing pressure using the system of the present invention. As shown therein, using the methods and systems of the present invention, the determined pulse amplitude ratio equals 0.1 and the LVEDP equals 4.

FIG. 8 illustrates a graphical view of LVEDP by catheter versus Average Pulse Amplitude Ratio for a patient study, where the pulse amplitude ratios were determined using the system of the present invention.

Although a preferred embodiment of the invention has been described using specific terms, such description is for illustrative purposes only, and it is to be understood that changes and variations may be made without departing from the spirit or scope of the following claims.While this method has been described for use in determining cardiac filling pressure non-invasively, it need not be limited to this application and could be used for any other suitable purpose known to one of skill in the art. The many features and advantages of the invention are apparent from the detailed specification, and thus, it is intended by the appended claims to cover all such features and advantages of the invention which fall within the true spirit and scope of the invention. Further, since numerous modifications and variations will readily occur to those skilled in the art, it is not desired to limit the invention to the exact construction and operation illustrated and described, and accordingly, all suitable modifications and equivalents may be resorted to, falling within the scope of the invention.

What is claimed is:

1. A method for automating a process for determining cardiac filling pressure non-invasively, comprising:

analyzing a photoplethysmography signal having a pulse amplitude, said analyzing being done to determine a point in time that the pulse amplitude of the photoplethysmography signal does not vary by a predetermined amount over a first predetermined time period;

displaying a first instruction on a user interface to inform a user that a second instruction to initiate an expiratory effort will be displayed;

displaying the second instruction on the user interface informing the user to begin an expiratory effort;

comparing the expiratory effort of the user to a predetermined goal range for expiratory effort; and

displaying an indicator of the user's expiratory effort relative to the predetermined goal range on the user interface.

2. The method of claim 1further comprising instructing the user to sustain the expiratory effort for a second predetermined period of time.

3. The method of claim 2 further comprising displaying an elapsed time for the expiratory effort as well as a time remaining in the second predetermined period of time.

4. The method of claim 1 further comprising indicating to the user that the data acquisition sequence is invalid when the expiratory effort does not meet the predetermined goal range within a third predetermined period of time.

5. The method of claim 1 further comprising indicating to the user that the data acquisition sequence is invalid when the expiratory effort exceeds the predetermined range for expiratory effort.

6. The method of claim 1 further comprising displaying that the user can cease the expiratory effort.

7. The method of claim 1 further comprising calculating a first average of the pulse amplitude of the photoplethysmography signal for a fourth predetermined period of time before the user ceases the expiratory effort.

8. The method of claim 7 further comprising calculating a second average of the pulse amplitude of the photoplethysmograpy signal for a fifth period of time before an initiation of the expiratory effort.

9. The method of claim 8 further comprising calculating a pulse amplitude ratio of the first average of the pulse amplitude to the second average of the pulse amplitude.

10. A method for automating a process for determining cardiac filling pressure non-invasively, comprising:

programming a computer readable medium to execute steps comprising:

analyzing a photoplethysmography signal having a pulse amplitude, said analyzing being done to determine a point in time that the pulse amplitude of the photoplethysmography signal does not vary by a predetermined amount over a first predetermined time period;

transmitting a first instruction to be displayed on a user interface, said first instruction informing a user that a second instruction to initiate an expiratory effort will be displayed;

transmitting the second instruction to be displayed on the user interface, said second instruction informing the user to begin an expiratory effort;

comparing the expiratory effort of the user to a predetermined goal range for expiratory effort; and

transmitting a third instruction to be displayed on the user interface, said third instruction indicating the user's expiratory effort relative to the predetermined goal range on the user interface.

11. The method of claim 10 further comprising instructing the user to sustain the expiratory effort for a second predetermined period of time.

12. The method of claim 11 further comprising displaying an elapsed time for the expiratory effort as well as a time remaining in the second predetermined period of time.

13. The method of claim 10 further comprising indicating to the user that the data acquisition sequence is invalid when the expiratory effort does not meet the predetermined goal range within a third predetermined period of time.

14. The method of claim 10 further comprising indicating to the user that the data acquisition sequence is invalid when the expiratory effort exceeds the predetermined range for expiratory effort.

15. The method of claim 10 further comprising displaying that the user can cease the expiratory effort.

16. The method of claim 10 further comprising calculating a first average of the pulse amplitude of the photoplethysmography signal for a fourth predetermined period of time before the user ceases the expiratory effort.

17. The method of claim 16 further comprising calculating a second average of the pulse amplitude of the photoplethysmograpy signal for a fifth period of time before an initiation of the expiratory effort.

18. The method of claim 17 further comprising calculating a pulse amplitude ratio of the first average of the pulse amplitude to the second average of the pulse amplitude.

19. An apparatus for automating a process for determining cardiac filling pressure non-invasively, comprising:

a device including a housing, said device including a user interface disposed within said housing, an expiratory effort reception apparatus being coupled to said housing, a photoplethysmograph, and a computer readable medium, wherein said computer readable medium is programmed with steps comprising:

programming a computer readable medium to execute steps comprising:

analyzing a signal from the photoplethysmograph, said signal having a pulse amplitude, said analyzing being done to determine a point in time that the pulse amplitude of the signal does not vary by a predetermined amount over a first predetermined time period;

transmitting a first instruction to be displayed on a user interface, said first instruction informing a user that a second instruction to initiate an expiratory effort will be displayed;

transmitting the second instruction to be displayed on the user interface, said second instruction informing the user to begin an expiratory effort;

comparing the expiratory effort of the user to a predetermined goal range for expiratory effort; and

transmitting a third instruction to be displayed on the user interface, said third instruction indicating the user's expiratory effort relative to the predetermined goal range on the user interface.

20. The device of claim 19 further comprising said computer readable medium being disposed within the housing of the device.

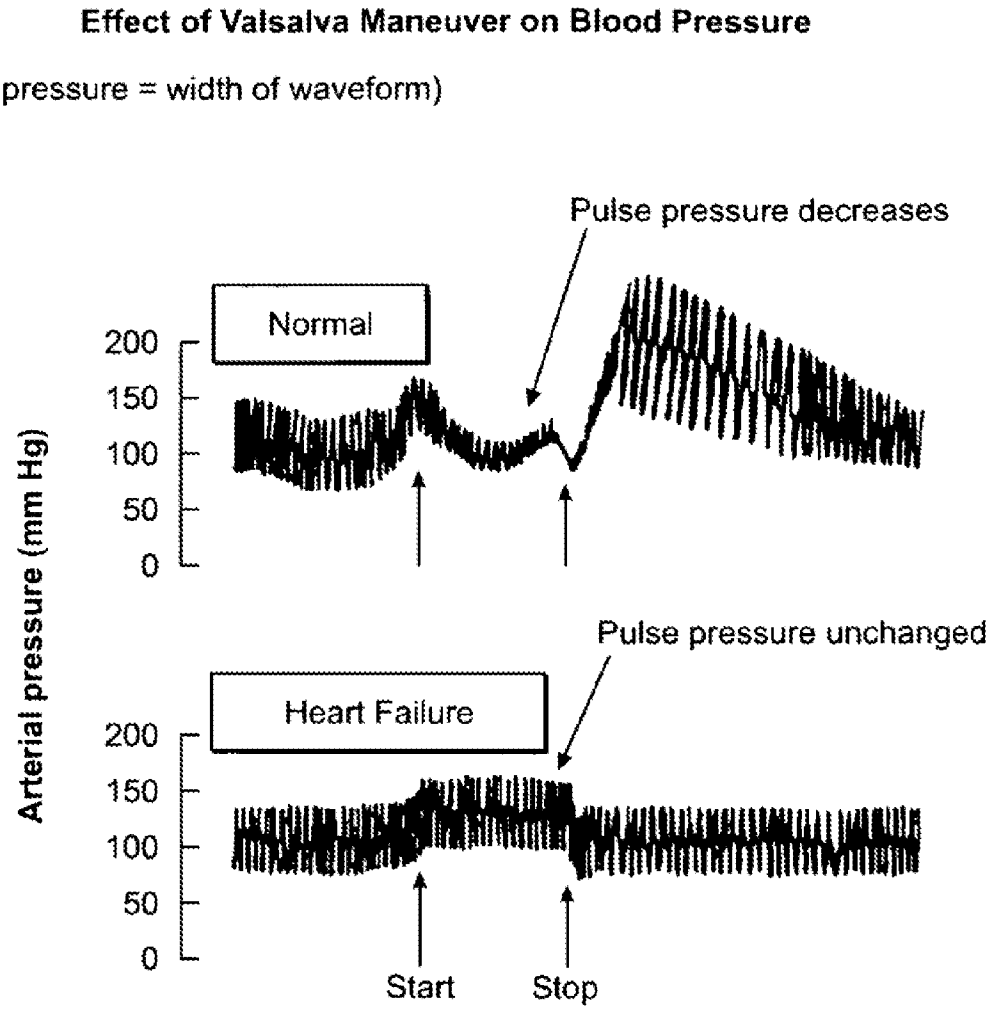

Effect of Valsalva Maneuver on Blood Pressure
(Pulse pressure = width of waveform)
Pulse pressure decreases
Normal
200
150
100
50
0
Arterial pressure (mm Hg)
Pulse pressure unchanged
Heart Failure
200
150
100
50
0
Start
Stop

FIG. 1

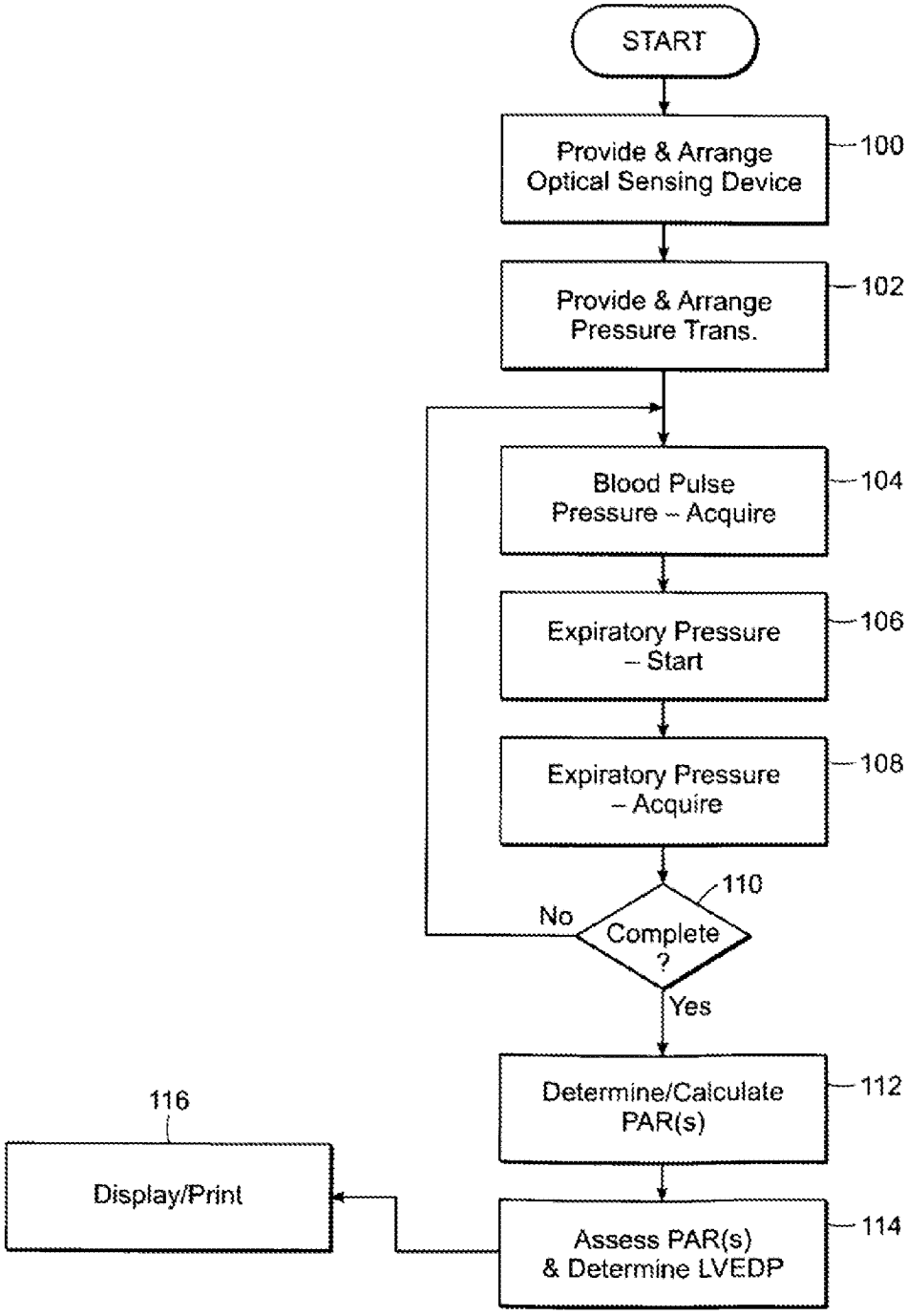

START
Provide & Arrange Optical Sensing Device
100
Provide & Arrange Pressure Trans.
102
Blood Pulse Pressure – Acquire
104
Expiratory Pressure – Start
106
Expiratory Pressure – Acquire
108
110
No
Complete ?
Yes
Determine/Calculate PAR(s)
112
116
Display/Print
Assess PAR(s) & Determine LVEDP
114

FIG. 2

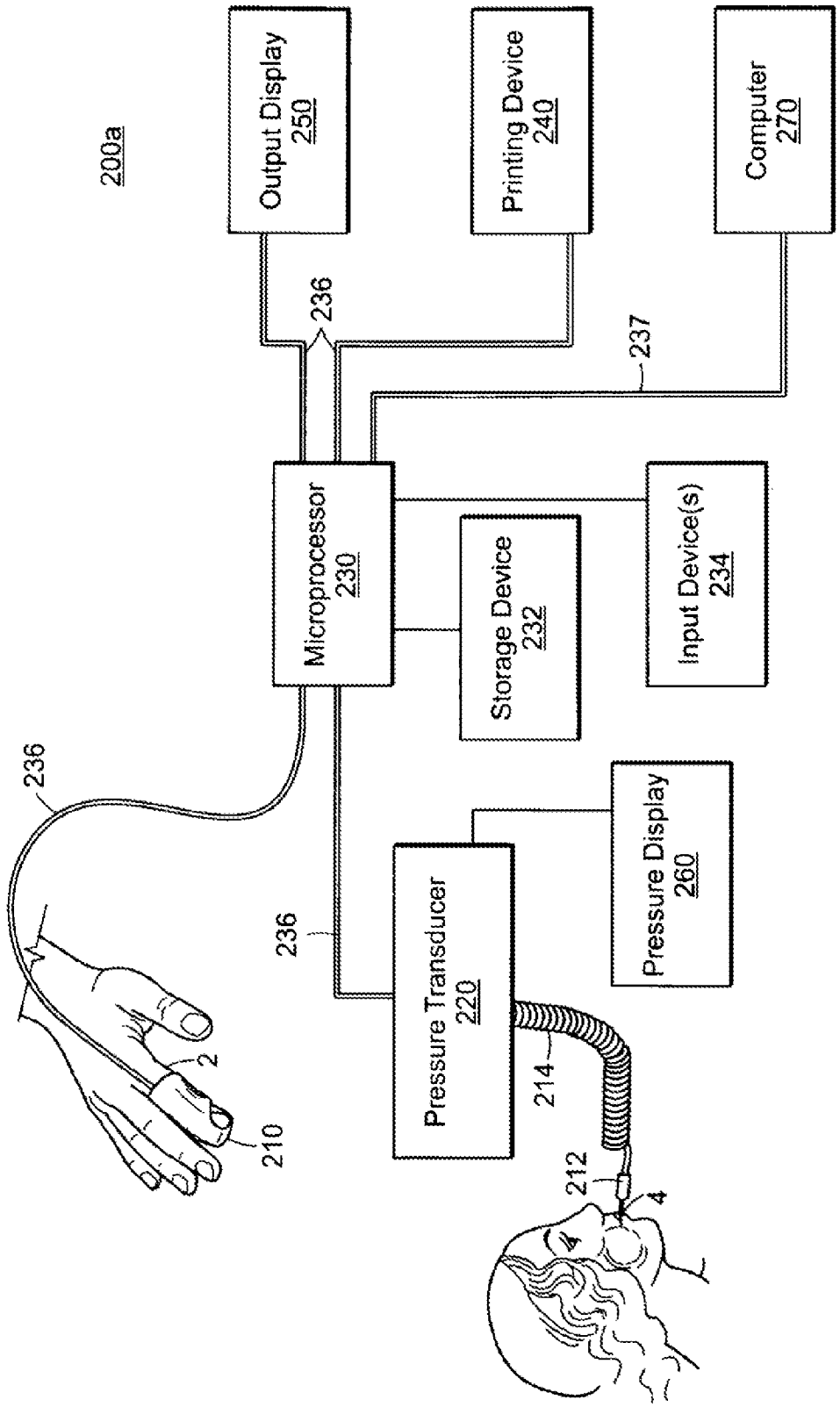

200a
Output Display 250
Printing Device 240
Computer 270
236
237
Microprocessor 230
Storage Device 232
Input Device(s) 234
236
Pressure Display 260
236
Pressure Transducer 220
214
212
4
2
210

FIG. 3A

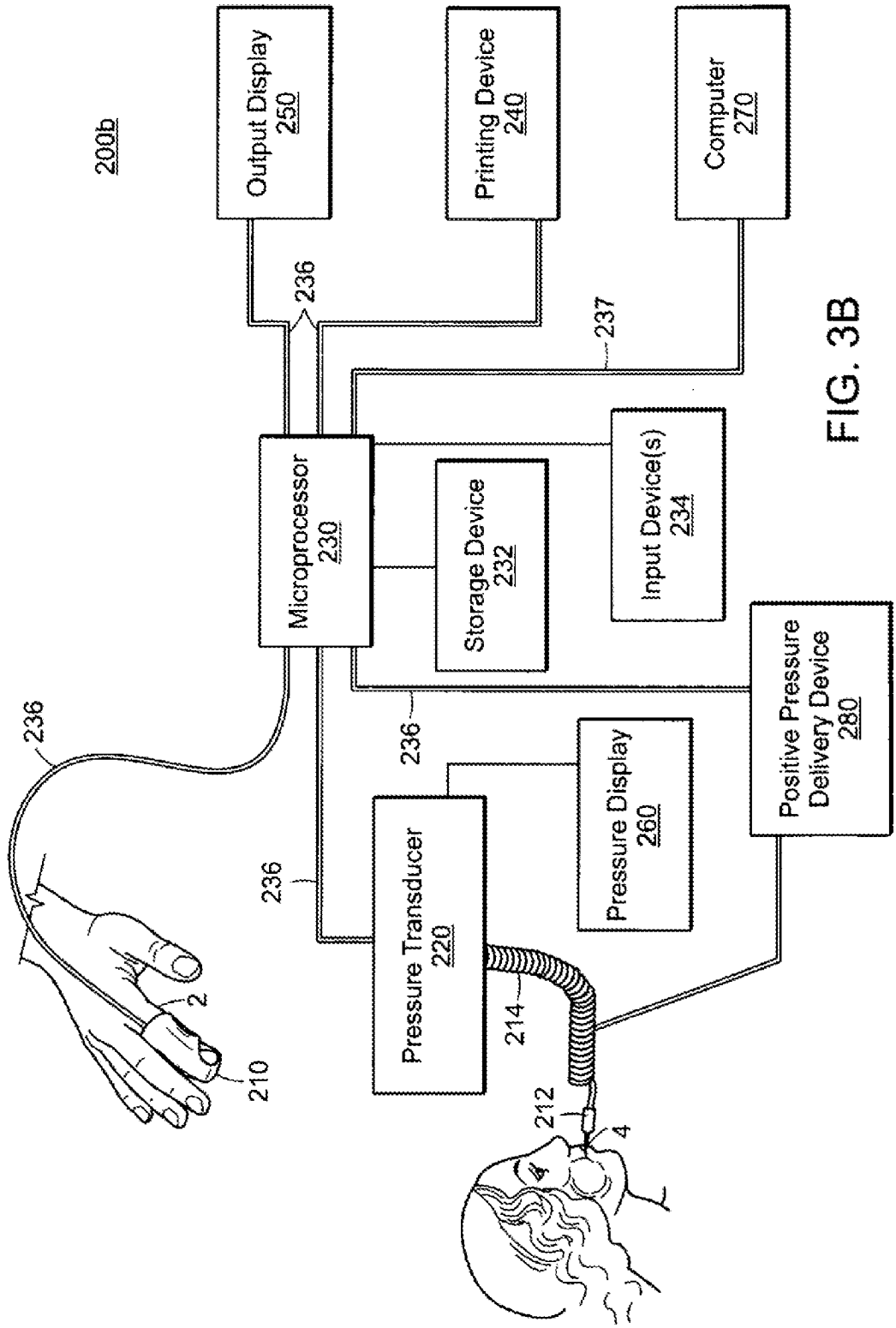

200b
Output Display 250
Printing Device 240
Computer 270
236
237
Microprocessor 230
Storage Device 232
Input Device(s) 234
Positive Pressure Delivery Device 280
236
236
Pressure Transducer 220
Pressure Display 260
214
212
4
2
210

FIG. 3B

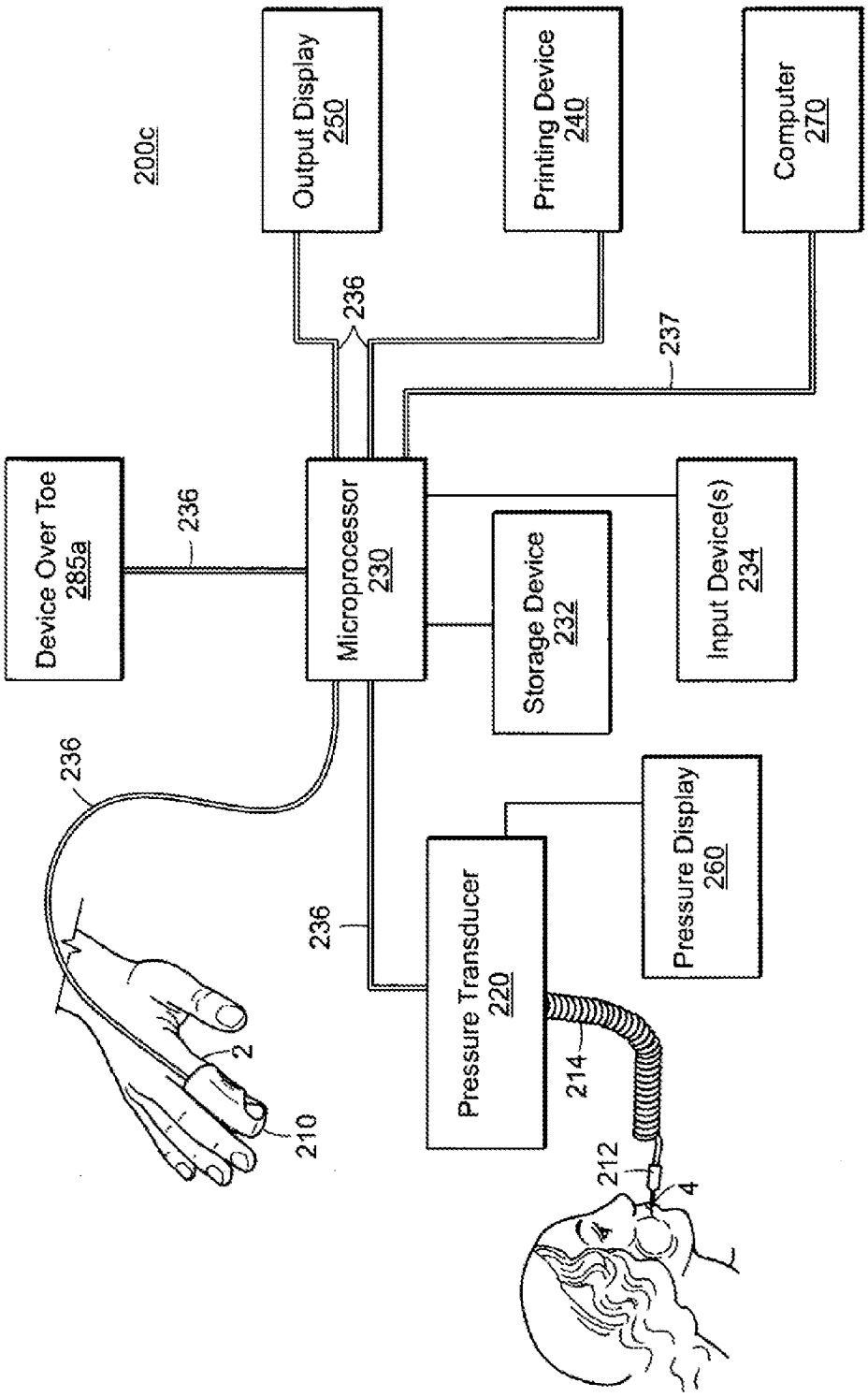

200c
Output Display 250
Printing Device 240
Computer 270
236
237
Device Over Toe 285a
236
Microprocessor 230
Storage Device 232
Input Device(s) 234
236
Pressure Transducer 220
Pressure Display 260
214
212
4
2
210

FIG. 3C

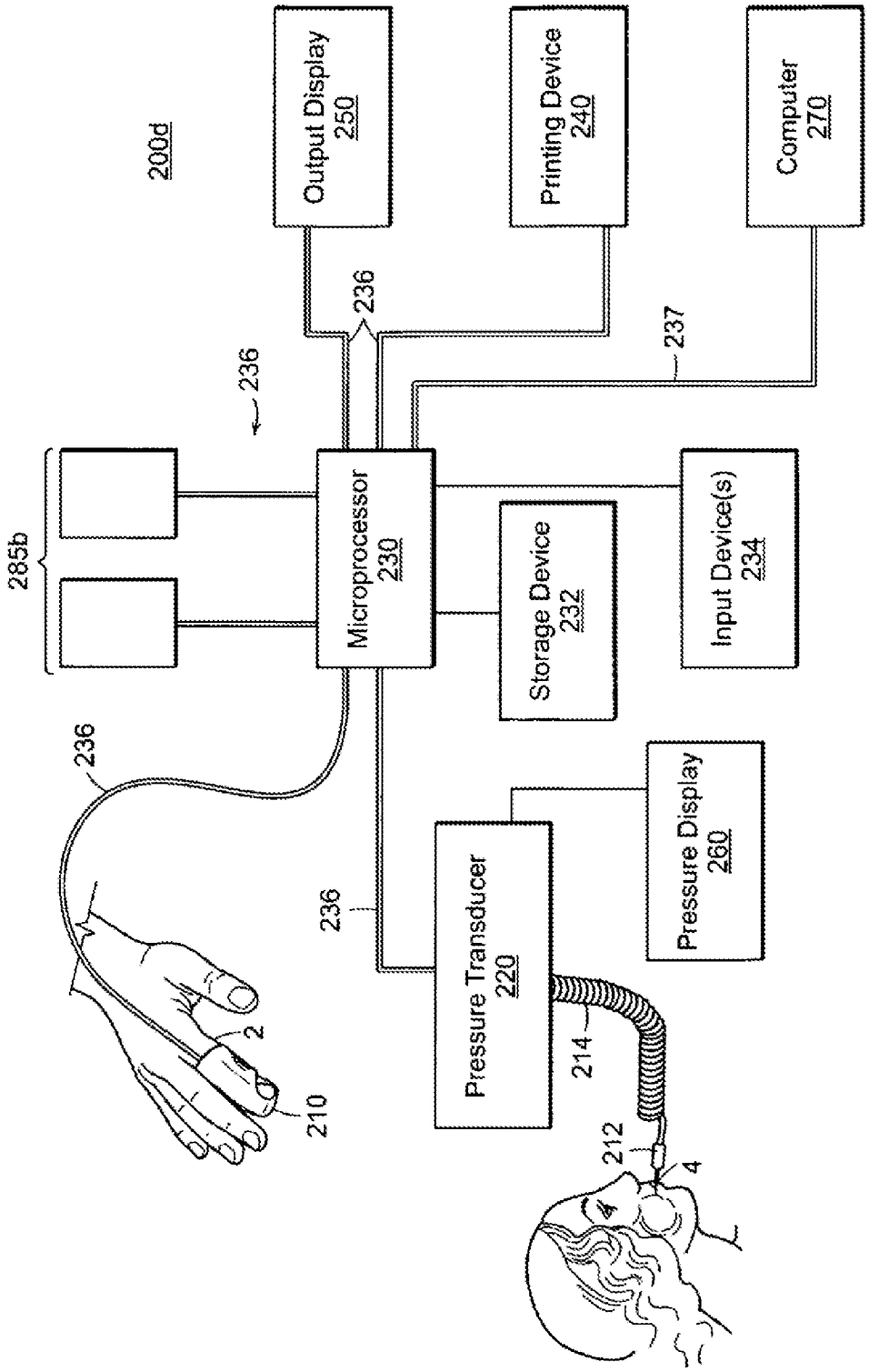

200d
Output Display 250
Printing Device 240
Computer 270
236
237
236
285b
Microprocessor 230
Storage Device 232
Input Device(s) 234
236
Pressure Display 260
236
Pressure Transducer 220
214
212
4
2
210

FIG. 3D

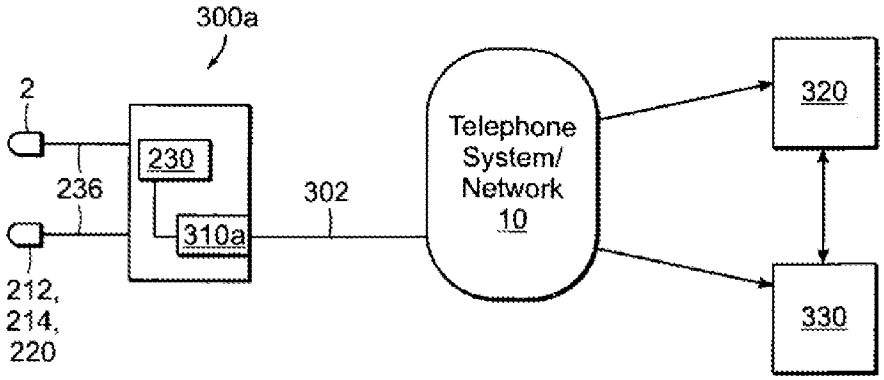

300a
2
230
236
310a
302
212,
214,
220
Telephone
System/
Network
10
320
330

FIG. 3E

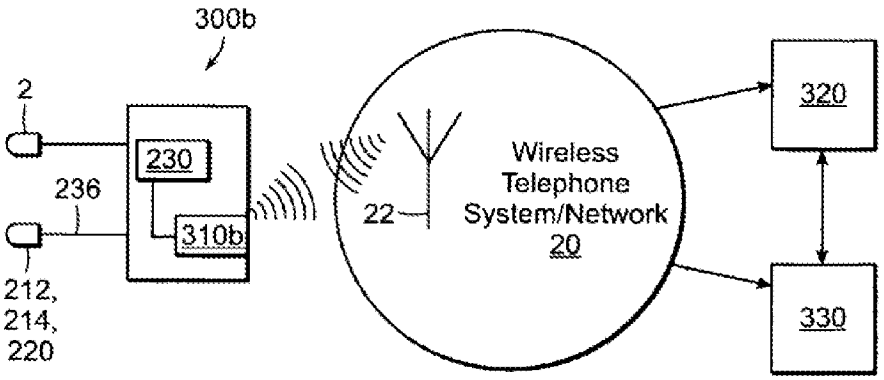

300b
2
230
236
310b
212,
214,
220
22
Wireless
Telephone
System/Network
20
320
330

FIG. 3F

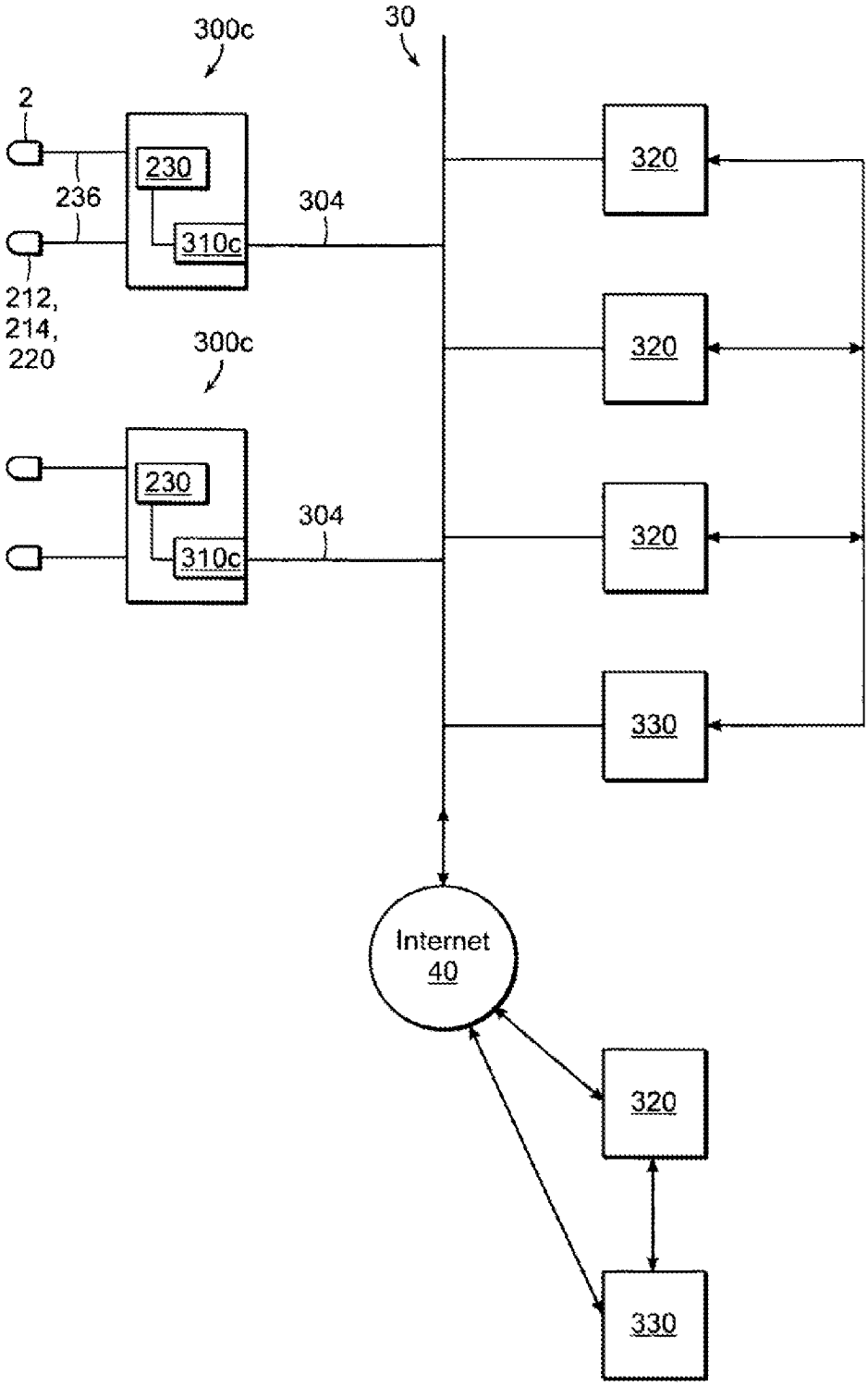

300c
30
2
230
236
304
310c
320
212,
214,
220
300c
320
230
304
310c
320
330
Internet
40
320
330

FIG. 3G

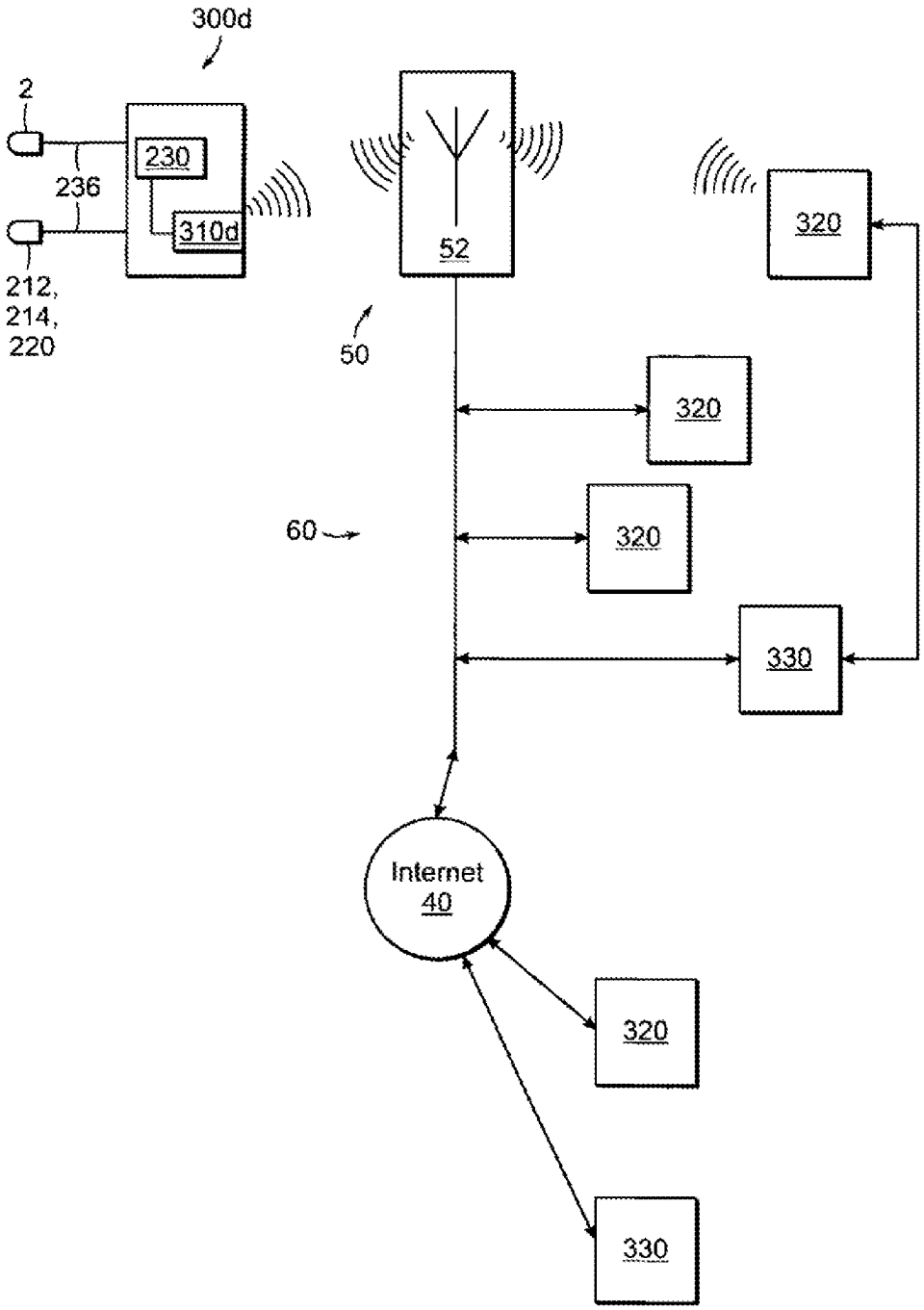

300d
2
230
236
310d
212,
214,
220
52
50
320
320
320
60
330
Internet
40
320
330

FIG. 3H

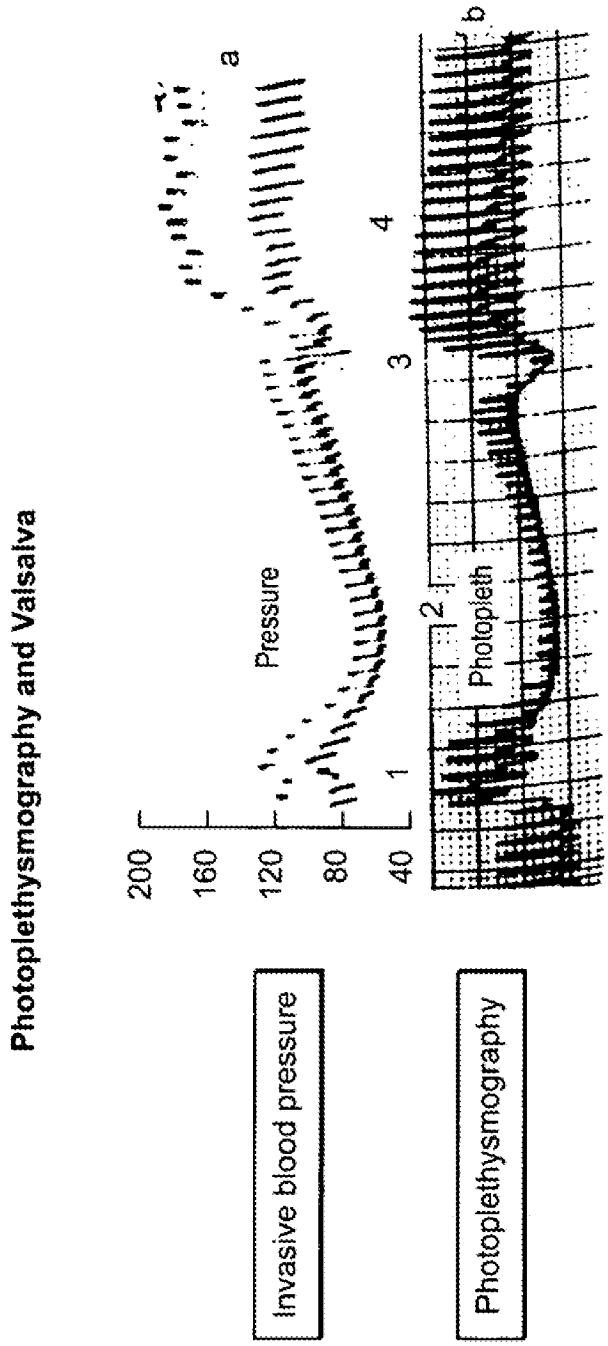

Photoplethysmography and Valsalva
Invasive blood pressure
Photoplethysmography
200
160
120
80
40
Pressure
Photopleth
1
2
3
4
a
b
The photoplethysmography signal closely resembles the invasively measured blood pressure signal during the Valsalva maneuver.

FIG. 4

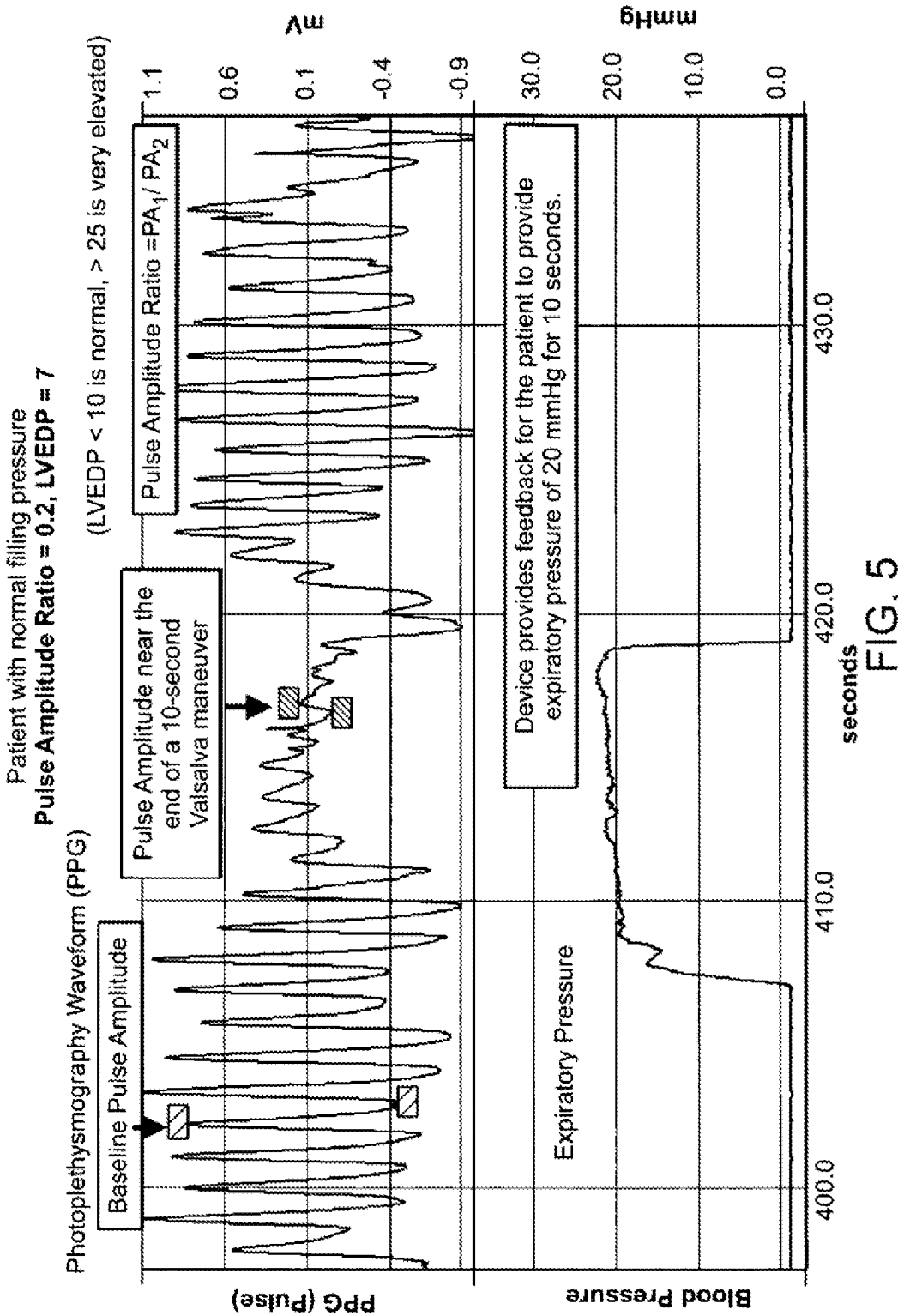

Patient with normal filling pressure
Pulse Amplitude Ratio = 0.2, LVEDP = 7
(LVEDP < 10 is normal, > 25 is very elevated)
Photoplethysmography Waveform (PPG)
Baseline Pulse Amplitude
Pulse Amplitude near the end of a 10-second Valsalva maneuver
Pulse Amplitude Ratio =PA1/ PA2
Device provides feedback for the patient to provide expiratory pressure of 20 mmHg for 10 seconds.
Expiratory Pressure
PPG (Pulse)
Blood Pressure
mV
1.1
0.6
0.1
-0.4
-0.9
mmHg
30.0
20.0
10.0
0.0
400.0
410.0
420.0
430.0
seconds

FIG. 5

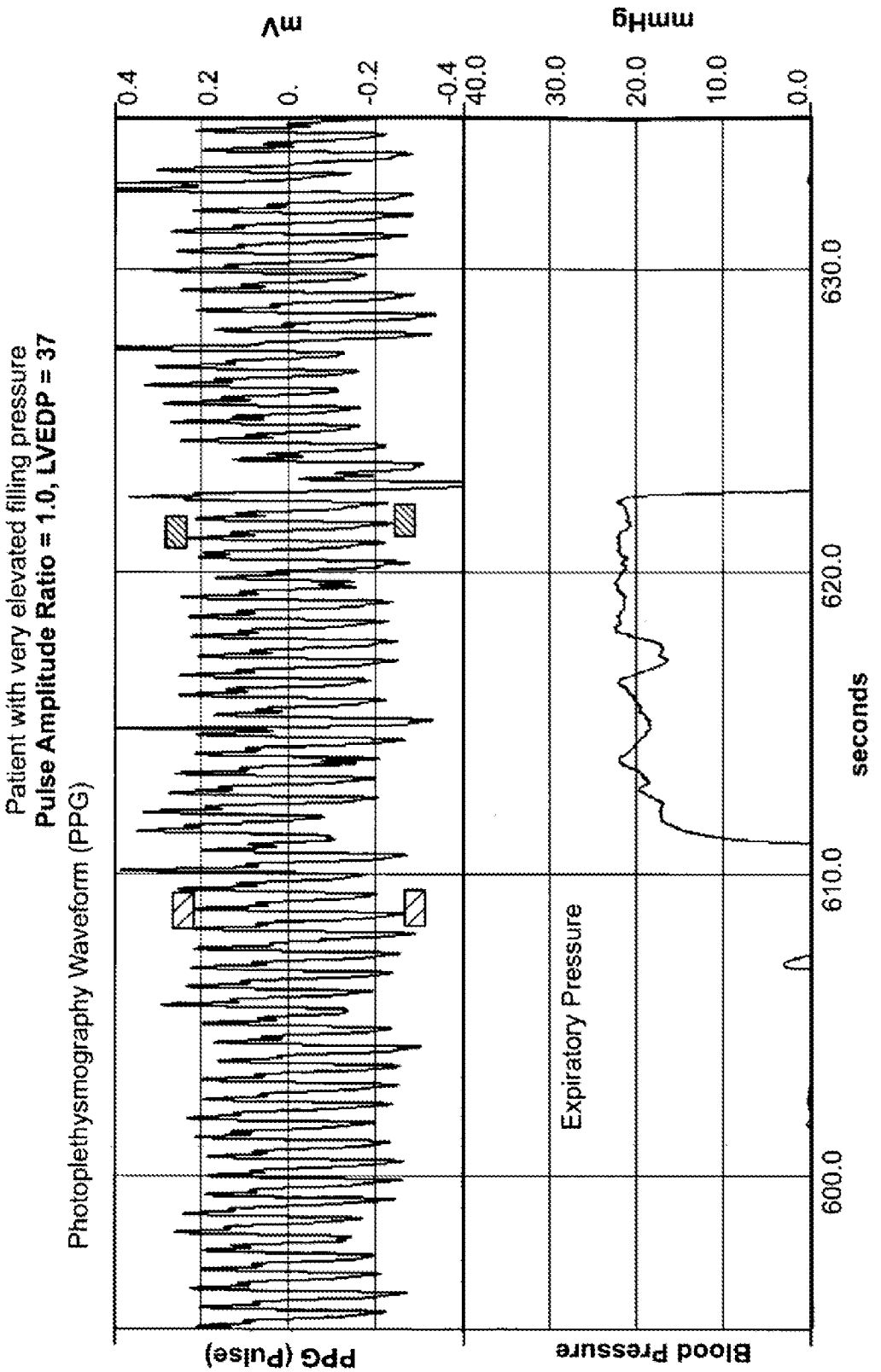

Patient with very elevated filling pressure
Pulse Amplitude Ratio = 1.0, LVEDP = 37
Photoplethysmography Waveform (PPG)
mV
0.4
0.2
0.
-0.2
-0.4
PPG (Pulse)
mmHg
40.0
30.0
20.0
10.0
0.0
Blood Pressure
Expiratory Pressure
600.0
610.0
620.0
630.0
seconds

FIG. 6

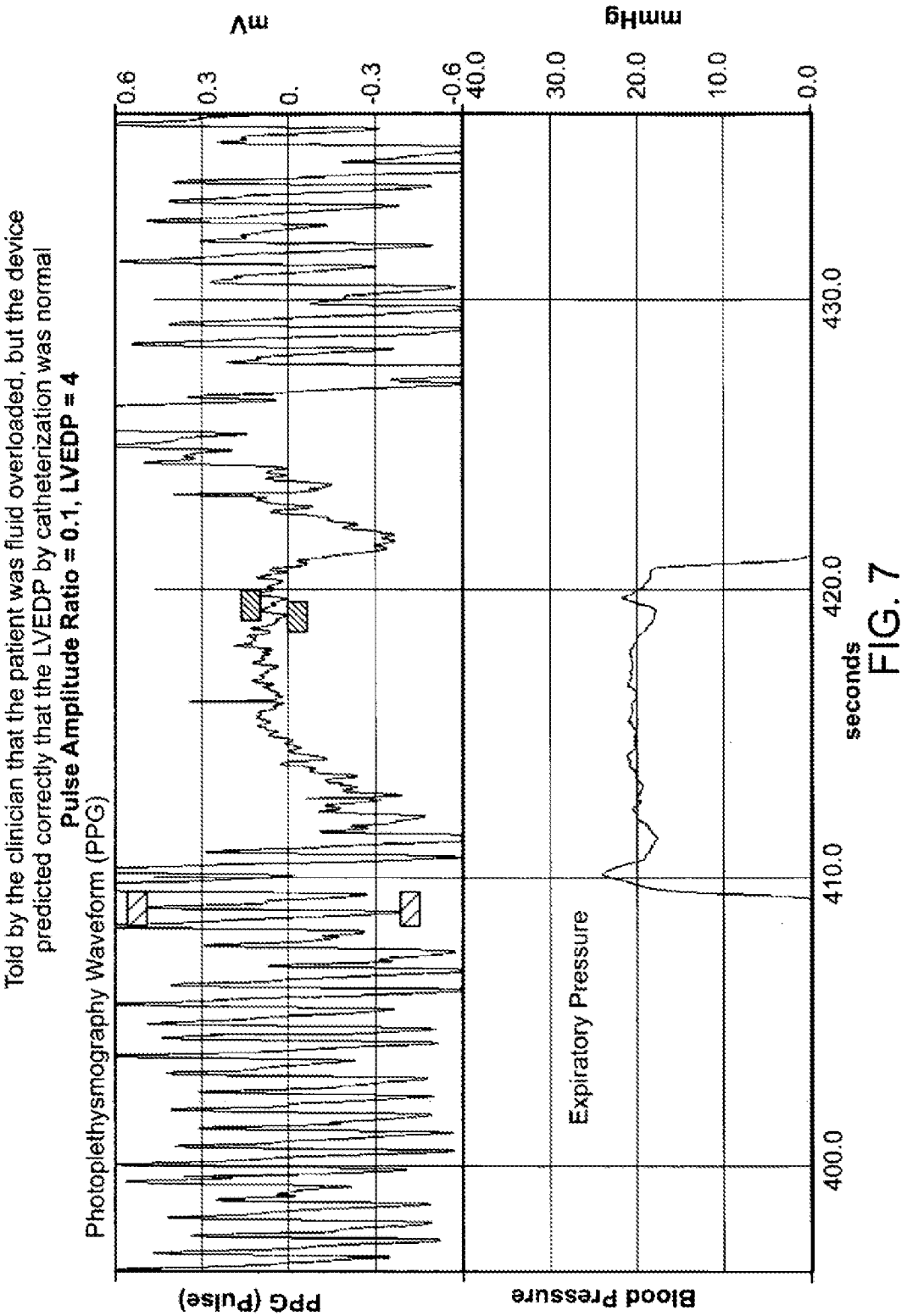

Told by the clinician that the patient was fluid overloaded, but the device predicted correctly that the LVEDP by catheterization was normal
Pulse Amplitude Ratio = 0.1, LVEDP = 4
Photoplethysmography Waveform (PPG)
mV
0.6
0.3
0.
-0.3
-0.6
PPG (Pulse)
mmHg
40.0
30.0
20.0
10.0
0.0
Blood Pressure
Expiratory Pressure
400.0
410.0
420.0
430.0
seconds

FIG. 7

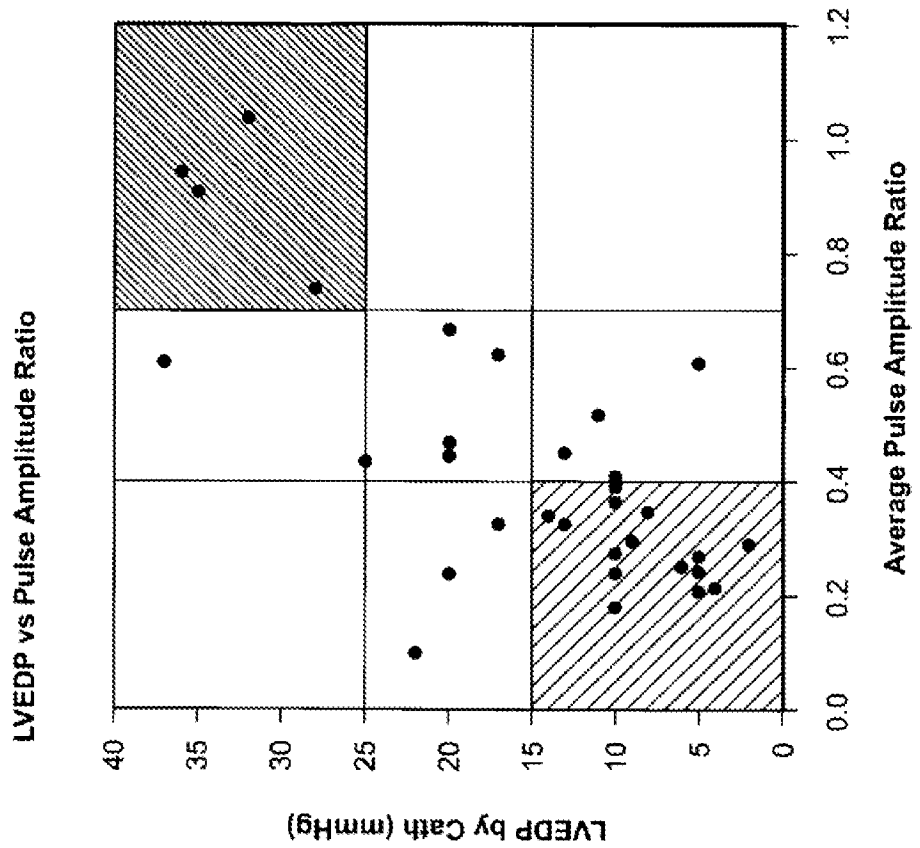

LVEDP vs Pulse Amplitude Ratio
LVEDP by Cath (mmHg)
Average Pulse Amplitude Ratio
0
5
10
15
20
25
30
35
40
0.0
0.2
0.4
0.6
0.8
1.0
1.2
Based on our study of 33 patients (r = 0.7, p<0.0001)
Sensitivity and Specificity:
PAR <= 0.4 indicating LVEDP <= 15 Sensitivity 80%, Specificity 77%
PAR >= 0.7 indicating LVEDP >= 25 Sensitivity 80%, Specificity 100%

FIG. 8

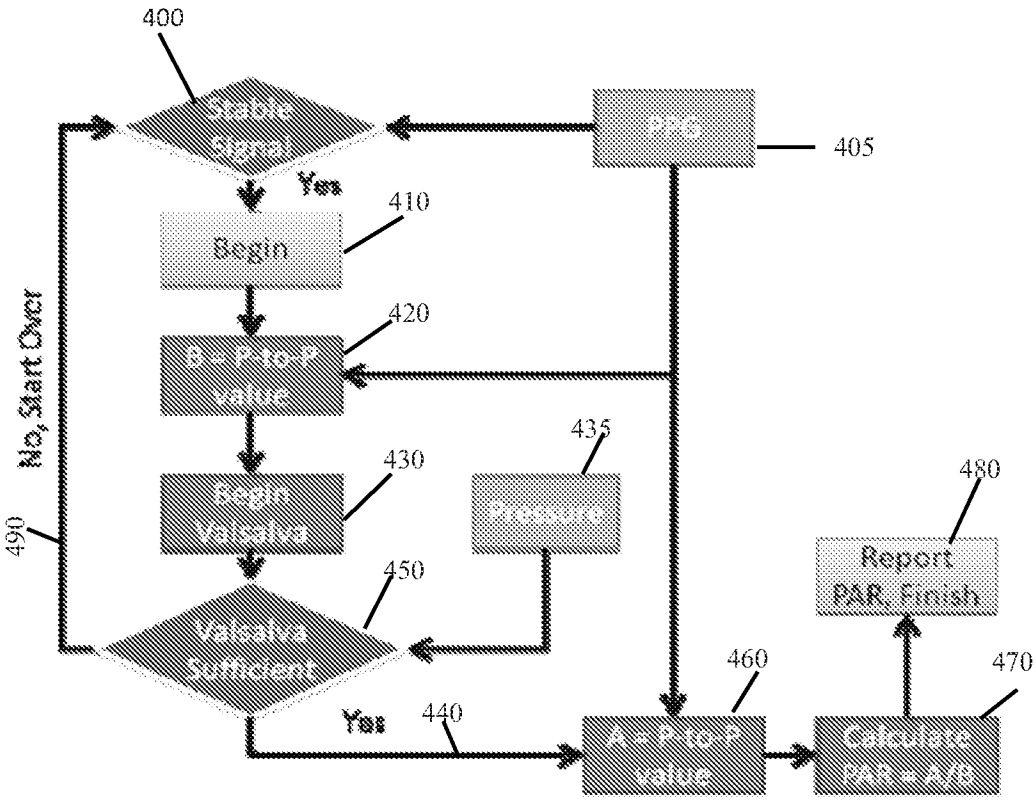

400
Stable Signal
Yes
No, Start Over
490
PPG
405
410
Begin
420
B = P-to-P value
435
Pressure
430
Begin Valsalva
480
Report PAR, Finish
450
Valsalva Sufficient
460
470
Yes
440
A = P-to-P value
Calculate PAR = A/B

FIG. 9

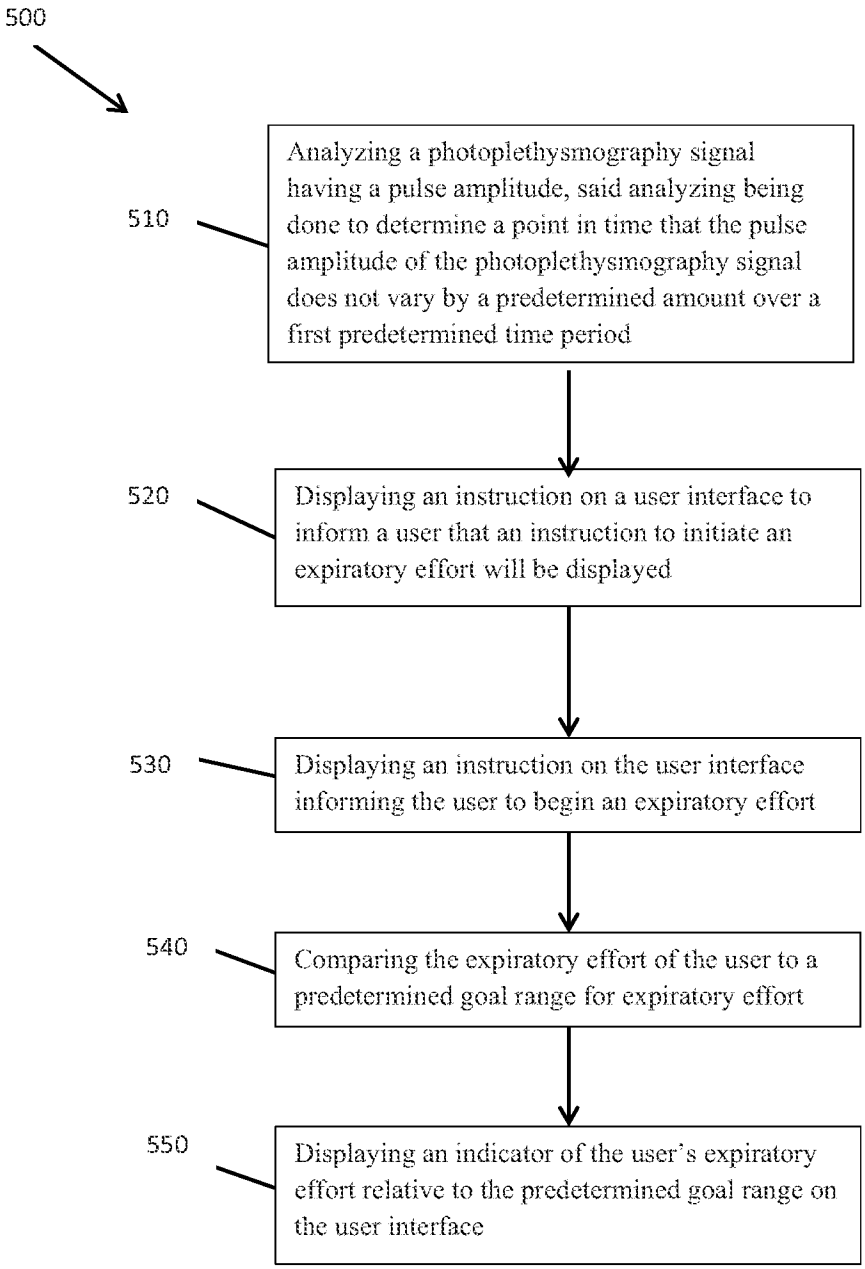

500
510
Analyzing a photoplethysmography signal having a pulse amplitude, said analyzing being done to determine a point in time that the pulse amplitude of the photoplethysmography signal does not vary by a predetermined amount over a first predetermined time period
520
Displaying an instruction on a user interface to inform a user that an instruction to initiate an expiratory effort will be displayed
530
Displaying an instruction on the user interface informing the user to begin an expiratory effort
540
Comparing the expiratory effort of the user to a predetermined goal range for expiratory effort
550
Displaying an indicator of the user's expiratory effort relative to the predetermined goal range on the user interface

FIG. 10