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(54) Title: MECHANICAL VENTILATION WITH AUTOMATIC CONTROL OF PATIENT'S WORK OF BREATHING USING CLASSICAL FEEDBACK CONTROL

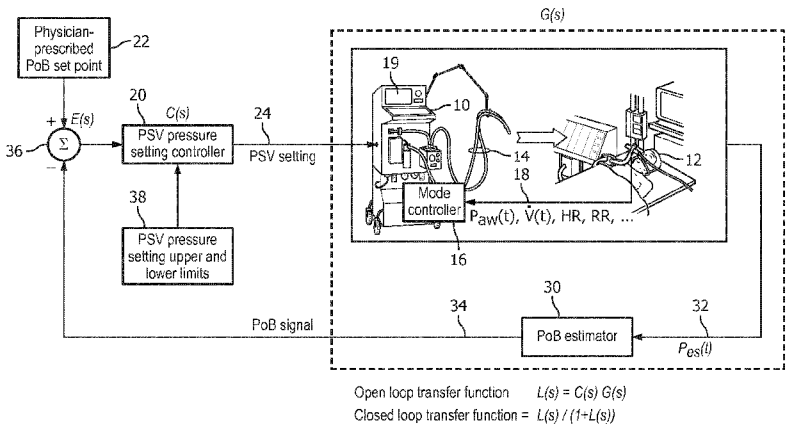


FIG. 1

(57) Abstract: A mechanical ventilator (10) provides pressure support ventilation (PSV) to a patient (12). A power of breathing (PoB) or work of breathing (WoB) estimator (30) generates a PoB or WoB signal (34) for the patient. An error calculator (36) computes an error signal as a difference between the PoB or WoB signal and a set point PoB or WoB value (22). A controller (20) inputs a PSV control signal (24) equal to the product of the controller transfer function and the error signal to the mechanical ventilator. A patient adaptation component (52, 54, 56, 60) fits parameters of a model of a controlled mechanical ventilation system comprising the mechanical ventilator and the patient to data comprising the PoB or WoB signal and the PSV control signal generated by the operating closed loop controller, and adjusts parameters of the controller transfer function to maintain stability of the operating closed loop controller.

MECHANICAL VENTILATION WITH AUTOMATIC CONTROL OF PATIENT'S WORK OF BREATHING USING CLASSICAL FEEDBACK CONTROL

FIELD

The following relates generally to the mechanical ventilation arts, respiratory health arts, and related arts.

BACKGROUND

Mechanical ventilators are life-saving machines that help patients with impaired respiratory drive, or lack of respiratory drive, on a temporary or long term basis. In both cases, the level of respiratory support strongly impacts patient outcome. It is estimated that about 1-in-5 patients who receive mechanical ventilation develop some form of ventilator-related lung injury attributable to the ventilator providing too much support. Another problem with the providing too much ventilator support is that the patient may become overly dependent on the ventilator machine, which can lead to more difficult wean-off from the ventilator and longer recovery time for the patient. On the other hand, if the ventilator provides too little support, then the patient overexerts to breathe producing detrimental patient stress. Too little ventilation support can also lead to insufficient respiration and potential adverse conditions such as hypoxia.

In the case of a patient who is unable to spontaneously breath, a ventilation mode such as continuous mandatory ventilation (CMV) is typically employed. In CMV, the ventilator initiates mandatory breaths at a programmed respiration rate, and each mandatory breath is driven to a pre-set inflation volume by action of the mechanical ventilator. This ensures adequate ventilation, but it is difficult to later wean the patient off the ventilator as CMV does not support any spontaneous respiration effort by the patient.

In the case of a patient who is spontaneously breathing, the goal of mechanical ventilation is to support the spontaneous respiration without providing too much support. Mechanical ventilation using pressure support, i.e. Pressure Support Ventilation (PSV), is a common operating mode for supporting spontaneous breathing. In PSV, the ventilator controller detects the onset of spontaneous inspiration as a decrease in airway pressure or an abrupt increase in air flow. The ventilator then applies pressure at a PSV pressure setting to support the patient's spontaneous inhalation effort. In PSV, the patient controls respiration rate and inflation volume, with the mechanical ventilator being limited to providing pressure

support at the PSV pressure setting to assist the spontaneous breaths. PSV is thus well-suited to providing ventilator assistance for a spontaneously breathing patient.

When PSV is used alone, the patient initiates all breaths. This is beneficial to encourage the patient's respiratory effort, but PSV cannot provide effective ventilation if the patient fails to spontaneously initiate breaths at a sufficient rate. To provide a safety net, PSV may be combined with an intermittent mandatory ventilation (IMV) mode that triggers ventilator-driven (i.e. mandatory) breaths if the spontaneous breaths alone are determined by the ventilator to provide insufficient ventilation for the patient.

Typical ventilator settings of a ventilator operating in a PSV or PSV/IMV mode include the PSV pressure setting, one or more trigger parameters (specifying how the ventilator detects spontaneous breaths), one or more mandatory breath cycling parameters (controlling timing of IMV-initiated mandatory breaths), and fraction of inspired oxygen (FiO_2, for oxygenated patients). These ventilator settings are prescribed by the physician. During mechanical ventilation, airway pressure and flow, fraction or percent of respired carbon dioxide (CO_2, via capnography, e.g. end-tidal CO_2 or $etCO_2$), heart rate, respiratory rate, peripheral capillary oxygen saturation (SpO_2), and/or so forth are monitored. During physician visits to the patient's hospital room (usually occurring one or more times per day), the prescribed ventilator settings may be adjusted based on the patient's current condition as indicated by the various physiological measurements.

However, the patient's condition may change significantly between successive physician visits. This can lead to the patient being mechanically ventilated under significantly non-optimal ventilator settings until the next physician visit. Ventilation using non-optimal ventilator settings, in turn, enhances the likelihood of ventilator-related lung injury.

Chbat et al., U.S. Pub. No. 2015/0059754 published March 5, 2015 discloses an improvement in which the patient's Power of Breathing (PoB) is estimated in real-time and, if different from a physician-prescribed PoB, one or more ventilator setting adjustments are made (optionally automatically) based on the identified PoB difference. The ventilator setting adjustments may include, for example, changing settings such as tidal volume, respiratory rate, pressure readings, airflow, or so forth, and/or may also include changes to an operating mode of the ventilator. The approach of Chbat et al. is generally applicable to ventilator modes including but not limited to: volume controlled continuous mandatory ventilation, volume controlled intermittent mandatory ventilation, pressure controlled continuous mandatory ventilation, pressure controlled intermittent mandatory ventilation, continuous spontaneous ventilation, high frequency ventilation systems, or so forth.

The following discloses a new and improved systems and methods that address the above referenced issues, and others.

SUMMARY

Notwithstanding the foregoing, there remains a need in the art to provide improved automated ventilator control for spontaneously breathing patients, which can rapidly adapt to changes in the patient's physiological condition, is readily implemented, and is easily comprehended by the physician and nursing staff.

In one disclosed aspect, a respiratory therapy device comprises: a mechanical ventilator configured to provide mechanical ventilation to a patient in a pressure support ventilation (PSV) or pressure support ventilation/intermittent mandatory ventilation (PSV/IMV) mode in accordance with a PSV pressure setting; a power of breathing (PoB) or work of breathing (WoB) estimator configured to generate a PoB or WoB signal for the patient; an error calculator configured to compute an error signal $E(s)$ as a difference between the PoB or WoB signal and a set point PoB or WoB value; and a controller having a controller transfer function $C(s)$ and configured to input the PSV pressure setting equal to $C(s)E(s)$ to the mechanical ventilator. By way of illustration, the mechanical ventilator, the PoB or WoB estimator, the error calculator, and the controller may be operatively interconnected to form a single-input, single-output (SISO) closed loop feedback control system in which the mechanical ventilator and a connected patient and the PoB or WoB estimator define the controlled system whose single input is the PSV pressure setting and whose single controlled output is the PoB or WoB signal. The respiratory therapy device may further include a patient adaptation component comprising an electronic device programmed to fit parameters of a model of the controlled system transfer function to PoB or WoB signal and PSV pressure setting data generated by the operating SISO closed loop feedback control system and to adjust parameters of the controller transfer function $C(s)$ to maintain stability of the closed loop transfer function of the SISO closed loop feedback control system.

In another disclosed aspect, a single input, single output (SISO) closed loop controller is disclosed for controlling a mechanical ventilator configured to provide mechanical ventilation to a patient in a PSV or PSV/IMV mode in accordance with a PSV pressure setting. The closed-loop controller comprises: a PoB or WoB estimator configured to generate a signal representing PoB or WoB of the patient; an error calculator configured to compute an error signal $E(s)$ as a difference between the signal representing PoB or WoB of the patientand a set point value; and a controller having a controller transfer function $C(s)$

and configured to generate the PSV pressure setting as the product $C(s)E(s)$. In some embodiments the SISO closed loop controller further comprises a patient adaptation component comprising an electronic device programmed to fit parameters of a model of the controlled system transfer function $G(s) = \frac{PoB(s)}{PSV(s)}$ of a ventilator providing ventilation to a patient under control of the SISO closed-loop controller to $PoB(s)$ and $PSV(s)$ data generated by the operating SISO closed loop controller and to adjust parameters of the controller transfer function $C(s)$ to maintain stability of the closed loop transfer function $\frac{C(s)G(s)}{1+C(s)G(s)}$.

In another disclosed aspect, a closed loop controller is disclosed for controlling a mechanical ventilator configured to provide mechanical ventilation to a spontaneously breathing patient. The closed-loop controller comprises: a PoB or WoB estimator configured to generate a PoB or WoB signal for the patient; an error calculator configured to compute an error signal $E(s)$ as a difference between the PoB or WoB signal and a set point PoB or WoB value; a controller having a controller transfer function *C(s)* and configured to input a pressure support ventilation (PSV) control signal equal to the product $C(s)E(s)$ to the mechanical ventilator to control the mechanical ventilation provided to the spontaneously breathing patient; and a patient adaptation component comprising an electronic device programmed to fit parameters of a model of a controlled mechanical ventilation system comprising a ventilator and a spontaneously breathing patient ventilated by the mechanical ventilator under control of the closed loop controller to data comprising the PoB or WoB signal and the PSV control signal generated by the operating closed loop controller and to adjust parameters of the controller transfer function $C(s)$ to maintain stability of the operating closed loop controller.

In another disclosed aspect, a closed loop control method is disclosed for controlling mechanical ventilation provided by a mechanical ventilator to a spontaneously breathing patient. The closed-loop control method comprises: measuring a PoB or WoB signal for the patient being provided mechanical ventilation; computing an error signal as a difference between the measured PoB or WoB signal and a set point PoB or WoB value; and setting pressure support of the mechanical ventilation to a control signal computed as a product of a controller transfer function and the error signal.

One advantage resides in providing improved automated ventilator control for mechanically ventilated spontaneously breathing patients.

Another advantage resides in providing such automated ventilator control with physician-prescribed constraints having physiological bases.

Another advantage resides in providing such automated ventilator control that is adaptive to changing patient condition.

Another advantage resides in providing such automated ventilator control that is robust against noise and system disturbances.

Another advantage resides in providing such automated ventilator control with zero steady state error.

A given embodiment may provide none, one, two, more, or all of the foregoing advantages, and/or may provide other advantages as will become apparent to one of ordinary skill in the art upon reading and understanding the present disclosure.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention may take form in various components and arrangements of components, and in various steps and arrangements of steps. The drawings are only for purposes of illustrating the preferred embodiments and are not to be construed as limiting the invention.

FIGURE 1 diagrammatically illustrates a mechanical ventilator system providing Pressure Support Ventilation (PSV) and further including an outer control loop which controls the PSV pressure setting to achieve patient spontaneous respiration with a physician-prescribed Power of Breathing (PoB) level.

FIGURES 2-6 show experimental PoB data (top plot) and PSV pressure setting (bottom plot) for ventilator/patient systems including a Patient #1 (FIGURE 2), a Patient #2 (FIGURE 3), a Patient #3 (FIGURE 4), a Patient #4 (FIGURE 5), and a Patient #5 (FIGURE 6).

FIGURE 7 shows Bode plots (magnitude, upper plot and phase, lower plot) for ventilator/patient system data of Patients #1-#5 presented in respective FIGURES 2-6 fitted to a ventilator-patient system transfer function modeled as $G(s) = \frac{PoB(s)}{PSV(s)} = K/(\tau s + 1)$.

FIGURE 8 shows step responses for the ventilator-patient system transfer functions $G(s)$ of FIGURE 7.

FIGURE 9 shows Bode plots of the closed-loop SISO system transfer functions $L(s)$ for a controller designed as described in the text operating with the ventilator/patient systems of FIGURES 7 and 8

FIGURE 10 plots simulated PoB (top plot) for input PSV pressure setting (bottom plot) for the closed-loop transfer function $L(s)/(1 + L(s))$ where $L(s)$ are the five open-loop system transfer functions of FIGURE 9.

FIGURE 11 illustrates a patient adaptation component optionally added to the single input, single output (SISO) closed loop controller of FIGURE 1.

DETAILED DESCRIPTION

In illustrative examples herein, a mechanically ventilated spontaneously breathing patient is ventilated using pressure support ventilation (PSV), with or without intermittent mandatory ventilation (IMV). In the applied PSV or PSV/IMV ventilation mode, the mechanical ventilator detects the onset of a spontaneous breath and provides pressure support for the breath in accord with a PSV pressure setting. The pressure support waveform may take various forms, e.g. a square wave of amplitude equal to the PSV pressure setting, or an increasing pressure ramp in which the ramp peak equals the PSV pressure setting (or the ramp average or other ramp amplitude characteristic equals the PSV pressure setting), or a decreasing pressure ramp, parabolic pressure waveform, or so forth. The ventilator settings of the applied PSV or PSV/IMV ventilation mode may also include one or more trigger parameters, such as (by way of illustration) a negative pressure threshold wherein airway pressure falling below this threshold is detected as onset of a spontaneous breath, and/or an air flow threshold wherein airway air flow rate above this threshold is detected as onset of a spontaneous breath. If the patient is being oxygenated, the fraction of inspired oxygen (FiO_2) is another ventilator setting. If a PSV/IMV mode is being applied, then one or more IMV mandatory breath cycle settings are also provided. Still further ventilator settings may be provided, such as a maximum inflation volume or other safety-related limits.

It is recognized herein that, of these PSV or PSV/IMV parameters, the PSV pressure setting is the primary parameter for effectively tailoring the PSV or PSV/IMV ventilation to elicit the desired work of breathing (WoB) or power of breathing (PoB) from the patient. Accordingly, in embodiments disclosed herein the PSV pressure setting is the only automatically controlled ventilator setting.

It is further recognized herein that the PSV pressure setting can be controlled based on measured WoB or PoB using a classical feedback control system in which the

combination of the ventilator and the patient, along with the PoB or WoB estimator, is treated as the controlled system having a transfer function $G(s)$ which is controlled by a controller having a transfer function $C(s)$. A transfer function is the ratio of the output to the input of a system (or sub-system), and a transfer function is represented herein in the (complex) frequency domain by its Laplace transform, i.e. for a time-domain transfer function $f(t) = \frac{output(t)}{input(t)}$ where t denotes time, the corresponding s-domain representation of this transfer function is formally computed as its Laplace transform $F(s) = \int_0^\infty e^{-st} f(t)dt$ where s is the complex frequency. In quantitative examples herein the time domain is measured in seconds (sec) and the s-domain is in units of sec^{-1}, although of course other time/frequency units can be employed. Using this classical control paradigm for controlling a mechanical ventilator providing mechanical ventilation to a patient in a PSV or PSV/IMV mode in accordance with a PSV pressure setting, the output of the controlled ventilator/patient system is a WoB or PoB signal, and the control input to the controlled ventilator/patient system is the PSV pressure setting. The WoB or PoB signal is represented herein as $PoB(s)$ in the s-domain, that is, in illustrative examples presented herein the power of breathing (PoB) is employed. The PoB is power per unit time (e.g. having units of Joules/sec), whereas WoB is power per breath (e.g. having units of Joules/breath). Either PoB or WoB can be used as the output signal of the controlled ventilator/patient system, but PoB has an advantage in that it does not depend on the generally non-uniform breath interval of a spontaneously breathing patient. In a suitable approach, if WoB is measured it may be converted to PoB using the breath time interval.

The transfer function of the controlled ventilator/patient system is represented as transfer function $G(s) = \frac{PoB(s)}{PSV(s)}$. It is recognized that a difficulty with the disclosed classical control approach is that $G(s)$ is, in part, a function of the patient. This means that the characteristics of the controlled system will change each time the mechanical ventilator is connected with a different patient, and any time the current patient's respiratory characteristics change in a material way. Depending upon the patient, or the patient's current condition, it is therefore possible that the closed loop transfer function $\frac{C(s)G(s)}{1+C(s)G(s)}$ could become unstable. Control instability in the control of life-sustaining mechanical ventilation is generally unacceptable. This difficulty is addressed herein by two approaches, which may optionally be combined. First, it is shown herein that by appropriate empirical design of the controller transfer function $C(s)$ using measured ventilated patient data comprising the

measured $PoB(s)$ and control signal $PSV(s)$, the controller transfer function $C(s)$ can be designed so that the closed loop transfer function is stable for a wide range of patients.

Second, in some embodiments disclosed herein the controller is adaptive. In these embodiments, the controlled ventilator/patient system transfer function $G(s) = \frac{PoB(s)}{PSV(s)}$ is modeled using $PoB(s)$ and $PSV(s)$ data are collected for the current patient over a representative time interval. The controller transfer function $C(s)$ is then adjusted, if needed, in order to ensure the closed loop system transfer function $\frac{C(s)G(s)}{1+C(s)G(s)}$ is stable for the current patient. This adaptation can be updated periodically to ensure the controller remains a stable.

With reference to FIGURE 1, a respiratory therapy device includes a mechanical ventilator **10** that provides mechanical ventilation to a patient **12** via air hoses **14**. The mechanical ventilator **10** can be of any design capable of delivering mechanical ventilation in a Pressure Support Ventilation (PSV) or pressure support ventilation/intermittent mandatory ventilation (PSV/IMV) mode. The mechanical ventilator **10** may include various ancillary components such as an air filter, a medical oxygen supply to deliver a prescribed fraction of inspired oxygen (FiO_2), a humidifier, or so forth. It will be appreciated that the mechanical ventilator includes a controller, diagrammatically shown and labeled as a "mode" controller **16**, which is a microprocessor or microcontroller and ancillary sensors and electronics programmed to operate the mechanical ventilator **10** in a PSV or PSV/IMV mode based on sensor data **18** such as an airway pressure $P_{aw}(t)$ measured by an airway pressure gauge, and airway air flow $\dot{V}(t)$ measured by an airway air flow sensor. Another common control parameter is the respired air volume $V(t)$ which can be computed from the air flow as $V(t) = \int \dot{V}(t)dt$ (where the integral is computed over a single breath, or over a time from start of inspiration of a current breath to the present time, or over some other time interval of interest). The sensor data **18** may include various other physiological parameters may also be monitored by suitable sensors such as heart rate (HR), respiratory rate (RR), end-tidal carbon dioxide ($etCO_2$, measured by capnography), or so forth. These data may be displayed on a display component **19** of the mechanical ventilator **10**, and/or on a bedside patient monitor or so forth. To provide pressure support in the PSV or PSV/IMV mode, the mode controller **16** detects the onset of spontaneous inspiration (i.e. start of a breath intake), for example as an abrupt decrease in airway pressure $P_{aw}(t)$ and/or an abrupt increase in air flow $\dot{V}(t)$. Thresholds for this detection may be physician-prescribed parameters or default values of the mechanical ventilator **10**. Upon detection of onset of a spontaneous breath intake, the mechanical ventilator **10** applies pressure at a PSV pressure

setting to support the patient's spontaneous inhalation effort. This pressure may be provided in accord with a prescribed or default pressure support-over-time profile, e.g. a square wave (pressure support at a constant magnitude over the breath) or with some ramp or other profile feature(s). The pressure support may be terminated after a fixed time interval, or may be terminated based on detection of the end of the patient's spontaneous breath intake effort.

If the mode controller **16** is implementing a PSV/IMV mode, then in addition to providing the foregoing pressure support for spontaneous breaths, the mode controller **16** additionally triggers ventilator-driven (i.e. mandatory) breaths if the spontaneous breaths alone do not provide a prescribed or default minimum level of ventilation for the patient (which may be measured based on total number of breaths, and/or inspired air volume, or so forth). In some embodiments, the mode controller **16** implements a PSV/IMV mode in which the intermittent mandatory ventilation is provided in accordance with a synchronized intermittent mandatory ventilation (SIMV) approach in which the timing of any mandatory breaths is synchronized with the spontaneous breaths.

It is to be appreciated that the PSV or PSV/IMV mode may be implemented in the respiratory therapy device of FIGURE 1 without modification from conventional PSV or PSV/IMV mode mechanical ventilation. Thus, the physician may prescribe various trigger thresholds or other PSV or PSV/IMV mode parameters as is conventional in the respiratory therapy arts, and the mechanical ventilator **10** implements the PSV or PSV/IMV mode in a conventional manner.

The respiratory therapy device of FIGURE 1 differs from a conventional mechanical ventilation device in that it provides an "outer" control loop, that is, a control loop that is "outside" of the control loop of the mode controller **16**. This outer control loop is referred to hereinafter as a single-input, single-output (SISO) closed loop feedback control system or using similar phraseology. The SISO control loop employs classical feedback control using a controller **20** having a transfer function designated herein without loss of generality as $C(s)$. The SISO control loop receives as input a physician-prescribed power of breathing (PoB) set point **22**, which is the desired respiratory effort for the patient **12**. The controller **20** outputs a control signal **24** in the form of a PSV setting **24** that is input to the mechanical ventilator **10**. The ventilator/patient system **26** comprising the mechanical ventilator **10** and the patient **12** operates in accord with the PSV or PSV/IMV settings prescribed by the physician but with the PSV setting equal to the control signal **24**. A PoB estimator **30** estimates the PoB exerted by the patient **12** based on sensor data **32**. The PoB estimator **30** outputs a measured PoB signal **34** which is compared with the set point PoB **22**

by an error calculator **36** configured to compute an error signal $E(s)$ as a difference between the PoB signal **34** and the set point PoB value **22**. This error signal $E(s)$ is input to the PSV pressure setting controller **20** which computes the PSV setting **24** as $C(s)E(s)$, that is, the product of the controller transfer function $C(s)$ of the controller **20** and the error signal $E(s)$.

To ensure patient safety, the physician may optionally prescribe lower and upper limits **38** on the PSV setting **24**, so that if the product $C(s)E(s)$ goes below the lower limit the control signal is set to the lower limit, and similarly if the product $C(s)E(s)$ goes above the upper limit the control signal is set to the upper limit. Reaching these (or optionally other) physician-prescribed upper or lower limits optionally also sets off an alarm, e.g. a warning displayed on the display component **19** of the mechanical ventilator **10** that the pressure support provided by the mechanical ventilator **10** has reached (or is approaching) an upper or lower limit. More generally, the lower and upper PSV limits **38** may be physician-prescribed values, or may be default limits of the respiratory therapy device. In another embodiment, both are contemplated, e.g. default upper and lower limits and additionally the physician can choose to prescribe a narrower limit (e.g. a lower upper limit than the default, or a higher lower limit than the default).

In a suitable embodiment, the PoB estimator **30** computes the PoB by integrating the respiratory muscle pressure $P_{mus}(t)$, which is the pressure applied by the patient's muscles (primarily the thoracic diaphragm though other thoracic muscles may contribute) over time, i.e. $PoB = \int P_{mus}(t)dt$. In the illustrative embodiment, the respiratory muscle pressure $P_{mus}(t)$ is measured using an esophageal pressure measurement employing a balloon that is inserted inside the esophagus of the patient **12** and outputs sensor data **32** comprising measured esophageal pressure $P_{es}(t)$. The esophageal pressure is assumed to be a good proxy for the pleural pressure and is used, in conjunction with an estimate of respiratory system chest wall compliance C_{rs}, to compute the WoB via the so-called Campbell diagram or, equivalently, via explicit computation of $P_{mus}(t)$ and then of PoB. In another contemplated embodiment, respiratory muscle pressure $P_{mus}(t)$ is estimated using an Equation of Motion of the Lungs, e.g. using a first-order Equation of the Lungs given by:

$$P_{aw}(t) = R_{rs}\dot{V}(t) + \left(\frac{1}{C_{rs}}\right)V(t) + P_{mus}(t) + P_0 \qquad (1)$$

where $P_{aw}(t)$ is the measured airway pressure, $\dot{V}(t)$ is the measured air flow, $V(t)$ is the respired air volume, i.e. $V(t) = \int \dot{V}(t)dt$, R_{rs} is the respiratory system resistance, C_{rs} is the

respiratory system complance (or, equivalently, elastance $E_{rs} = 1/C_{rs}$ can be substituted in Equation (1)), and P_0 is a constant term to account for the pressure at the end of expiration. Thus, in the illustrative embodiment the sensor inputs **32** to the PoB estimator **30** include airway pressure $P_{aw}(t)$ and flow $\dot{V}(t)$. In one approach, the flow-interrupter technique, also called End Inspiratory Pause (EIP), is used to determine the respiratory system parameters R_{rs} and C_{rs} (or E_{rs}) after which $P_{mus}(t)$ is obtained directly from Equation (1). A disadvantage of this approach is that it is invasive insofar as it involves occasional interruption of flow through the airway to perform the EIP respiratory system assessment. Alternatively, Equation (1) may be solved to simultaneously determine $P_{mus}(t)$, R_{rs}, and C_{rs} (or E_{rs}). In this case Equation (1) is underdetermined since for N samples there are $N + 2$ unknowns (the values of $P_{mus}(t)$ for each of the N samples plus R_{rs} and C_{rs}). A piecewise approximation of $P_{mus}(t)$ or other approach for reducing the number of unknowns is contemplated to make the simultaneous solution tractable.

As indicated in FIGURE 1, the controlled system has a transfer function $G(s) = \frac{PoB(s)}{PSV(s)}$ where $PSV(s)$ is the control input **24** (i.e. the PSV setting) and $PoB(s)$ is the POB signal **34** output by the PoB estimator **30**. In accord with classical control theory, the open loop transfer function $L(s)$ of the SISO closed loop control system is $L(s) = C(s)G(s)$. The closed loop transfer function is $\frac{L(s)}{(1+L(s))} = \frac{C(s)G(s)}{(1+C(s)G(s))}$. This closed loop system becomes unstable if $C(s)G(s) \rightarrow -1$ and is stable otherwise.

The transfer function $G(s) = \frac{PoB(s)}{PSV(s)}$ is, in general, different from patient to patient, and also depends on the patient's current respiratory system condition and general health, state of consciousness, or so forth. Furthermore, the transfer function $G(s)$ may depend on the physician-prescribed or default settings of the PSV or PSV/IMV mode currently in force, such as the trigger settings for triggering pressure support. (As an example, if the operational trigger setting results in some delay in the initiation of pressure support this can lead to increased patient effort and hence higher PoB). This means that $G(s)$ can vary significantly, and the transfer function $C(s)$ of the controller **20** is preferably designed to provide large operational margins for $G(s)$ that encompass a wide range (and preferably all) of the credible variants of the system transfer function $G(s)$. To this end, a representative database is generated for "training" patients under mechanical ventilation. For each training patient, input PSV and output PoB data are collected for different PSV settings. These training data are used for optimizing the controller $C(s)$. In the following, an illustrative

design approach for designing the controller **20**, and more particularly its transfer function $C(s)$, is described.

With reference to Table 1, in this controller design example training data for five patients designated P1, P2, P3, P4, and P5, respectively, were used for the system modeling. Table 1 lists the age, gender, height, weight, and disease/medical issue of each of these five training patients.

Table 1 – training patients

Patient #	Age	Gender	Height	Weight	Disease, Issue
P1	79	Male	68 inches	70 kg	Ischemic gut
P2	70	Female	60 inches	60 kg	Sepsis, COPD
P3	55	Male	67 inches	71 kg	Hemopneumothorax
P4	54	Male	67 inches	76 kg	Sepsis (candidemia)
P5	77	Male	70 inches	71 kg	Bilateral Pneumonia

With reference to FIGURES 2-6, each training patient was mechanically ventilated under PSV mode and during the ventilation, the level of pressure support was changed a few times. Also, during the ventilation time, the esophageal pressure is measured using an esophageal balloon. The respiratory muscle pressure $P_{mus}(t)$ was calculated using an estimated value of chest wall compliance, and the PoB was calculated from $P_{mus}(t)$. These acquired training data are plotted in FIGURES 2-6 for patients P1-P5, respectively. Referring back to FIGURE 1, the data of FIGURES 2-6 can be understood to have been acquired running the system of FIGURE 1 open loop, that is, without using the controller **20**. In each of FIGURES 2-6, the top plot shows the measured PoB signal **34** (in units of Joules/min) and the bottom plot shows the input PSV setting **24** (in units of cmH_2O), again operating in open loop without use of the controller **20**. As seen in FIGURES 2-6, the level of noise or disturbance in the ventilator/patient/PoB estimator system is high, and this noise information was taken into account in the design of the control system.

With reference to FIGURES 7 and 8 and with further reference to Table 2, the training data of FIGURES 2-6 were fitted to a first order dynamic model of the transfer function $G(s)$ of the form:

$$G(s) = \frac{PoB(s)}{PSV(s)} = \frac{K_p}{\tau s + 1} \qquad (2)$$

where $PoB(s)$ is the (open loop) PoB signal **34**, $PSV(s)$ is the (open loop) input PSV setting **24**, K_p is a gain parameter, and τ is a time parameter. Table 2 lists the fitted values for K_p and τ for the ventilator/patient system for each of the five patients P1-P5. FIGURE 7 shows the Bode plots of the five open loop ventilator/patient systems. FIGURE 8 shows the time-domain step responses of the five open loop ventilator/patient systems. It is noteworthy that although these five ventilator/patient systems are very different in terms of time responses (FIGURE 8), the DC gain K_p of all five ventilator/patient systems are within a relatively small range between -0.80 and -1.05. This simplifies the gain selection for the controller transfer function $C(s)$.

Table 2 – System models for training ventilator/patient systems

Patient #	K_p (DC gain)	τ (Time constant)
P1	-0.90	33.3
P2	-0.90	27.7
P3	-0.87	491
P4	-1.02	50.6
P5	-0.81	203.5

With reference now to FIGURE 9, design of the controller transfer function $C(s)$ based on the five ventilator/patient training systems is described. From the training data of FIGURES 2-6, it is seen that the noise in the system is at a relatively low frequency. This motivates providing a non-zero, positive-valued pole at relatively low frequency, e.g. a non-zero, positive pole $P \leq 200$ sec^{-1} in some contemplated embodiments. Furthermore, the controller **20** should provide zero steady state error – this motivates placing another pole at the origin of the s-plane. A suitable controller model is thus:

$$C(s) = \frac{K}{s(s+P)} \tag{3}$$

where P is the noise-suppressing non-zero, positive pole. Designing the values of the controller gain K and noise-suppressing pole P for control of the training systems of Table 2 and FIGURES 7-9 yielded $K = -0.002$ and $P = 100$ sec^{-1} so that the designed controller transfer function was:

$$C(s) = \frac{-0.002}{s(s+100)} \quad (4)$$

The gain $K = -0.002$ and the location $P = 100$ sec^{-1} of the noise-suppressing pole were selected to maximize gain and phase margin for the five training ventilator/patient systems of Table 2 and FIGURES 2-6. FIGURE 9 shows the Bode plots of the closed-loop SISO system transfer functions $L(s)$ for the controller $C(s)$ of Equation (4) operating with the ventilator/patient systems of FIGURES 7 and 8. Table 3 lists the gain margin (GM), phase margin (PM), and bandwidth (BW) achieved for each patient by the designed controller.

Table 3 – margins of stability

Patient #	GM (dB)	PM (Deg)	BW (rad/sec)
P1	29	76	(.00178)
P2	28	77.1	(.00177)
P3	16.8	47.1	(.00142)
P4	23.3	73	(.00199)
P5	19.3	64	(.00153)

With reference now to FIGURE 10, the controller design of Equation (4) was simulated on the ventilator/patient models of Equation (2) and Table 2. In these simulations, the PSV level was updated every 5 minutes, with the PSV updates discretized to a minimum PSV level change of 1 cmH_2O up or down. The maximum allowable PSV change step was 5 cmH_2O (that is, the largest change in PSV setting at a single 5 minute interval). The PSV lower and upper limits **38** were 0 cmH_2O and 25 cmH_2O, respectively. FIGURE 10 shows the simulation results, which exhibited stable responses for all five ventilator/patient systems.

With returning reference to FIGURE 1, when the respiratory therapy device is started an initial or starting PSV setting is suitably chosen, e.g. prescribed by the physician (preferably) or a default initial PSV setting may be used. The controller **20** then adjusts the PSV setting **24** based on accumulating history of the PoB signal **34** and thereby accumulating error history $E(s)$.

It will be appreciated that the controller represented by the transfer function $C(s)$ of Equation (3) is an illustrative example which has been demonstrated to work well for the representative ventilator/patient systems used in the training. Other controller designs are

contemplated. For example, adding a zero to the controller transfer function is contemplated to provide a faster transient response. Another contemplated variant is to add a second, higher frequency positive pole, e.g. at a value greater than 200 sec^{-1}, which could beneficially suppress higher frequency noise if present.

The respiratory therapy device of FIGURE 1 using a controller transfer function in accord with Equation (3) has been shown to provide large margins for the five training ventilator/patient systems. However, it is further disclosed herein that additional stability can be obtained by constructing the controller **20** to be an adaptive controller. This may be useful, for example, if the controller **20** is to be used with a wider range of patient types (e.g. both infants and elderly patients), or with a number of different types of mechanical ventilators, patient accessories, or so forth.

With continuing reference to FIGURE 1 and with further reference to FIGURE 11, an adaptive variant of the controller **20** is described. Diagrammatically indicated in FIGURE 11 are the controller **20** (grouped with the error calculator **36** as a unit in FIGURE 11), the physician-prescribed PoB set point **22**, and the estimated PoB signal **34**. Also indicated in FIGURE 11 is the PSV setting **24** output by the controller **20**. The start of patient ventilation is indicated in FIGURE 1 by a "start" block **50**. The variant of FIGURE 11 adds a patient adaptation component including blocks **52**, **54**, **56**, **60**. After ventilator startup **50**, the SISO closed-loop feedback controller runs for a pre-set time (two hours, i.e. 120 min, in the illustrative example of FIGURE 11) to collect sufficient data to perform controller adaptation. A delay block **52** diagrammatically shows implementation of this initial delay. During this delay, PoB and PSV setting data are collected and stored in operation **54**. When the pre-set time interval (e.g. 120 min) has passed, flow passes to a ventilator/patient model update operation **56**, which updates $G(s)$. In the illustrative example of using a first-order dynamic model of the transfer function $G(s)$, this can be done by fitting the first-order model of Equation (2) to optimize K_p and τ respective to the collected (PSV(t), PoB(t)) data after transforming PSV(t) and PoB(t), respectively, into the s-domain using the Laplace transform. The resulting updated $G(s)$ **58** is input to a controller update operation **60** which updates the controller transfer function $C(s)$ to provide large-margin control of the ventilator/patient represented by the updated $G(s)$ **58**. For the controller transfer function model of Equation (3), this can be done by optimizing the controller gain K and pole P parameters so that the closed-loop transfer function $\frac{C(s)G(s)}{(1+C(s)G(s))}$ with the updated $G(s)$ **58** provides large gain and

phase operating margins. The resulting updated controller transfer function $C(s)$ **62** is loaded into the controller **20** for subsequent use in controlling the mechanical ventilator **10**.

The outer loop components (e.g. controller **20**, PoB estimator **30**, error calculator **36**, and optional controller adaptation components shown in FIGURE 11) may be implemented as one or more electronic components separate from the mechanical ventilator **10**. For example, in one embodiment the controller **20**, PoB estimator **30**, and error calculator **36** are constructed as a unitary add-on control box including a microprocessor or microcontroller and ancillary circuitry, and having a port outputting the PSV setting **24** via a cable to the mechanical ventilator **10** and having an input port receiving the esophageal pressure reading **32** from an esophageal catheter.

Alternatively, some or all of the outer loop components can be integrated with the mechanical ventilator **10**. In this case the controller **20**, PoB estimator **30**, and error calculator **36** are suitably implemented on the same microprocessor that is programmed to implement the mode controller **16**. In this embodiment the PSV setting **24** is conveyed to the mode controller **16** in software, e.g. as an argument of a call function or so forth, and the mechanical ventilator **10** is modified only in providing an input port to receive the esophageal pressure reading **32**. In a variant embodiment, if the PoB signal **34** is calculated using an Equation of Motion of the Lungs (e.g. the first order Equation of Motion of the Lungs of Equation (1)), and as the mechanical ventilator **10** typically already receives the airway pressure $P_{aw}(t)$ and air flow $\dot{V}(t)$ as inputs, the outer loop can be implemented on the same microprocessor of the mechanical ventilator **10** which implements the mode controller **16** without adding any additional input or output ports or other hardware.

It will be further appreciated that various functionality of the outer loop (and optionally also the mode controller **16**) may be implemented as a non-transitory storage medium storing instructions executable on the microprocessor of the mechanical ventilator **10** and/or on a separate microprocessor to perform the disclosed control functionality (optionally with a adaptation as described with reference to FIGURE 11). The non-transitory storage medium may, for example, comprise a flash memory or other solid state electronic storage device or component, a magnetic disk or other magnetic storage device or component, an optical disk or other optical storage device or component, or so forth.

The invention has been described with reference to the preferred embodiments. Modifications and alterations may occur to others upon reading and understanding the preceding detailed description. It is intended that the invention be

construed as including all such modifications and alterations insofar as they come within the scope of the appended claims or the equivalents thereof.

CLAIMS:

1. A respiratory therapy device comprising:

a mechanical ventilator (10) configured to provide mechanical ventilation to a patient (12) in a pressure support ventilation (PSV) or pressure support ventilation/intermittent mandatory ventilation (PSV/IMV) mode in accordance with a PSV pressure setting (24);

a power of breathing (PoB) or work of breathing (WoB) estimator (30) configured to generate a PoB or WoB signal (34) for the patient;

an error calculator (36) configured to compute an error signal $E(s)$ as a difference between the PoB or WoB signal and a set point PoB or WoB value (22); and

a controller (20) having a controller transfer function $C(s)$ and configured to input the PSV pressure setting (24) equal to $C(s)E(s)$ to the mechanical ventilator.

2. The respiratory therapy device of claim 1 wherein the mechanical ventilator (10), the PoB or WoB estimator (30), the error calculator (36), and the controller (20) are operatively interconnected to form a single-input, single-output (SISO) closed loop feedback control system in which the mechanical ventilator and a connected patient (12) and the PoB or WoB estimator define the controlled system whose single input is the PSV pressure setting (24) and whose single controlled output is the PoB or WoB signal (34).

3. The respiratory therapy device of claim 2 wherein the controlled system has a controlled system transfer function

$$G(s) = \frac{PoB(s)}{PSV(s)} = \frac{K_p}{\tau s + 1}$$

where $PoB(s)$ is the PoB or WoB signal and $PSV(s)$ is the PSV pressure setting, and the respiratory therapy device further comprises:

a patient adaptation component (52, 54, 56, 60) comprising an electronic device programmed to fit K_p and τ to $(PoB(s), PSV(s))$ data generated by the operating SISO closed loop feedback control system and to adjust parameters of the controller transfer function $C(s)$ to maintain stability of the closed loop transfer function

$$\frac{C(s)G(s)}{1 + C(s)G(s)}$$

of the SISO closed loop feedback control system.

4. The respiratory therapy device of claim 2 further comprising:

a patient adaptation component (52, 54, 56, 60) comprising an electronic device programmed to fit parameters of a model of the controlled system transfer function

$$G(s) = \frac{PoB(s)}{PSV(s)}$$

where $PoB(s)$ is the PoB or WoB signal (34) and $PSV(s)$ is the PSV pressure setting (24) to $(PoB(s), PSV(s))$ data generated by the operating SISO closed loop feedback control system and to adjust parameters of the controller transfer function $C(s)$ to maintain stability of the closed loop transfer function

$$\frac{C(s)G(s)}{1 + C(s)G(s)}$$

of the SISO closed loop feedback control system.

5. The respiratory therapy device of claim 2 further comprising:

a patient adaptation component (52, 54, 56, 60) comprising an electronic device programmed to fit parameters of a model of the controlled system transfer function to PoB or WoB signal (34) and PSV pressure setting data (24) generated by the operating SISO closed loop feedback control system and to adjust parameters of the controller transfer function $C(s)$ to maintain stability of the closed loop transfer function of the SISO closed loop feedback control system.

6. The respiratory therapy device of any one of claims 1-5 wherein the controller (20) has programmed upper and lower PSV pressure setting limits (38) and the controller is configured to limit the PSV pressure setting input (24) to the mechanical ventilator (10) to an allowable PSV pressure setting range bounded by the upper and lower PSV pressure setting limits.

7. The respiratory therapy device of any one of claims 1-6 wherein:

$$C(s) = \frac{-K}{s(s + P)}$$

where K is a positive value and P is a positive value.

8. The respiratory therapy device of any one of claims 1-6 wherein $C(s)$ includes a pole at zero and a pole with a positive value P.

9. The respiratory therapy device of any one of claims 7-8 wherein $P \leq 200$ sec^{-1}.

10. A single input, single output (SISO) closed-loop controller for controlling a mechanical ventilator (10) configured to provide mechanical ventilation to a patient (12) in a pressure support ventilation (PSV) or pressure support ventilation/intermittent mandatory ventilation (PSV/IMV) mode in accordance with a PSV pressure setting (24), the closed-loop controller comprising:

a power of breathing (PoB) or work of breathing (WoB) estimator (30) configured to generate a signal (34) representing PoB or WoB of the patient;

an error calculator (36) configured to compute an error signal $E(s)$ as a difference between the signal representing PoB or WoB of the patient and a set point value (22); and

a controller (20) having a controller transfer function $C(s)$ and configured to generate the PSV pressure setting (24) as the product $C(s)E(s)$.

11. The SISO closed-loop controller of claim 10 further comprising:

a patient adaptation component (52, 54, 56, 60) comprising an electronic device programmed to fit parameters of a model of the controlled system transfer function $G(s) = \frac{PoB(s)}{PSV(s)}$ of the mechanical ventilator (10) providing ventilation to the patient (12) under control of the SISO closed-loop controller to $PoB(s)$ and $PSV(s)$ data generated by the operating SISO closed loop controller, where $PoB(s)$ are signal data representing the PoB or WoB of the patient and $PSV(s)$ are PSV pressure setting data, and to adjust parameters of the controller transfer function $C(s)$ to maintain stability of the closed loop transfer function $\frac{C(s)G(s)}{1+C(s)G(s)}$.

12. The SISO closed-loop controller of claim 10 further comprising:

a patient adaptation component (52, 54, 56, 60) comprising an electronic device programmed to fit parameters of a model of the controlled system transfer function of the mechanical ventilator (10) providing ventilation to the patient (12) under control of the operating SISO close-loop controller to $PoB(s)$ and $PSV(s)$ data generated by the operating SISO closed loop controller, where $PoB(s)$ are signal data representing the PoB or WoB of

the patient and $PSV(s)$ are PSV pressure setting data, and to adjust parameters of the controller transfer function $C(s)$ to maintain stability of the operating SISO closed-loop controller.

13. The SISO closed-loop controller of any one of claims 10-12 wherein the controller (20) has programmed upper and lower limits (38) for the PSV pressure setting (24).

14. The SISO closed-loop controller of any one of claims 10-13 wherein:

$$C(s) = \frac{-K}{s(s+P)}$$

where K is a positive value and P is a positive value.

15. The SISO closed-loop controller of any one of claims 10-13 wherein $C(s)$ includes a pole at zero and a pole with a positive value P.

16. The SISO closed-loop controller of any one of claims 14-15 wherein $P \leq 200$ sec^{-1}.

17. A closed-loop ventilator controller for controlling a mechanical ventilator (10) configured to provide mechanical ventilation to a spontaneously breathing patient (12), the closed-loop controller comprising:

a power of breathing (PoB) or work of breathing (WoB) estimator (30) configured to generate a PoB or WoB signal (34) for the patient;

an error calculator (36) configured to compute an error signal $E(s)$ as a difference between the PoB or WoB signal and a set point PoB or WoB value (22);

a controller (20) having a controller transfer function $C(s)$ and configured to input a pressure support ventilation (PSV) control signal (24) equal to the product $C(s)E(s)$ to the mechanical ventilator to control the mechanical ventilation provided to the spontaneously breathing patient; and

a patient adaptation component (52, 54, 56, 60) comprising an electronic device programmed to fit parameters of a model of a controlled mechanical ventilation system comprising the mechanical ventilator (10) and the spontaneously breathing patient (12) ventilated by the mechanical ventilator under control of the closed-loop controller to data

comprising the PoB or WoB signal and the PSV control signal generated by the operating closed loop controller and to adjust parameters of the controller transfer function $C(s)$ to maintain stability of the operating closed-loop controller.

18. The closed-loop controller of claim 17 wherein the controlled mechanical ventilation system has a controlled system transfer function

$$G(s) = \frac{PoB(s)}{PSV(s)}$$

where $PoB(s)$ is the PoB or WoB signal (34) for the patient and $PSV(s)$ is the PSV control signal (24) input by the controller (20) to the mechanical ventilator (10).

19. The closed-loop controller of claim 18 wherein the patient adaptation component (52, 54, 56, 60) is programmed to adjust parameters of the controller transfer function $C(s)$ to maintain stability of

$$\frac{C(s)G(s)}{1 + C(s)G(s)}$$

which is the closed loop transfer function of the closed-loop controller.

20. The closed-loop controller of any one of claims 17-20 wherein the patient adaptation component (52, 54, 56, 60) is programmed to adjust parameters of the controller transfer function $C(s)$ including at least one non-zero and positive pole of the controller transfer function $C(s)$ to maintain stability of the operating closed-loop controller.

21. A closed-loop control method for controlling mechanical ventilation provided by a mechanical ventilator (10) to a spontaneously breathing patient (12), the closed-loop control method comprising:

measuring a power of breathing (PoB) or work of breathing (WoB) signal (34) for the patient being provided mechanical ventilation;

computing an error signal as a difference between the measured PoB or WoB signal and a set point PoB or WoB value (22); and

setting pressure support of the mechanical ventilation to a control signal (24) computed as a product of a controller transfer function and the error signal.

22. The closed-loop control method of claim 21 further comprising:

fitting parameters of a model of a transfer function $G(s) = \frac{PoB(s)}{PSV(s)}$ of the mechanical ventilation provided by the mechanical ventilator (10) to the spontaneously breathing patient (12) to data including the PoB or WoB signal $PoB(s)$ and the control signal $PSV(s)$ generated over time by the performing of the closed-loop control method; and

adjusting the controller transfer function to maintain stability of the closed-loop control provided by the closed-loop control method.

23. The closed-loop control method of any one of claims 21-22 wherein the controller transfer function includes at least one noise-suppressing non-zero positive pole whose value is 200 sec^{-1} or lower.

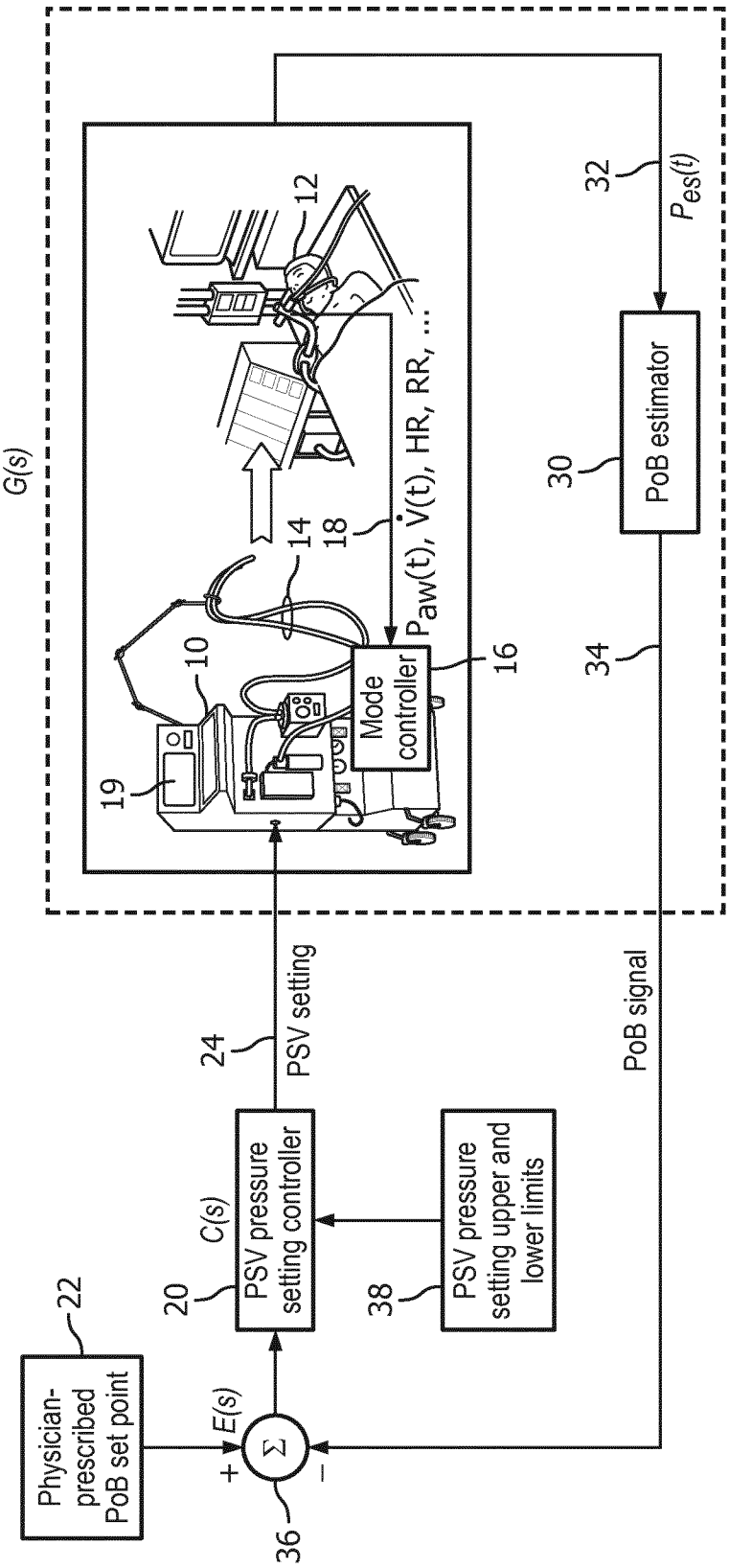

G(s)
12
14
18
10
19
Mode controller
16
$P_{aw}(t)$, $\dot{V}(t)$, HR, RR, ...
32
$P_{es}(t)$
30
PoB estimator
34
PoB signal
24
PSV setting
20
C(s)
PSV pressure setting controller
38
PSV pressure setting upper and lower limits
22
Physician-prescribed PoB set point
E(s)
+
−
36
Open loop transfer function L(s) = C(s) G(s)
Closed loop transfer function = L(s) / (1+L(s))

FIG. 1

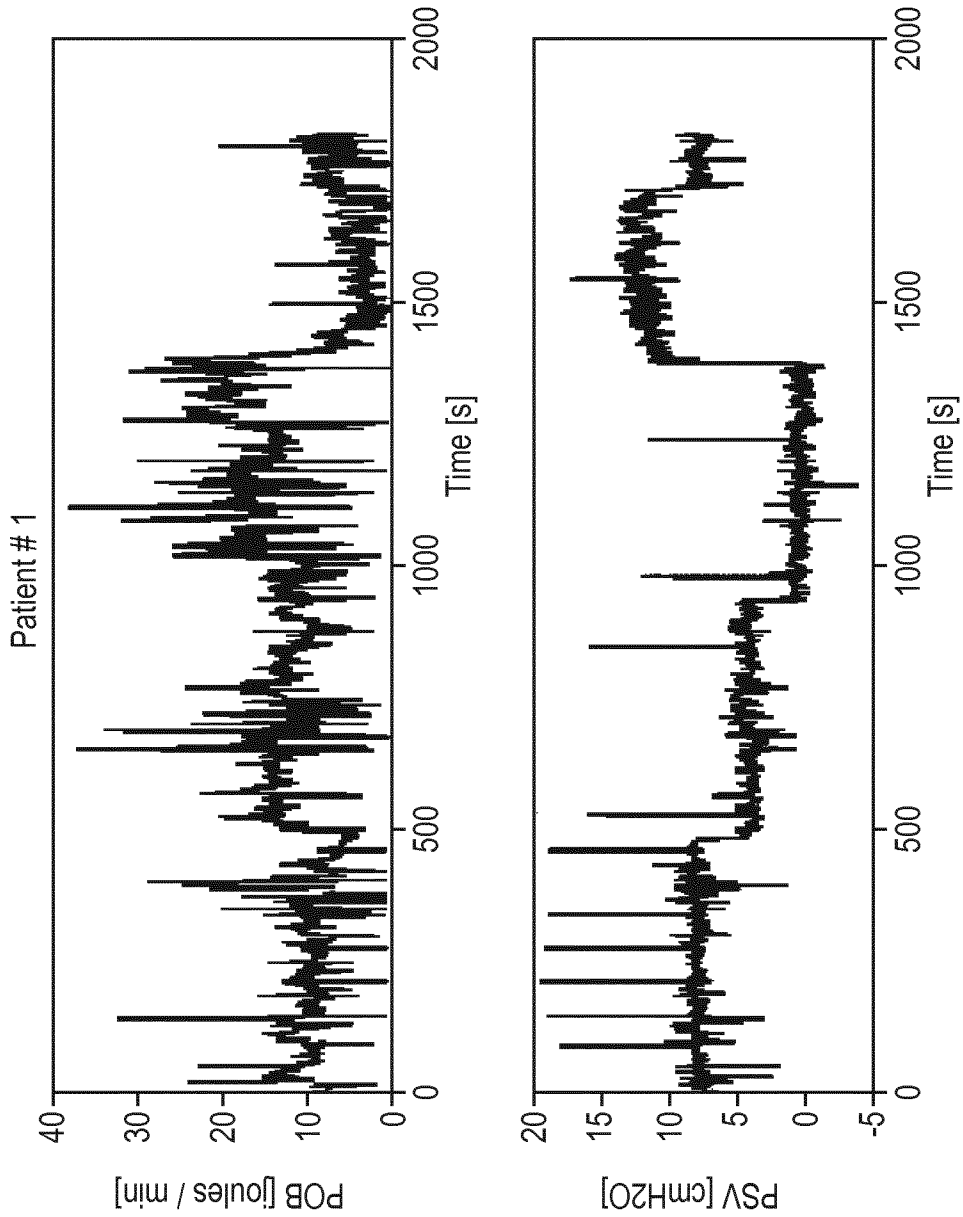

Patient # 1
POB [joules / min]
40
30
20
10
0
0
500
1000
1500
2000
Time [s]
PSV [cmH2O]
20
15
10
5
0
-5
0
500
1000
1500
2000
Time [s]

FIG. 2

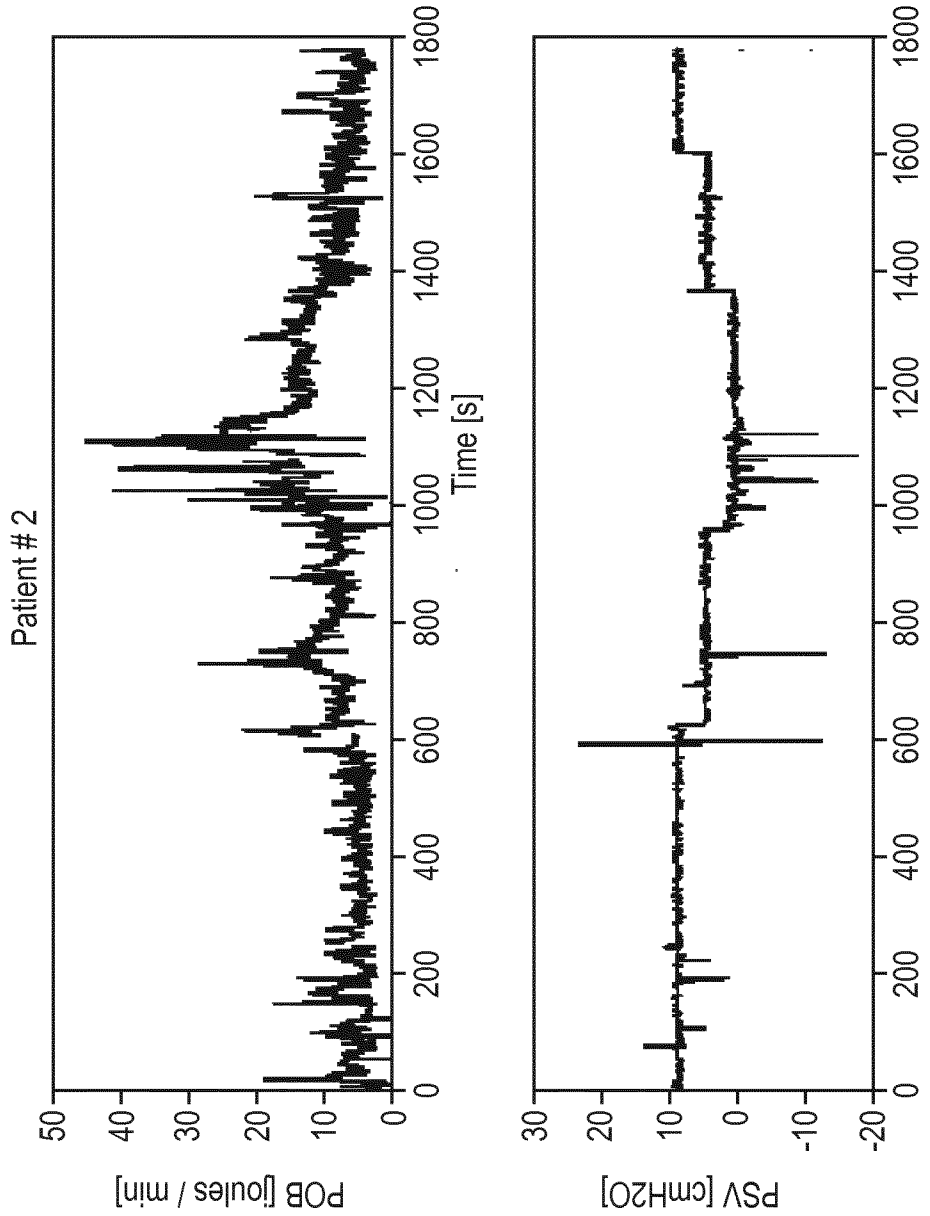


FIG. 3

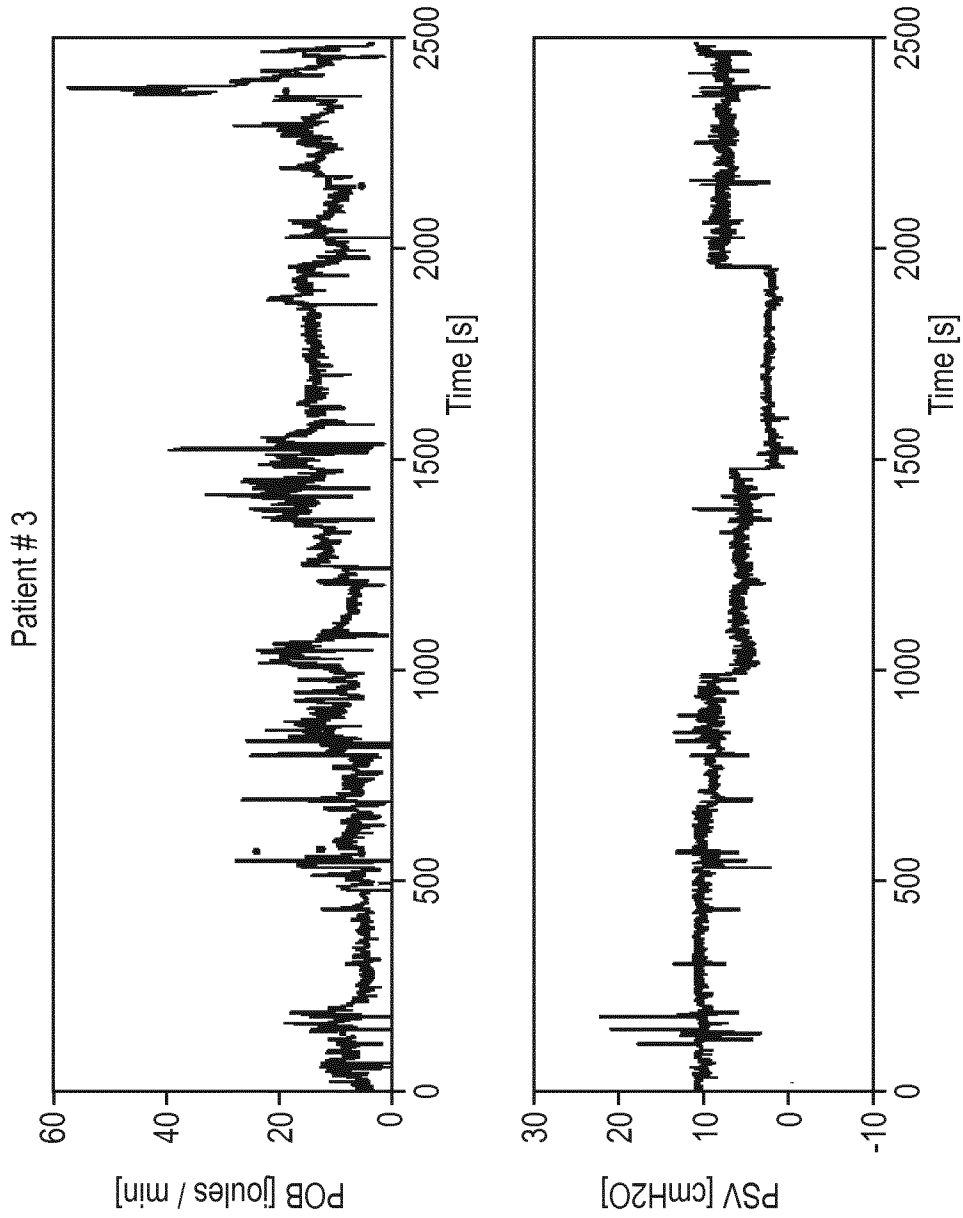

Patient # 3
POB [joules / min]
60
40
20
0
0
500
1000
1500
2000
2500
Time [s]
PSV [cmH2O]
30
20
10
0
-10
0
500
1000
1500
2000
2500
Time [s]

FIG. 4

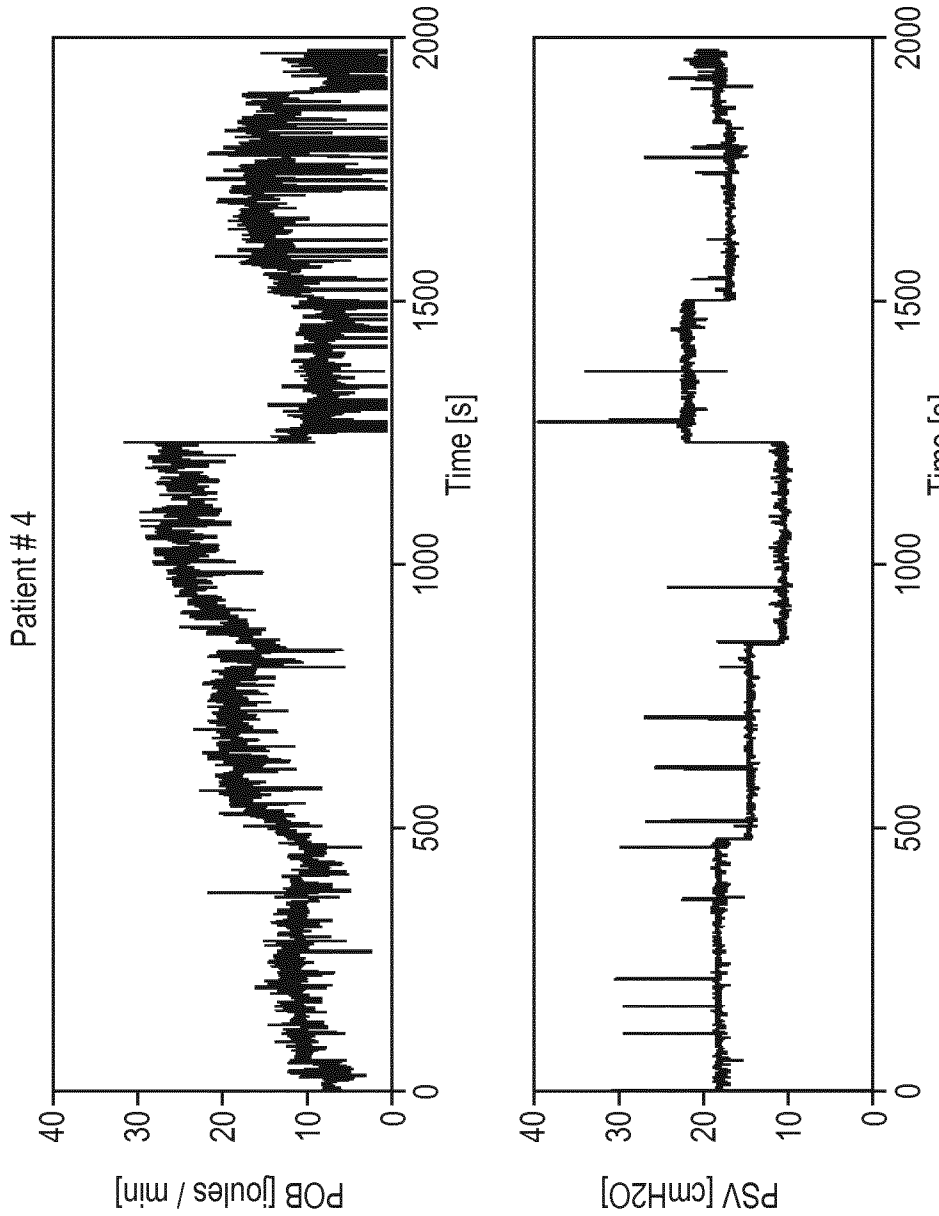

Patient # 4
POB [joules / min]
PSV [cmH2O]
Time [s]
Time [s]
0
10
20
30
40
0
500
1000
1500
2000

FIG. 5

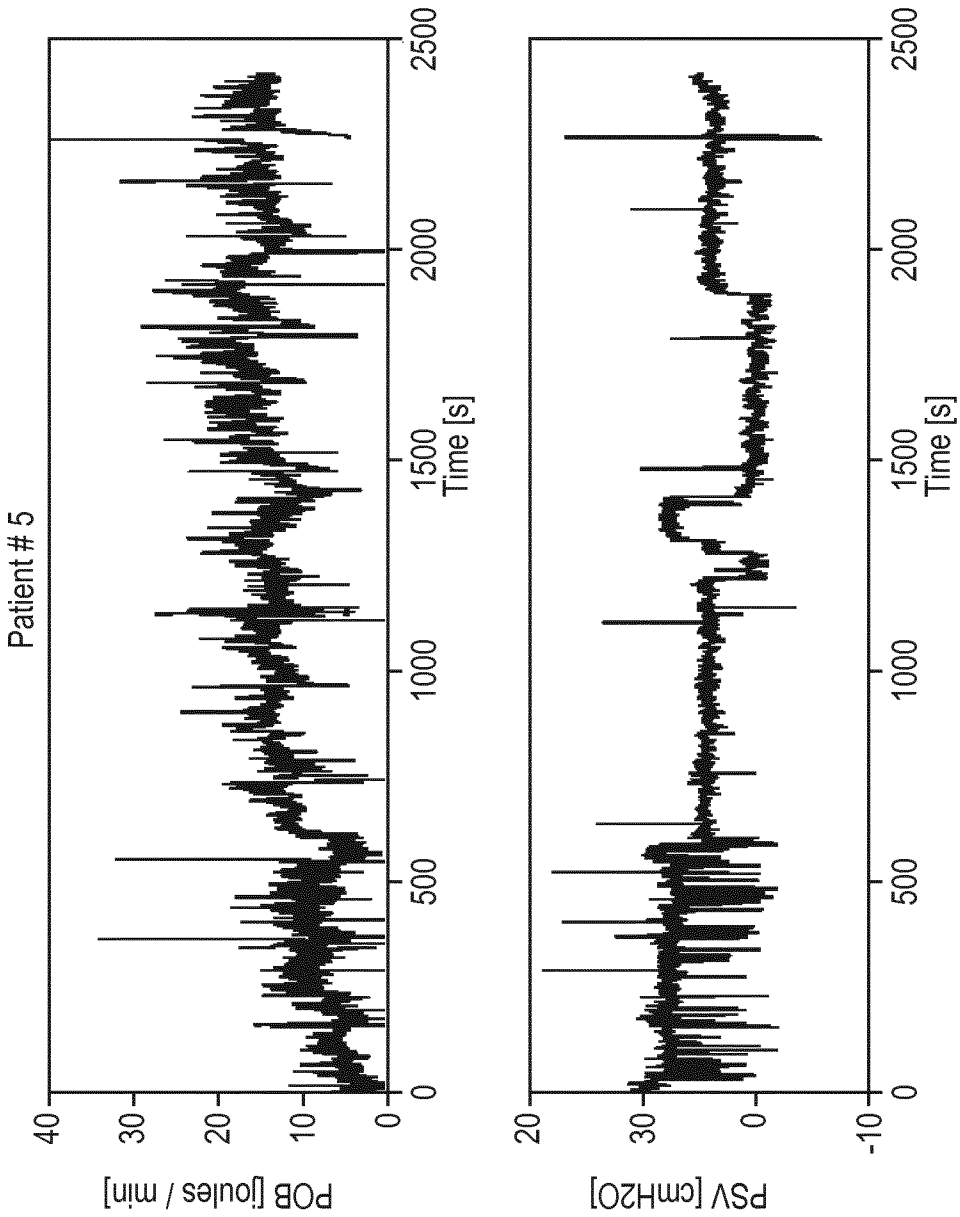

Patient # 5
POB [Joules / min]
0
10
20
30
40
0
500
1000
1500
2000
2500
Time [s]
PSV [cmH2O]
20
30
0
-10
0
500
1000
1500
2000
2500
Time [s]

FIG. 6

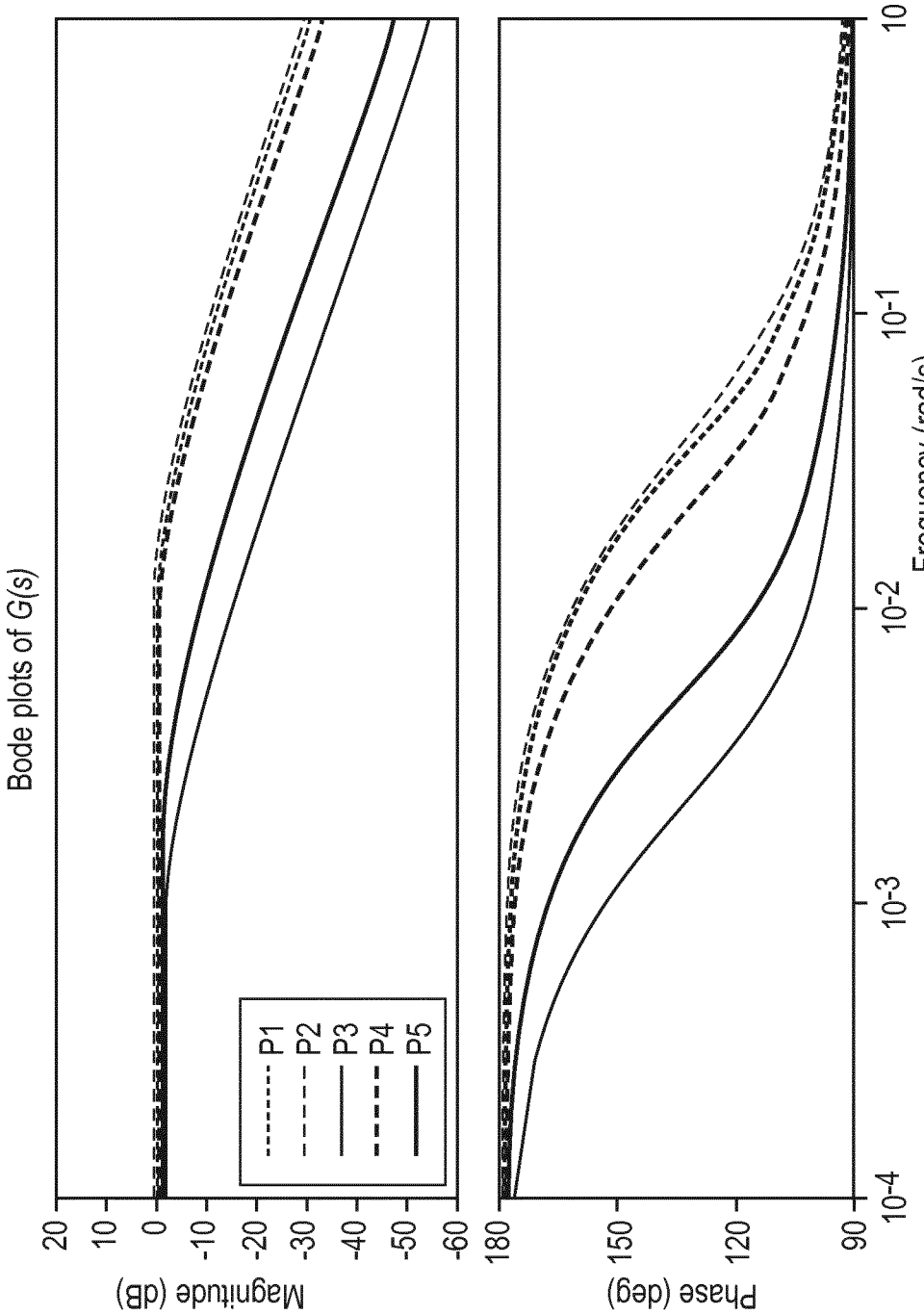

Bode plots of G(s)
Magnitude (dB)
20
10
0
-10
-20
-30
-40
-50
-60
P1
P2
P3
P4
P5
Phase (deg)
180
150
120
90
10-4
10-3
10-2
10-1
10
Frequency (rad/s)

FIG. 7

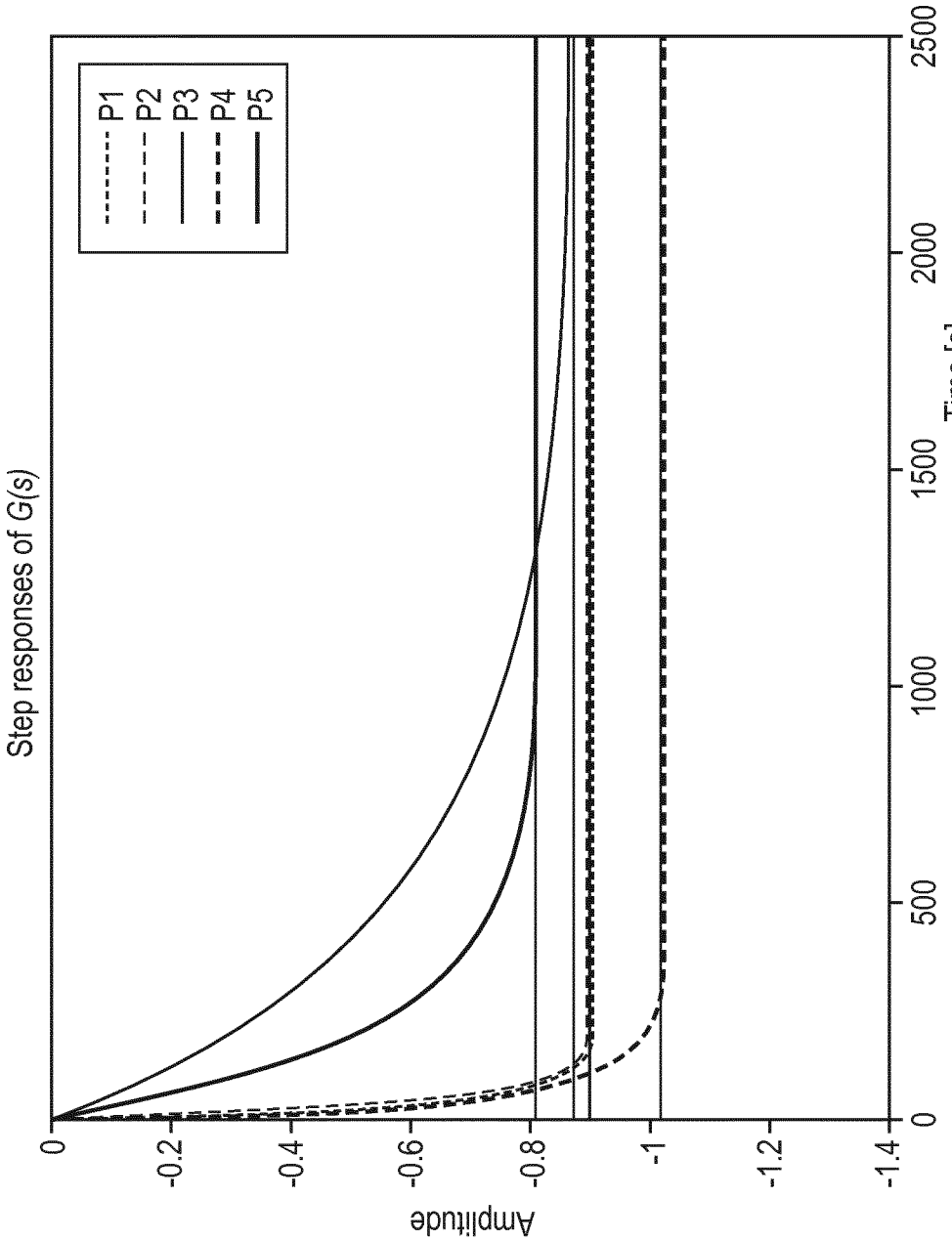

Step responses of G(s)
P1
P2
P3
P4
P5
Amplitude
0
-0.2
-0.4
-0.6
-0.8
-1
-1.2
-1.4
Time [s]
0
500
1000
1500
2000
2500

FIG. 8

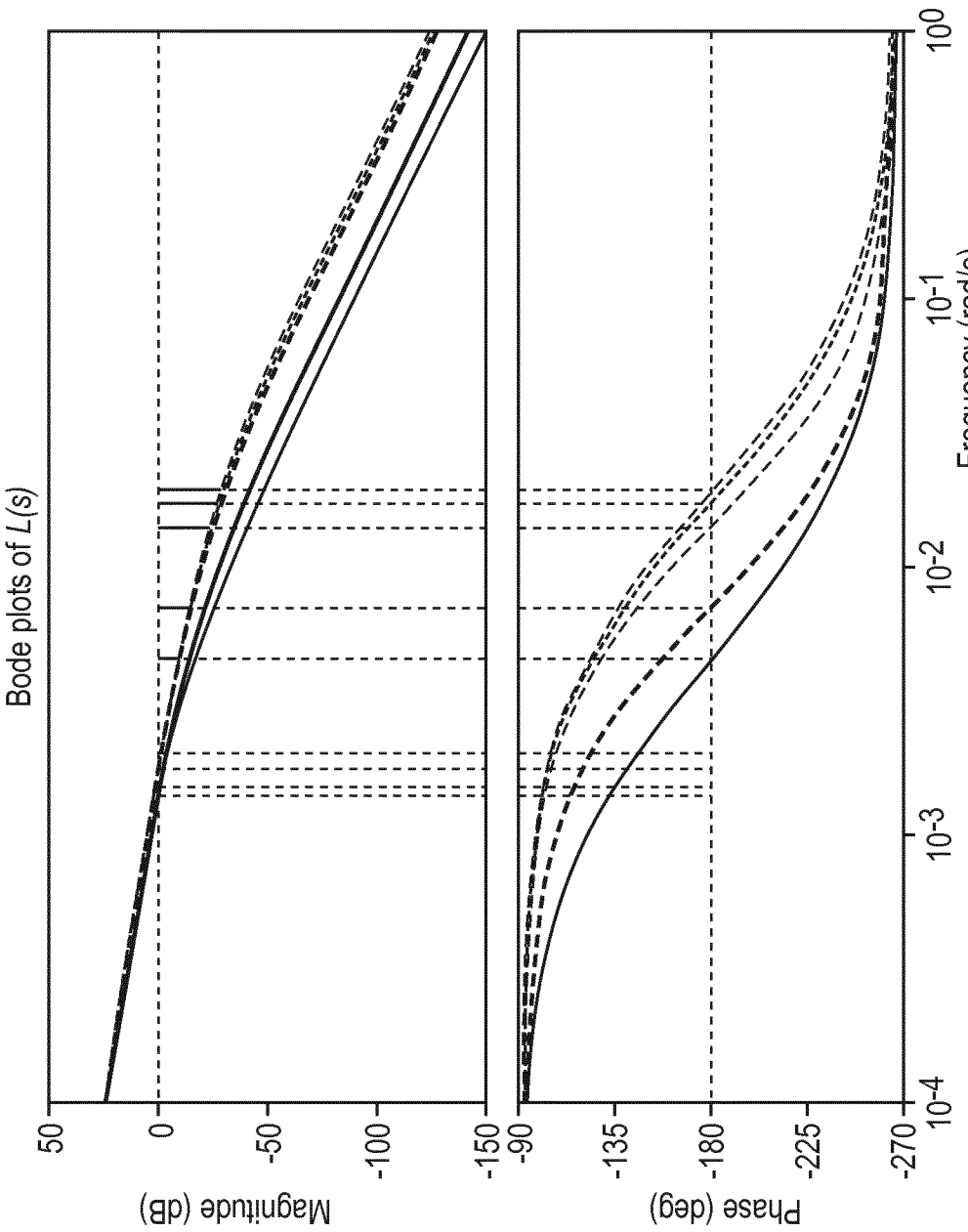

Bode plots of L(s)
Magnitude (dB)
50
0
-50
-100
-150
Phase (deg)
-90
-135
-180
-225
-270
10-4
10-3
10-2
10-1
100
Frequency (rad/s)

FIG. 9

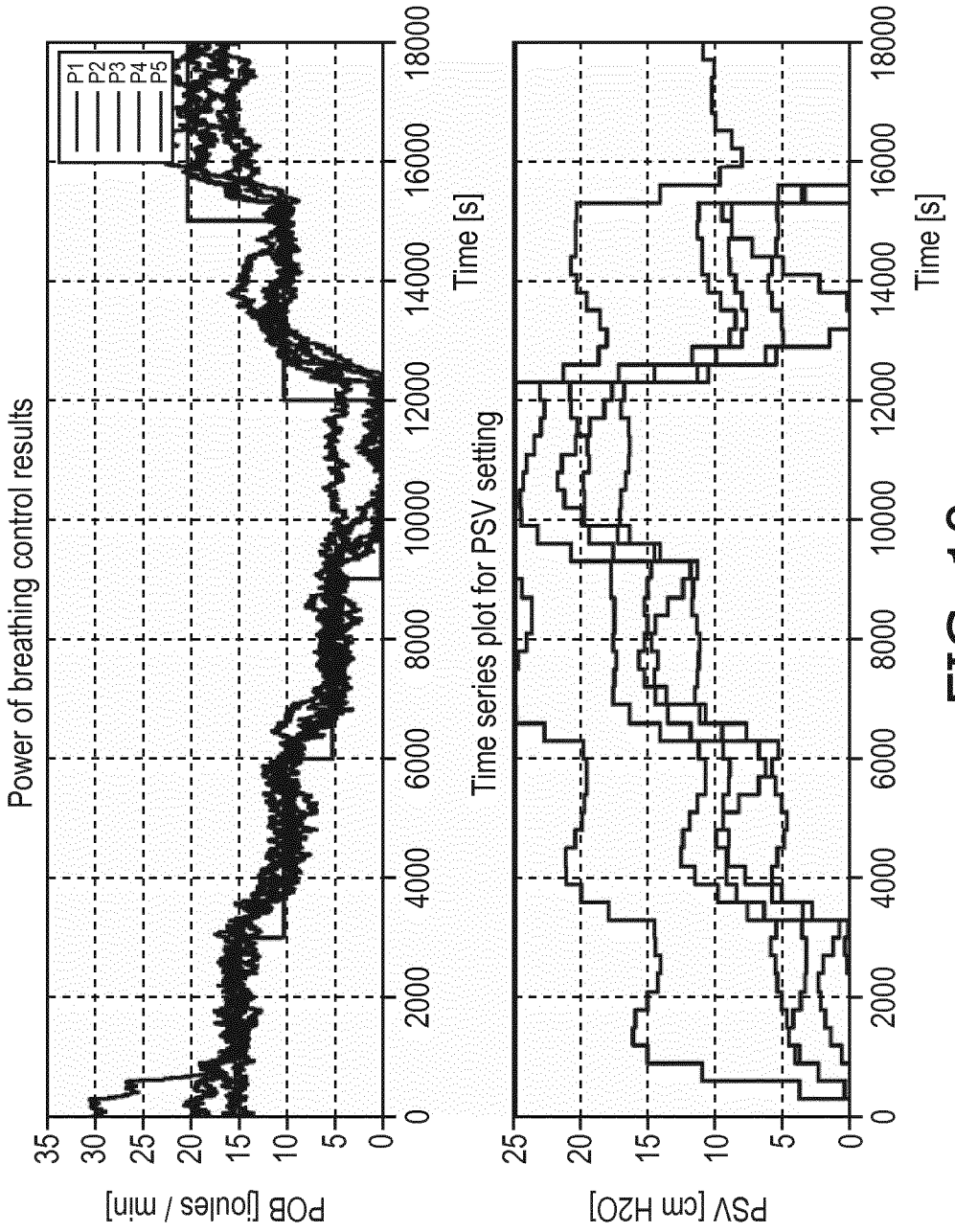

Power of breathing control results
POB [joules / min]
Time [s]
P1
P2
P3
P4
P5
Time series plot for PSV setting
PSV [cm H2O]
Time [s]

FIG. 10

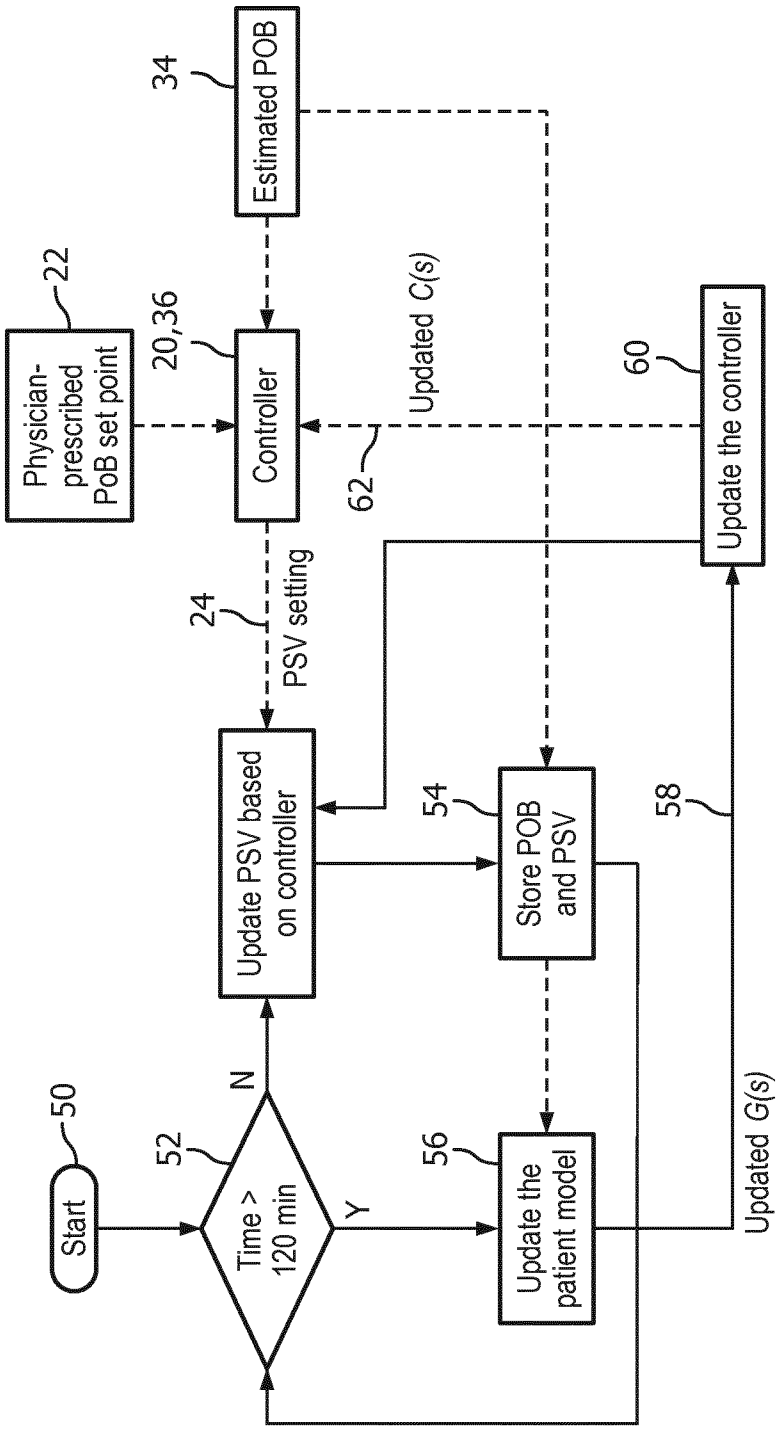

Start
50
Time > 120 min
52
N
Y
Update PSV based on controller
24
PSV setting
Update the patient model
56
Store POB and PSV
54
Updated G(s)
58
Update the controller
60
Updated C(s)
62
Controller
20,36
Physician-prescribed PoB set point
22
Estimated POB
34

FIG. 11

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2016/074342

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M16/00 G06F19/00 A61B5/085 A61B5/00 G05B13/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M G06F A61B G05B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2013/276787 A1 (MARTIN ANATOLE D [US] ET AL) 24 October 2013 (2013-10-24)	1,2, 6-10, 13-16
Y	paragraph [0003] - paragraph [0023] paragraph [0031] - paragraph [0044] paragraph [0046] - paragraph [0060] figures 1,4	3-9, 11-20

X	WO 2014/207623 A2 (KONINKL PHILIPS NV [NL]) 31 December 2014 (2014-12-31)	1,2, 6-10, 13-16
Y	page 1, line 1 - page 2, line 31 page 4, line 2 - page 10, line 2 page 10, line 25 - page 13, line 5 figures 1-5, 12-16	3-9, 11-20

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 November 2016	06/12/2016

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Aguado, Miguel

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2016/074342

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US 2015/059754 A1 (CHBAT NICOLAS WADIH [US] ET AL) 5 March 2015 (2015-03-05) cited in the application paragraph [0001] - paragraph [0005] paragraph [0013] - paragraph [0045] figures 1-7	1,2, 6-10, 13-16 3-9, 11-20

X Y	US 2015/090264 A1 (DONG NANCY F [US]) 2 April 2015 (2015-04-02) paragraph [0001] - paragraph [0044] paragraph [0058] - paragraph [0117] paragraph [0119] - paragraph [0129] paragraph [0131] - paragraph [0142] paragraph [0144] - paragraph [0153] paragraph [0155] - paragraph [0156] paragraph [0158] - paragraph [0162] figures 1-6	1-20 3-9, 11-20

X Y	US 2007/151563 A1 (OZAKI KENJI [JP] ET AL) 5 July 2007 (2007-07-05) paragraph [0001] - paragraph [0085] paragraph [0114] - paragraph [0157] paragraph [0159] - paragraph [0229] figures 1-27	1-20 3-9, 11-20

Y	WO 02/20076 A2 (MALLINCKRODT INC [US]) 14 March 2002 (2002-03-14) page 1, line 3 - page 4, line 6 page 4, line 21 - page 15, line 10 figures 1-3	3-9, 11-20

Y	US 5 303 698 A (TOBIA RONALD L [US] ET AL) 19 April 1994 (1994-04-19) column 1, line 5 - column 5, line 37 column 6, line 25 - column 16, line 20 figures 1-7	3-9, 11-20

Y	WO 2009/115949 A1 (PHILIPS INTELLECTUAL PROPERTY [DE]; KONINKL PHILIPS ELECTRONICS NV [NL] 24 September 2009 (2009-09-24) page 1, line 6 - page 5, line 31 page 6, line 6 - page 9, line 22 figure 1	3-9, 11-20

E	WO 2016/166709 A1 (KONINKLIJKE PHILIPS NV [NL]) 20 October 2016 (2016-10-20) page 1, line 4 - page 5, line 19 page 7, line 13 - page 27, line 13 figures 1-4	1,2,10

A	US 2015/157816 A1 (FREEMAN GARY A [US] ET AL) 11 June 2015 (2015-06-11) paragraph [0042]	1-20

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2016/074342

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 21-23
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

Continuation of Box II.1

Claims Nos.: 21-23

Pursuant to Article 17(2)(a)(i) and (b) PCT, no search report has been established for claims 21-23, because these claims are directed to methods for treatment of the human or animal body by therapy and/or surgery in the sense of Rule 39.1(iv) PCT. This is because claim 21, on which claims 22-23 are dependent, defines a closed-loop control method "for controlling mechanical ventilation provided by a mechanical ventilator to a spontaneously breathing patient". This functional indication defines one of the steps of the method specified in claim 21, which is, consequently, a step of therapy and/or surgery. Moreover, the method step "setting pressure support of the mechanical ventilation to a control signal computer as a product of a controller transfer function and the error signal" in claim 21 is explicitly a step of therapy. Therefore, the whole methods defined in each of claims 21-23 are rendered therapeutical and/or surgical.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2016/074342

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