



- (51) International Patent Classification:  
A61B 5/00 (2006.01)
- (21) International Application Number:  
PCT/IB2016/056115
- (22) International Filing Date:  
13 October 2016 (13.10.2016)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
62/243,174 19 October 2015 (19.10.2015) US
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- (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, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, 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, ST, 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, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

Published:

— with international search report (Art. 21(3))

(54) Title: ANOMALY DETECTION DEVICE AND METHOD FOR RESPIRATORY MECHANICS PARAMETER ESTIMATION

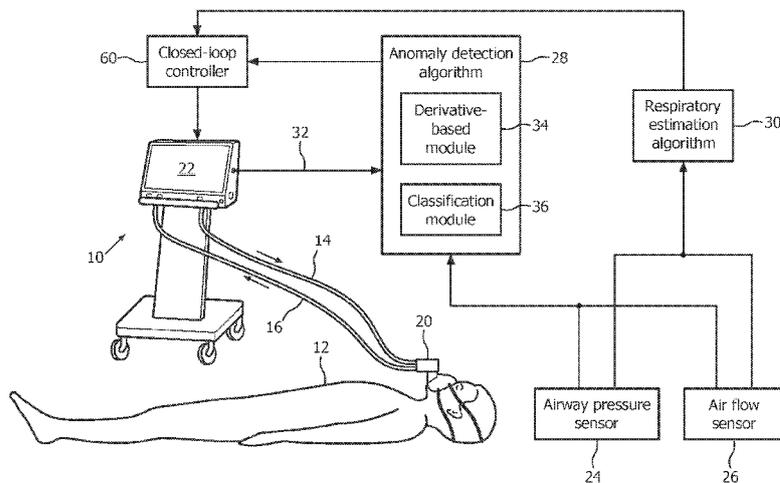


FIG. 1

(57) Abstract: A mechanical ventilation device (10) includes a mechanical ventilator. At least one airway sensor (24, 26) is configured to measure at least one of airway pressure and airway air flow as a function of time for a patient on the mechanical ventilator. At least one microprocessor (28, 30) is programmed to analyze at least one of airway pressure and airway air flow measured by the airway sensor to detect a spontaneous respiration anomaly in respiratory muscle pressure as a function of time generated by a patient on the mechanical ventilator. A display component (22) is configured to display an indication of a spontaneous respiration anomaly detected by the anomaly detection component.

WO 2017/068464 A1

**ANOMALY DETECTION DEVICE AND METHOD FOR RESPIRATORY  
MECHANICS PARAMETER ESTIMATION**

**FIELD**

The following relates to the medical therapy arts, respiratory therapy arts, medical ventilation arts, and related arts.

**BACKGROUND**

In a spontaneously breathing patient receiving mechanical ventilation, the goal is to configure the mechanical ventilator to support the patient's spontaneous respiration. To this end, it is desirable to minimize patient-ventilator dyssynchrony. Some examples of potentially problematic patient-ventilator dyssynchrony include early cycling off and double effort. In early cycling off, the ventilator cycles off, so as to begin the expiration phase, before the patient completes his or her inspiration effort. In double effort, the patient makes two distinct inhalation efforts in a single inspiration period. Active exhalation is another condition that is useful to detect. During normal respiratory effort, the patient's diaphragm operates to expand the lungs to cause inhalation; the exhalation phase is normally passive and relies upon the elastance of the respiratory system to expel air from the lungs. In active exhalation, the patient's respiratory muscles actively operate to compress the lung volume during exhalation. These and other respiratory anomalies are difficult to assess for a patient on mechanical ventilation because the patient's respiratory effort is normally not measured.

The need for estimation of the respiratory system parameters (e.g., resistance  $R$  and elastance  $E$ ) and patient inspiratory efforts (e.g., respiratory muscle pressure  $P_{\text{mus}}$ ) is well-known in the medical community. Estimating  $P_{\text{mus}}$  as a function of time ( $P_{\text{mus}}(t)$ ) is especially important in patient-ventilator support modalities of mechanical ventilation, such as a Pressure Support Ventilation (PSV) mode, where a patient and a ventilator share the mechanical work performed on the respiratory system. A quantitative assessment of  $P_{\text{mus}}(t)$  can be used to select the appropriate level of ventilation support delivered by the ventilator in order to prevent both atrophy and fatigue of patient respiratory muscles. The clinical parameter commonly used to assess the effort made by the patient per breath is known as Work of Breathing (WoB) and can be computed once the estimate of  $P_{\text{mus}}(t)$  is available for the breath. WoB can be obtained from

$P_{\text{mus}}(t)$  by integration of the latter over the inhaled volume. However, respiration anomalies can occur during mechanical ventilation, which can result in an inaccurate estimation of  $P_{\text{mus}}(t)$ ,  $R$ , and/or  $E$ . Detecting such anomalies can improve the estimation of these parameters.

The following provides new and improved systems and methods which overcome the foregoing problems and others.

### **BRIEF SUMMARY**

In accordance with one aspect, a mechanical ventilation device includes a mechanical ventilator. At least one airway sensor is configured to measure at least one of airway pressure and airway air flow as a function of time for a patient on the mechanical ventilator. At least one microprocessor is programmed to analyze at least one of airway pressure and airway air flow measured by the airway sensor to detect a spontaneous respiration anomaly in respiratory muscle pressure as a function of time generated by a patient on the mechanical ventilator. A display component is configured to display an indication of a spontaneous respiration anomaly detected by the anomaly detection component.

In accordance with another aspect, a non-transitory storage medium stores instructions readable and executable by one or more microprocessors to perform a method of detecting a spontaneous respiration anomaly. The method includes detecting peaks in an airway pressure versus time signal acquired for a patient on a mechanical ventilator; and detecting a patient-ventilator dyssynchrony indicated, for instance, by a double peak in the airway pressure versus time signal within a single breath.

In accordance with another aspect, a method of detecting a spontaneous respiration anomaly includes detecting peaks in an airway pressure versus time signal acquired for a patient on a mechanical ventilator; and detecting a patient-ventilator dyssynchrony indicated by a double peak in the airway pressure versus time signal within a single breath.

One advantage resides in improved monitoring for anomalies in patient respiratory effort during mechanical ventilation of a spontaneously respiring patient.

Another advantage resides in detecting such an anomaly in patient respiratory effort without determining the patient respiratory muscle pressure  $P_{\text{mus}}(t)$ .

Another advantage resides in automatically adjusting settings of a ventilator responsive to a detected anomaly.

Another advantage resides in classifying breaths into favorable and unfavorable breaths from the perspective of the estimation of respiratory mechanics.

Further advantages of the present invention will be appreciated to those of ordinary skill in the art upon reading and understand the following detailed description. It will be appreciated that any given embodiment may achieve none, one, more, or all of the foregoing advantages and/or may achieve other advantages.

### **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 shows a medical ventilation system including respiratory effort anomaly detection.

FIGURE 2 shows a signal that is analyzed by one or more algorithms of the medical ventilation system of FIGURE 1.

FIGURE 3 shows another signal that is analyzed by one or more algorithms of the medical ventilation system of FIGURE 1.

FIGURE 4 diagrammatically shows an operations flow chart for the medical ventilation system of FIGURE 1.

### **DETAILED DESCRIPTION**

Estimates of R (resistance) and E (elastance) of the respiratory system are important since they provide quantitative information to a physician about the mechanical properties of the patient's respiratory system. They can also be used to diagnose respiratory diseases and better select the appropriate ventilation modalities and therapeutic paths. Moreover, R and E can also be used to non-invasively estimate  $P_{\text{mus}}(t)$  (respiratory muscle pressure) as a non-invasive alternative to the use of an esophageal catheter. Assuming R and E are known, it is indeed possible to estimate  $P_{\text{mus}}(t)$  via the following equation (known as the Equation of Motion of the Lungs):

$$P_{\text{aw}}(t) = R \dot{V}(t) + E V(t) + P_{\text{mus}}(t) + P_0 \quad (1)$$

where  $P_{aw}$  is the pressure measured at a Y-piece of the ventilator (also known as pressure at the airway opening or mouth of the patient),  $V$  is the flow of air into and out of the patient respiratory system (measured again at the Y-piece),  $V$  is the net volume of air delivered by the ventilator to the patient (measured by integrating the flow signal over time),  $P_0$  is a constant term to account for the pressure at the end of expiration/start of inhalation. In addition,  $1/E$  is often indicated as  $C$  (respiratory system compliance). In some embodiments,  $P_{mus}(t)$  is estimated simultaneously with  $R$  and  $E$ , relying on equation (1).

The inventors have found, however, that typical respiratory system parameters estimation algorithms can produce inferior results for mechanically ventilated patients under certain conditions, such as early ventilator cycling off, patient's double effort, and patient's active exhalation. Such respiratory effort anomalies are also often clinically problematic or call for corrective adjustment of the mechanical ventilator settings, e.g. adjusting the ventilator cycling to improve alignment with respiratory effort. Accordingly, detecting such anomalies has substantial benefits apart from improving respiratory system parameter estimation.

One or more algorithms in accordance with one aspect of the present disclosure can show occurrences of inferior estimation results for mechanically ventilated patients under certain conditions indicative of a spontaneous respiration anomaly in respiratory muscle pressure ( $P_{mus}(t)$ ). The respiration anomalies can be detected by analyzing the airway pressure. The air flow may also be impacted by these anomalies and thus may also be analyzed, but since air flow responds to these anomalies more slowly than airway pressure, stronger signatures are expected to be observed in the airway pressure signal. Such anomalies can include early cycling off, double effort, and active exhalation. These anomalies can also be referred to as a patient ventilator dyssynchrony.

As used herein, the term "early cycling off" refers to a spontaneous respiration anomaly in which the ventilator cycles off before the patient's respiratory effort ceases.

As used herein, the term "double effort" refers to a spontaneous respiration anomaly in respiratory muscle pressure in which the patient makes two distinct breath efforts in a single (ventilator) breath cycle.

As used herein, the term “active exhalation” refers to a spontaneous respiration anomaly in respiratory muscle pressure when that patient actively assists exhalation rather than passively allowing the elasticity of the lungs to push air out.

The present disclosure provides an anomaly detection algorithm that detects, for each breath, if the ventilator cycles off before the patient effort is over. In embodiments that further include estimation of respiratory parameters using an Equation of Motion of the Lungs, a flag may be raised if such an anomaly is detected to indicate that the estimates of R, E and  $P_{\text{mus}}(t)$  for that breath might be unreliable. The advantage of complementing respiratory mechanics estimation methods with anomaly detection algorithms is twofold. First, early cycling off of the ventilator is not a desirable clinical condition. Following detection of early cycling off, the clinician may choose to adjust the ventilator settings to align better with the patient’s inspiration effort. The adjustment of settings can in some embodiments be automatically done by a closed-loop controller. Second, the anomaly potentially affecting the presented non-invasive respiratory system parameter estimation technique would be detected to the benefit of the overall estimation method performance. The concept can be extended to other ventilation anomalies that may adversely impact the respiratory mechanics estimation methods, such as active exhalation and double patient effort within the same breath.

With reference to FIGURE 1, an illustrative mechanical ventilation device is used to provide mechanical ventilation to a patient via a mechanical ventilator **10** that delivers air flow and/or pressure in accordance with ventilator settings to a ventilated patient **12** via an inlet air hose **14**. Exhaled air returns to the ventilator **10** via an exhalation air hose **16**. A Y-piece or T-piece **20** (or alternatively a tracheal tube) couples air from the discharge end of the inlet air hose **14** to the ventilated patient **12** during inhalation and couples exhaled air from the ventilated patient **12** into the exhalation air hose **16** during exhalation. Not shown in FIGURE 1 are numerous other ancillary components that may be provided depending upon the ventilation mode and other therapy being received by the ventilated patient **12**. Such ancillary components may include, by way of illustration: an oxygen bottle or other medical-grade oxygen source for delivering a controlled level of oxygen to the air flow, usually controlled by a Fraction of Inspired Oxygen ( $\text{FiO}_2$ ) ventilator setting; a humidifier plumbed into the inlet line **14**; a nasogastric tube to provide the patient **12** with nourishment; and so forth. The mechanical ventilator **10** has a user interface including, in the illustrative example, a touch-sensitive display

component **22** via which the physician, respiratory specialist, or other medical personnel can visualize the ventilator settings and monitor measured physiological variables (e.g., airway pressure and air flow) and operating parameters of the mechanical ventilator **10**. Additionally or alternatively, the user interface may include physical user input controls (buttons, dials, switches, et cetera), a keyboard, a mouse, audible alarm device(s), indicator light(s), or so forth.

FIGURE 1 diagrammatically illustrates a system for detecting a spontaneous respiration anomaly of the ventilated patient **12**. For example, the mechanical ventilator **10** includes or is in communication with at least one air way sensor **24, 26**. These sensors **24, 26** are shown diagrammatically in FIGURE 1 and may, for example, be installed on the tubing **14, 16** or inside the ventilator unit **10**. The at least one air way sensor **24, 26** is configured to measure at least one of airway pressure and airway air flow as a function of time for the patient **12** on the mechanical ventilator **10**. For example, an airway pressure sensor **24** is configured to measure airway pressure as a function of time, and an airway air flow sensor **26** is configured to measure air flow as a function of time. The sensors **24, 26** are configured to measure airway pressure or air flow at the Y-piece **20** or at another appropriate point in the ventilator air flow circuit. It will be appreciated that only one of the sensors **24, 26** can be included, although usually both airway pressure and flow are monitored during mechanical ventilation. The data values of air pressure and/or air flow may be displayed on the display component **22** as an airway pressure (or air flow) versus time signal (e.g., a graphical signal), as numerical values updated in real time, or so forth. This data values of air pressure and/or air flow are also transferred to an anomaly detection algorithm **28** and, optionally, to a respiratory mechanics estimation algorithm **30** via a communication network (e.g., a wireless network, a local area network, a wide area network, a personal area network, BLUETOOTH®, and the like). Alternatively, the anomaly detection algorithm **28** and optional respiratory mechanics estimation algorithm **30** may be built into the mechanical ventilator **10** (e.g., executing on a microprocessor or microcontroller of the ventilator **10**) in which case data from the sensors **24, 26** are collected by the ventilator **10** and hence available to the algorithms **28, 30**. In another contemplated embodiment, the anomaly detection algorithm **28** and optional respiratory mechanics estimation algorithm **30** are implemented on the microprocessor of a patient monitor (not shown) that displays vital signs such as heart rate, respiration rate, blood pressure, or so forth, and the output of these algorithms **28, 30** are suitably displayed on the patient monitor display component.

The anomaly detection algorithm **28** is configured to receive as input the measured values of air pressure and/or air flow for the ventilated patient **12**. The anomaly detection algorithm **28** receives a start-of-breath signal **32** from the ventilator **10** to enable delineation of breath intervals. Alternatively, the airway pressure or air flow signal can be segmented into breath intervals based on expected features (e.g., start of breath is indicated by a rapid increase in airway pressure and air flow). The anomaly detection algorithm **28** is programmed to analyze airway pressure and/or airway air flow measured by the airway sensor **24, 26** to detect a spontaneous respiration anomaly in respiratory muscle pressure as a function of time (i.e.,  $P_{\text{mus}}(t)$ ) generated by the patient **12** on the mechanical ventilator **10**. The anomalies include at least an early cycling off anomaly, an active exhalation anomaly, and a double effort anomaly. To do so, the anomaly detection algorithm **28** is programmed to detect one or more peaks in an airway pressure (or air flow) versus time signal (see FIGURE 2). For example, the anomaly detection algorithm **28** can include any suitable peak detection hardware (e.g., a peak detector circuit with a diode and a capacitor) or software (e.g., a Matched Filtration with Experimental Noise Determination algorithm, a vectorized peak detection algorithm, a least-squares curve-fitting algorithm, an optimization peak detection algorithm, a derivative-based algorithm, or the like). In illustrative embodiments described herein, the anomaly detection algorithm **28** uses a derivative-based module **34** to detect peaks of an airway pressure (or air flow) versus time signal (not shown in FIGURE 1). It will be appreciated that the derivative-based module **34** also includes any suitable algorithms for signal processing processes (e.g., filtering, signal to noise ratio reduction, data smoothing, and the like). As described in more detail below, the derivative-based module **34** is configured to identify one or more anomalies based on abnormal peak detection readings, as described in more detail below. The derivative-based module **34** is configured to detect peak values (e.g., “y-axis” values of an airway pressure versus time signal, as described in more detail below) and the associated time values (e.g., “x-axis values”) at which these peaks occur, as described in more detail below.

As shown in FIGURE 1, the anomaly detection algorithm **28** also includes a classification module **36**. The classification module **36** is configured to receive an indication of an abnormal peak detection reading from the derivative-based module **34**. From the abnormal peak detection reading, the classification module **36** is configured to determine the type of spontaneous respiration anomaly (e.g., double effort, early cycling off, and active exhalation).

The classification module **36** then “flags” the anomaly, and assigns a corresponding flag value to the type of anomaly, as described in more detail below. The flag value is an indication of a spontaneous respiration anomaly detected by the derivative -based module **34**. The flag value is then transmitted to, and displayed on, the display component **22**.

FIGURE 2 shows one example display of an airway pressure versus time signal **38** shown on the display **22** of the mechanical ventilator **10**. The airway pressure data **38** are taken from “Noninvasive Estimation of Respiratory Mechanics in Spontaneously Breathing Ventilated Patients: A Constrained Optimization Approach”, *IEEE Trans Biomed Eng.*, 2015 (DOI [10.1109/TBME.2015.2470641](https://doi.org/10.1109/TBME.2015.2470641)). The signal **38** is based on experimental animal (i.e., pig) data. However, the signal **38** can instead be an air flow versus time signal. For illustrative and conciseness purposes only, the foregoing is described in regards to an airway pressure versus time signal. The anomaly detection algorithm **28** is programmed to detect at least one peak **40** of the signal **38**. For example, the anomaly detection algorithm **28** is programmed to analyze airway pressure measured by the airway pressure sensor **24** to detect a spontaneous respiration anomaly as a double peak in the airway pressure as a function of time within a single breath cycle. A breath of the signal **38** with a double peak configuration is indicative of a spontaneous respiration anomaly, while a breath with a single peak configuration in the signal is considered “normal.” The rationale underlying this approach is the expectation that, if the patient’s inspiration effort is a normal single exertion and the positive pressure applied by the ventilator **10** is well-aligned with the patient’s effort, then the airway pressure should exhibit a single peak corresponding to the nearly coincident termination of pressure applied by the ventilator and of the respiratory effort applied by the patient. On the other hand, if the ventilator cycles off early, then a double peak is expected – the first peak being due to the ventilator cycling off and thereby removing its applied pressure, and a second anomalous peak due to the subsequent end of patient respiratory effort. Similarly, a double effort by the patient will be observed as two peaks attributable to the patient’s two inspiration efforts.

As shown in FIGURE 2, at least one single (i.e., normal) peak **42** is indicative that the respiratory muscles of the patient **12** were completely released before the ventilator **10** cycled off. In other words, when the muscles are released,  $P_{\text{mus}}(t)$  rapidly returns back to 0. FIGURE 2 shows an illustrative example. In this example, a normal breath has peaks with values ranging between approximately 13.0-14.0 cmH<sub>2</sub>O. In this example, the mechanical

ventilator is operating in Pressure Support Ventilation (PSV) mode with pressure set around 10 cmH<sub>2</sub>O. When the patient releases the respiratory muscles, the corresponding change in effort  $\Delta P_{\text{mus}}$  generates an increase in the airway pressure leading to peak airway pressures that are 3-4 cmH<sub>2</sub>O higher than the 10 cmH<sub>2</sub>O setpoint. By contrast, referring back to the Equation of the Lungs (Equation (1)), if the ventilator **10** cycles off before patient effort is over,  $P_{\text{aw}}(t)$  first decreases immediately after the positive pressure applied by the ventilator is removed (i.e., from cycling off of the ventilator) and then increases due to quick release of patient effort  $\Delta P_{\text{mus}}$  (i.e., from patient effort), giving rise to a second (and lower) peak in the measured signal **38** over a single breath, as indicated by **44**.

The anomaly detection algorithm **28** is programmed to analyze airway pressure measured by the airway pressure sensor to detect a spontaneous respiration anomaly comprising an early cycling off event as a double peak in the airway pressure as a function of time coincident with the mechanical ventilator **10** cycling off. In particular, early cycling off is observed in the airway pressure waveform as a double peak in an airway pressure versus time signal acquired for the patient **12** on the mechanical ventilator **10** at about the time the ventilator cycles off. Normal breaths can be identified as the largest peak observed in the breath cycle (so that the double peak signifying early cycling off is a splitting of the largest peak of the breath cycle into two peaks), and/or the ventilator **10** can send a signal to the anomaly detection algorithm **28** when the ventilator **10** cycles off. The abnormal double peak **44** is due to an initial decline due to removal of the applied ventilator pressure followed by a second peak due to the release of patient respiratory effort after the ventilator has cycled off. The ventilator **10** only applies a positive pressure, so although pressure is controlled by the ventilator **10** in PSV mode, the ventilator cannot prevent (i.e. suppress) the second peak produced by the patient effort. To analyze the signal **38**, the derivative-based module **34** is configured to find each of the peaks **40** (e.g., the normal peaks **42** and the abnormal peaks **44**) of the signal **38**. The abnormal peaks **44** include a first peak **46** and a second peak **48**. The first peak **46** is indicative of cycling off of the ventilator (i.e., early cycling off), and the second peak **48** is indicative of continued effort by the patient **12**. The derivative-based module **34** then sends this data (i.e., the data associated with each of the peaks **42** and **44**) to the classification module **36**.

The classification module **36** then analyzes the signal **38** to determine a type of anomaly. In the example shown in FIGURE 2, the signal **38** includes multiple abnormal peaks

**44**, each of which includes the first and second peaks **46** and **48**. Due to the positioning of the first and second peaks **46** and **48** (described above), the classification module **36** determines that the abnormal peaks **44** are due to early-cycling off. The classification module **36** then flags this anomaly by assigning a flag value to the anomaly. For example, the classification module **36** assigns a flag value of “1” for an early-cycling off anomaly (this is merely an illustrative example). The classification module **36** sends the flag value to the display component **22**, where it is displayed for a medical professional (e.g., a nurse, a doctor, and the like).

In addition, the derivative-based module **34** optionally analyzes the double peak **44** to determine a cycling off time ( $t_{soe}$ ) **50** of the ventilator **10** and a patient effort end time ( $T_r$ ) **52**, under the assumption that the first peak corresponds to the ventilator cycling off and the second peak corresponds to the subsequent end of the patient’s inspiration effort. For example, as shown in FIGURE 2, the first peak **46** has a value of approximately 11.0 cmH<sub>2</sub>O, and a corresponding  $t_{soe}$  **50** of approximately 92 seconds. The second peak **48** has a value of approximately 12.0 cmH<sub>2</sub>O, and a corresponding  $t_r$  of approximately 93 seconds. Alternatively,  $t_{soe}$  may be acquired directly by the ventilator **10** as part of the breath cycle information **32** and this may be used to link one peak with the ventilator cycling off. Based on this information, a warning **53** of the detected early cycling off condition is displayed on the ventilator display **22**. A medical professional is notified by the warning **53**, and the setting of the ventilator **10** can be adjusted by the medical professional so that ventilator **10** cycles off at the same time that patient effort ends (i.e., by making  $t_{soe}$  **50** equal to  $t_r$  **52**). Automatic adjustment by the ventilator **10** is also contemplated, e.g. in the foregoing example the ventilator may increase  $t_{soe}$  by 1 second to align with the second peak at 93 sec indicating end of patient inspiration effort. As a result, the first and second peaks **46** and **48** would be equal as well, thereby producing a normal peak **42**.

Although the signal **38** has been described in terms of identifying a cycling off anomaly, it will be appreciated that similar features could be used to detect other anomalies, such as active exhalation or double effort. In one embodiment, in the case of active exhalation, the anomaly detection algorithm **28** is programmed to analyze airway pressure measured by the airway pressure sensor **24** to detect a spontaneous respiration anomaly comprising active exhalation as a deviation of an expiratory flow from exponential decay (which is determined from solving the Equation of the Lungs). For example, by solving the Equation of the Lungs during exhalation, the following exponential function is obtained.

$$\dot{V}(t) = \dot{V}(t_{min})\exp(-(t - t_{min})/\tau) \quad (2)$$

where  $t_{min}$  is the time at which the flow reaches its minimum value (negative peak flow  $\dot{V}(t_{min})$ ).  $\dot{V}(t_{min})$  and  $t_{min}$  are known from the measured flow waveform,  $\tau$  is the parameter to be adjusted to fit equation 2. The measured flow waveform during exponential fitting is expected to be a decaying exponential. The natural logarithm is then expected to be a line, as shown in Equation 3 below.

$$\ln(\dot{V}(t)) = a + bt \quad (3)$$

where  $a$  and  $b$  are two parameters related to  $\dot{V}(t_{min})$ ,  $t_{min}$ , and  $\tau$  to optimize the fit.

The derivative of the natural logarithm of the flow is then expected to be constant. Changes of such derivative during exhalation are then interpreted as a respiratory anomaly (for instance, patient's active exhalation). The derivative-based module **34** sends this data to the classification module **36**. In this example, the classification module **36** is programmed to assign a flag value of "2" for active exhalation occurrences. This flag value is sent to, and displayed on, the display component **22**.

In another embodiment, in the case of double effort the anomaly detection algorithm **28** is programmed to analyze airway pressure measured by the airway pressure sensor **24** to detect a spontaneous respiration anomaly comprising a double effort event as a double peak in the airway pressure as a function of time in which at least one peak of the double peak is not coincident with the mechanical ventilator **10** cycling off. Double effort, like early cycling off, is expected to be observed as a double peak in the airway pressure waveform signal during inhalation. In the case of double effort, the second peak is expected to precede the main (largest) peak at the cycle-off point, since it is most likely that the patient will exert both first and second efforts during the inspiration phase. However, the second effort of the double effort may occur elsewhere in the breathing cycle so that the second peak is more randomly located in the single breath. To detect the double effort on the basis of this analysis, the derivative-based module **34** is programmed to calculate instances when the second peak **48** is located away from the main ( $t_{soe}$ ) peak in the signal **38**. The derivative-based module **34** is also programmed to calculate the corresponding times of the two peaks of the double effort. The derivative-based module **34** sends this data to the classification module **36**. In this example, the classification module **36** is programmed to assign a flag value of "3" for double effort occurrences. This flag value is sent to, and displayed on, the display component **22**. In some embodiments, the classification module

**36** is programmed to assign a flag value of “0” when no anomaly is detected. This value can be continuously displayed on the display component **22**.

Referring back to FIGURE 1, the respiratory estimation algorithm **30** is programmed to calculate one or more variables of the Equation of the Lungs (reproduced here):

$$P_{aw}(t) = R V(t) + E V(t) + P_{mus}(t) + P_0 \quad (1)$$

As discussed above, the airway pressure sensor **24** is configured to measure  $P_{aw}(t)$ , and the air flow sensor **26** is configured to measure  $V(t)$ , while  $V(t)$  is the inspired air volume calculated as a time integral of air flow  $V(t)$ , and  $P_0$  is a constant. The respiratory estimation algorithm **30** is programmed to calculate at least one of  $R$ ,  $E$ , and  $P_{mus}(t)$  based on the airway pressure and the air flow as functions of time. The respiratory estimation algorithm **30** is programmed to calculate the values of  $R$ ,  $E$ , and/or  $P_{mus}(t)$  and compare them to corresponding threshold values (which are user-configurable on the ventilator **10**). Some suitable approaches for optimizing the parameters  $R$ ,  $E$ , and  $P_{mus}(t)$  for input  $V(t)$  and  $P_{aw}(t)$  data are given in: (1) Vicario et al., “Noninvasive Estimation of Respiratory Mechanics in Spontaneously Breathing Ventilated Patients: A Constrained Optimization Approach”, *IEEE Trans Biomed Eng.*, 2015 (DOI [10.1109/TBME.2015.2470641](https://doi.org/10.1109/TBME.2015.2470641)); and (2) Al-Rawas et al., “Expiratory Time Constant for Determinations of Plateau Pressure, Respiratory System Compliance, and Total Resistance”, *Critical Care*, 17:R23, 2013.

The variables  $R$ ,  $E$ , and  $P_{mus}(t)$  are optimized by the estimation algorithm **30** to balance the Equation of the Lungs. However, the inventors have found in numerical simulations that such estimation provides values with large error when the ventilator cycles off before the patient’s effort is over. For example, FIGURE 3 shows an example of respiratory estimation by the algorithm **30** optimizing the parameters  $R$ ,  $E$ , and  $P_{mus}(t)$  for simulated  $V(t)$  and  $P_{aw}(t)$  data, in which the simulation employed  $R=7.0000$ ,  $E=10.0000$ , and a  $P_{mus}(t)$  waveform **58** shown on the right-hand side of FIGURE 3. FIGURE 3 shows the results of simulations where the timing between the ventilator **10** cycling off and  $P_{mus}(t)$  is varied by changing the  $E_{cycle}$  setting of the ventilator as follows. The ventilator cycles off when the flow, after reaching the maximum positive value  $V_{max}$  decreases below a threshold given by  $E_{cycle}$  times  $V_{max}$ , with  $0 < E_{cycle} < 1$ . Therefore, lower values of  $E_{cycle}$  translate into longer time intervals before the ventilator cycles off. For low  $E_{cycle}$  values, the ventilator cycles off after the patient’s respiratory effort is completed, and the respiratory estimation algorithm **30** is able to estimate  $R$  and  $E$  exactly as

indicated by  $R_{est}=R=7.0000$  and  $E_{est}=E=10.0000$ . This corresponds to the example **54** shown in the upper right of FIGURE 3, where  $t_{SOE}$  (the time the ventilator cycles off) occurs later than  $t_r$  (the end of patient's inspiration effort).

On the other hand, for larger values of  $E_{cycle}$  the ventilator shuts off earlier, leading to early cycling off for sufficiently large  $E_{cycle}$ . Example **56** in the lower right of FIGURE 3 shows this early cycling off condition, for which the patient effort end time ( $t_r$ ) **52** occurs after the cycling off time ( $t_{SOE}$ ) **50** of the ventilator **10**. In this case, the respiratory estimation algorithm **30** calculates an abnormal values of R and E which begin to vary from their setting values of 7 and 10, respectively. This trend is seen for  $E_{cycle}=0.35$  for which  $t_{SOE}=t_r$  and for higher values of  $E_{cycle}$  for which  $t_{SOE}<t_r$ . As disclosed herein, this early cycling off condition can be detected, without estimating  $P_{mus}(t)$ , by observing a double peak in the airway pressure waveform at  $t_{SOE}$ . Thus, this condition in which the estimation values  $R_{est}$ ,  $E_{est}$  are likely to have large error is detected. (This condition cannot be detected for a real patient by analyzing the output of the estimation algorithm **30** because for a real patient the ground-truth values of R and E are not known *a priori*).

In some embodiments, the display component **22** is configured to indicate unreliability of the calculated respiratory system variables if an early cycling off anomaly, an active exhalation anomaly, or a double effort anomaly is detected. For example, the display component **22** is programmed to show the values of R, E, and  $P_{mus}(t)$  only when an anomaly is detected. In other embodiments, the display component **22** to continuously display values of R, E, and/or  $P_{mus}(t)$  based on the measured airway pressure and airway air flow. As a result, a medical professional can determine when an anomaly is occurring based on the displayed values of R, E, and/or  $P_{mus}(t)$ , in addition to the displayed flag value.

In some embodiments, when an anomaly is detected, the flag value and/or the displayed values of R, E, and  $P_{mus}(t)$  conveys to a medical professional that the anomaly is occurring. The medical professional can then adjust the settings of the ventilator **10** so that the anomaly no longer occurs.

In other embodiments, referring back to FIGURE 1, a power of breathing (or work of breathing) closed-loop controller **60** is included. The closed-loop controller **60** is programmed to calculate the actual patient's power (or work) of breathing by time integration of the estimated  $P_{mus}(t)$  and to adjust the ventilator setting based on the difference between the

actual and desired power or work of breathing in order to optimally support the patient's spontaneous respiratory effort. Such a closed-loop controller is described in U.S. Patent Publication No. 2015/0059754, which is incorporated in its entirety herein. In embodiments disclosed herein, the flag output by the anomaly detection algorithm **28** is also input to the closed loop ventilator controller **60**. If the flag indicates a respiratory anomaly that makes the output of the respiratory estimation algorithm **30** unreliable (as described with reference to FIGURE 3), then the closed loop ventilator controller **60** can take appropriate action, such as maintaining the current ventilator setting in an open-loop fashion, or adjusting ventilator settings based on the detected anomalous condition (e.g. reducing the  $E_{\text{cycle}}$  setting to bring  $t_{\text{SOE}}$  into alignment with  $t_r$  in the case of early cycling off).

Figure 4 shows a method **100** of detecting a spontaneous respiration anomaly. The method **100** includes: receiving at least one of an airflow pressure value and an air flow value from a corresponding airflow pressure sensor **24** and an air flow sensor **26** (step **102**); detecting peaks **40**, **42**, **44** in an airway pressure versus time signal **38** acquired for a patient **12** on a mechanical ventilator **10** (step **104**); detecting a patient-ventilator dyssynchrony indicated by a double peak **44** in the airway pressure versus time signal within a single breath (step **106**); determining a time **50** of ventilator cycling off from the signal **38** received from a mechanical ventilator **10** or estimated as the time of the largest peak in the ventilator cycle (step **108**); identifying a type of the patient-ventilator dyssynchrony based on at least one of: (1) a position of the double peak relative to the time of ventilator cycling off, (2) a position of the second peak of the double peak is after the time of ventilator cycling off, and (3) the double peak being the largest peak in the breath (step **110**); optionally calculating one or more respiratory system variables including resistance (R) and/or elastance (E) based on the measured airway pressure and airway air flow in which the detection of the patient-ventilator dyssynchrony does not use the calculated respiratory muscle pressure as a function of time (step **112**); and displaying at least one of unreliability of the calculated respiratory system variables if an early cycling off anomaly, an active exhalation anomaly, or a double effort anomaly is detected and values of one or more respiratory system variables including at least respiratory muscle pressure as a function of time based on the measured airway pressure and airway air flow (step **114**).

The various data processing components **28**, **30** are suitably implemented as a microprocessor programmed by firmware or software to perform the disclosed operations. In

some embodiments, the microprocessor is integral to the mechanical ventilator **10**, so that the data processing is directly performed by the ventilator **10**. In other embodiments the microprocessor is separate from the mechanical ventilator **10**, for example being the microprocessor of a desktop computer. The various data processing components **28, 30** of the ventilator settings optimization system may also be implemented as a non-transitory storage medium storing instructions readable and executable by a microprocessor (e.g. as described above) to implement the disclosed operations. The non-transitory storage medium may, for example, comprise a read-only memory (ROM), programmable read-only memory (PROM), flash memory, or other repository of firmware for the ventilator **10**. Additionally or alternatively, the non-transitory storage medium may comprise a computer hard drive (suitable for computer-implemented embodiments), an optical disk (e.g. for installation on such a computer), a network server data storage (e.g. RAID array) from which the ventilator **10** or a computer can download the system software or firmware via the Internet or another electronic data network, 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 mechanical ventilation device, comprising:
  - a mechanical ventilator (10);
  - at least one airway sensor (24, 26) configured to measure at least one of airway pressure and airway air flow as a function of time for a patient on the mechanical ventilator; and
  - at least one microprocessor (28, 30) programmed to analyze at least one of airway pressure and airway air flow measured by the airway sensor to detect a spontaneous respiration anomaly in respiratory muscle pressure as a function of time generated by a patient on the mechanical ventilator; and
  - a display component (22) configured to display an indication of a spontaneous respiration anomaly detected by the anomaly detection component.
  
2. The device of claim 1 wherein:
  - the at least one airway sensor (24, 26) includes an airway pressure sensor (24) configured to measure airway pressure as a function of time; and
  - the at least one microprocessor (28, 30) is programmed to analyze airway pressure measured by the airway pressure sensor to detect a spontaneous respiration anomaly comprising an early cycling off event as a double peak (46, 48) in the airway pressure as a function of time coincident with the mechanical ventilator cycling off.
  
3. The device of any one of claims 1-2 wherein:
  - the at least one airway sensor (24, 26) includes an airway pressure sensor (24) configured to measure airway pressure as a function of time; and
  - the at least one microprocessor (28, 30) is programmed to analyze airway pressure measured by the airway pressure sensor to detect a spontaneous respiration anomaly comprising a double effort event as a double peak in the airway pressure as a function of time in

which at least one peak of the double peak is not coincident with the mechanical ventilator (10) cycling off.

4. The device of any one of claims 1-3 wherein:

the at least one airway sensor (24, 26) includes an airway pressure sensor (24) configured to measure airway pressure as a function of time; and

the at least one microprocessor (28, 30) is programmed to analyze airway pressure measured by the airway pressure sensor to detect a spontaneous respiration anomaly comprising active exhalation as downward slope of the airway pressure following the mechanical ventilator (10) cycling off which is larger than a threshold value.

5. The device of any one of claims 2-4 wherein the at least one microprocessor (28, 30) receives a signal (38) indicative of the mechanical ventilator (10) cycling off and uses the signal to determine a time of the mechanical ventilator cycling off.

6. The device of claim 1 wherein:

the at least one airway sensor (24, 26) includes an airway pressure sensor (24) configured to measure airway pressure as a function of time; and

the at least one microprocessor (28, 30) is programmed to analyze airway pressure measured by the airway pressure sensor to detect a spontaneous respiration anomaly as a double peak (46, 48) in the airway pressure as a function of time within a single breath cycle.

7. The patient monitoring device of any one of claims 1-6, wherein the at least one airway sensor includes an airway pressure sensor (24) configured to measure airway pressure and an air flow sensor (26) configured to measure airway air flow, and the at least one microprocessor (28, 30) is further programmed to:

calculate one or more respiratory system variables including at least respiratory muscle pressure as a function of time based on the measured airway pressure and airway air flow; and

wherein the detection of the spontaneous respiration anomaly does not use the calculated respiratory muscle pressure as a function of time.

8. The patient monitoring device of claim 7, wherein:

the at least one microprocessor (**28, 30**) is programmed to detect spontaneous respiration anomalies including at least an early cycling off anomaly, an active exhalation anomaly, and a double effort anomaly; and

the display component (**22**) is configured to indicate unreliability of the calculated respiratory system variables if an early cycling off anomaly, an active exhalation anomaly, or a double effort anomaly is detected.

9. The patient monitoring device of any one of claims 1-8, further including a power of breathing closed-loop controller (**60**) programmed to:

adjust an output of the mechanical ventilator responsive to at least one flag value responsive to a detection at least one spontaneous respiration anomaly including at least an early cycling off anomaly, an active exhalation anomaly, and a double effort anomaly.

10. The patient monitoring device of claim 7, wherein the display component (**22**) is configured to display values of one or more respiratory system variables including at least respiratory muscle pressure as a function of time based on the measured airway pressure and airway air flow.

11. A non-transitory storage medium storing instructions readable and executable by one or more microprocessors (**28, 30**) to perform a method of detecting a spontaneous respiration anomaly, the method comprising:

detecting peaks (**40, 42, 44**) in an airway pressure versus time signal acquired for a patient on a mechanical ventilator; and

detecting a patient-ventilator dyssynchrony indicated by a double peak (**46, 48**) in the airway pressure versus time signal within a single breath.

12. The transitory storage medium of claim 11, wherein the method further comprises:

determining a time (**50**) of ventilator cycling off from a signal received from a mechanical ventilator; and

identifying a type of the patient-ventilator dyssynchrony based on position of the double peak (46, 48) respective to the time of ventilator cycling off.

13. The transitory storage medium of claim 12, wherein the identifying further includes:

identifying an early cycling off patient-ventilator dyssynchrony based on the position of the second peak (48) of the double peak being after the time (50) of ventilator cycling off.

14. The transitory storage medium of claim 11, wherein the method further comprises:

identifying an early cycling off patient-ventilator dyssynchrony based on the double peak being the largest peak in the breath.

15. The transitory storage medium any one of claims 11-14, wherein the method further comprises:

calculating one or more respiratory system variables including at least respiratory muscle pressure as a function of time based on the measured airway pressure and airway air flow; and

wherein the detection of the patient-ventilator dyssynchrony does not use the calculated respiratory muscle pressure as a function of time.

16. A method of detecting a spontaneous respiration anomaly, the method comprising:

detecting peaks (40, 42, 44) in an airway pressure versus time signal acquired for a patient on a mechanical ventilator; and

detecting a patient-ventilator dyssynchrony indicated by a double peak (46, 48) in the airway pressure versus time signal within a single breath.

17. The method of claim 16, further including:

determining a time (50) of ventilator cycling off from a signal received from a mechanical ventilator; and

identifying a type of the patient-ventilator dyssynchrony based on position of the double peak (46, 48) respective to the time of ventilator cycling off.

18. The method of claim 17, further including:

identifying an early cycling off patient-ventilator dyssynchrony based on the position of the second peak (48) of the double peak being after the time (50) of ventilator cycling off.

19. The method of claim 17, further including:

identifying an early cycling off patient-ventilator dyssynchrony based on the double peak being the largest peak in the breath.

20. The method of any one of claims 16-19, further including:

calculating one or more respiratory system variables including at least respiratory muscle pressure as a function of time based on the measured airway pressure and airway air flow; and

wherein the detection of the patient-ventilator dyssynchrony does not use the calculated respiratory muscle pressure as a function of time.

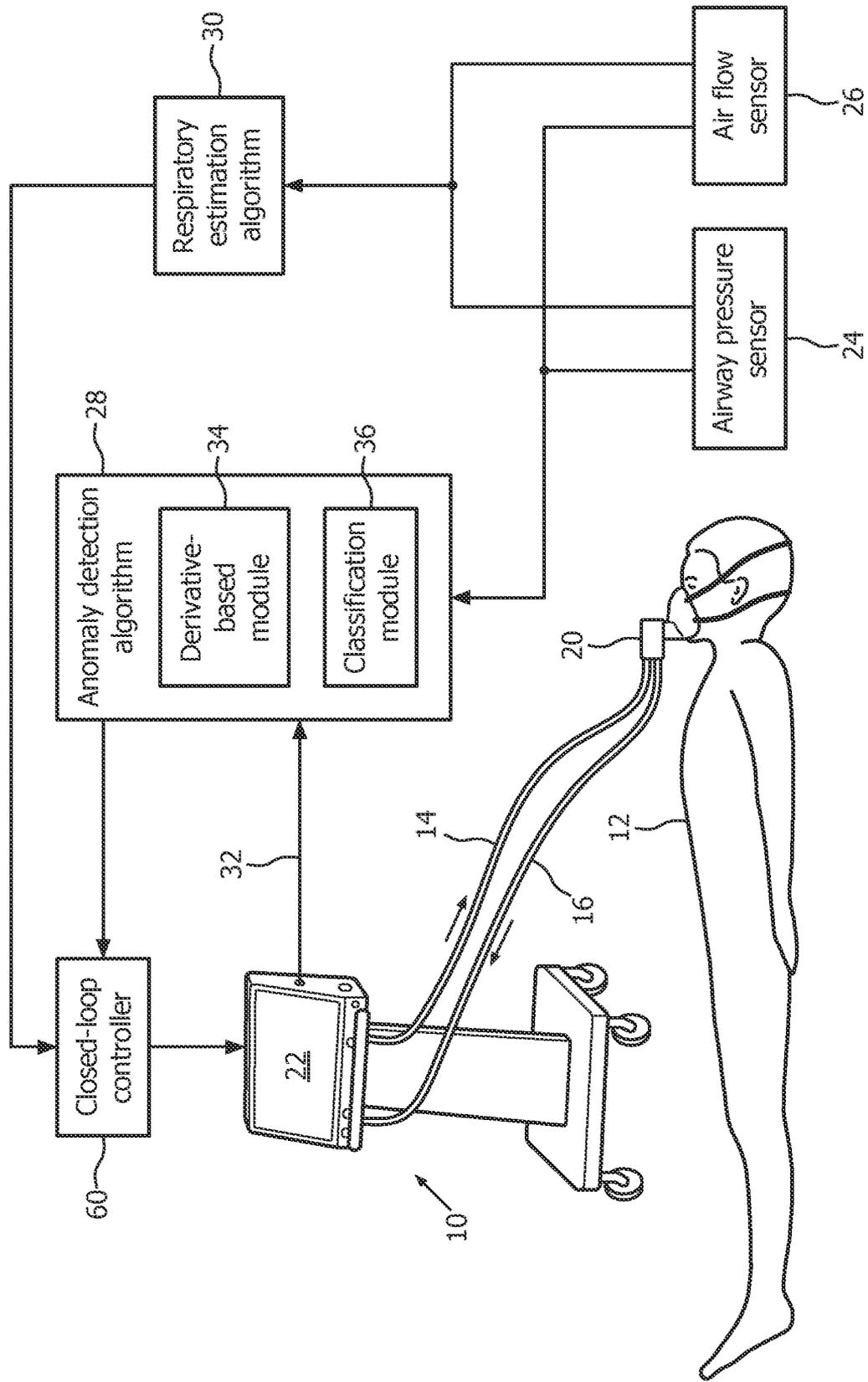


FIG. 1

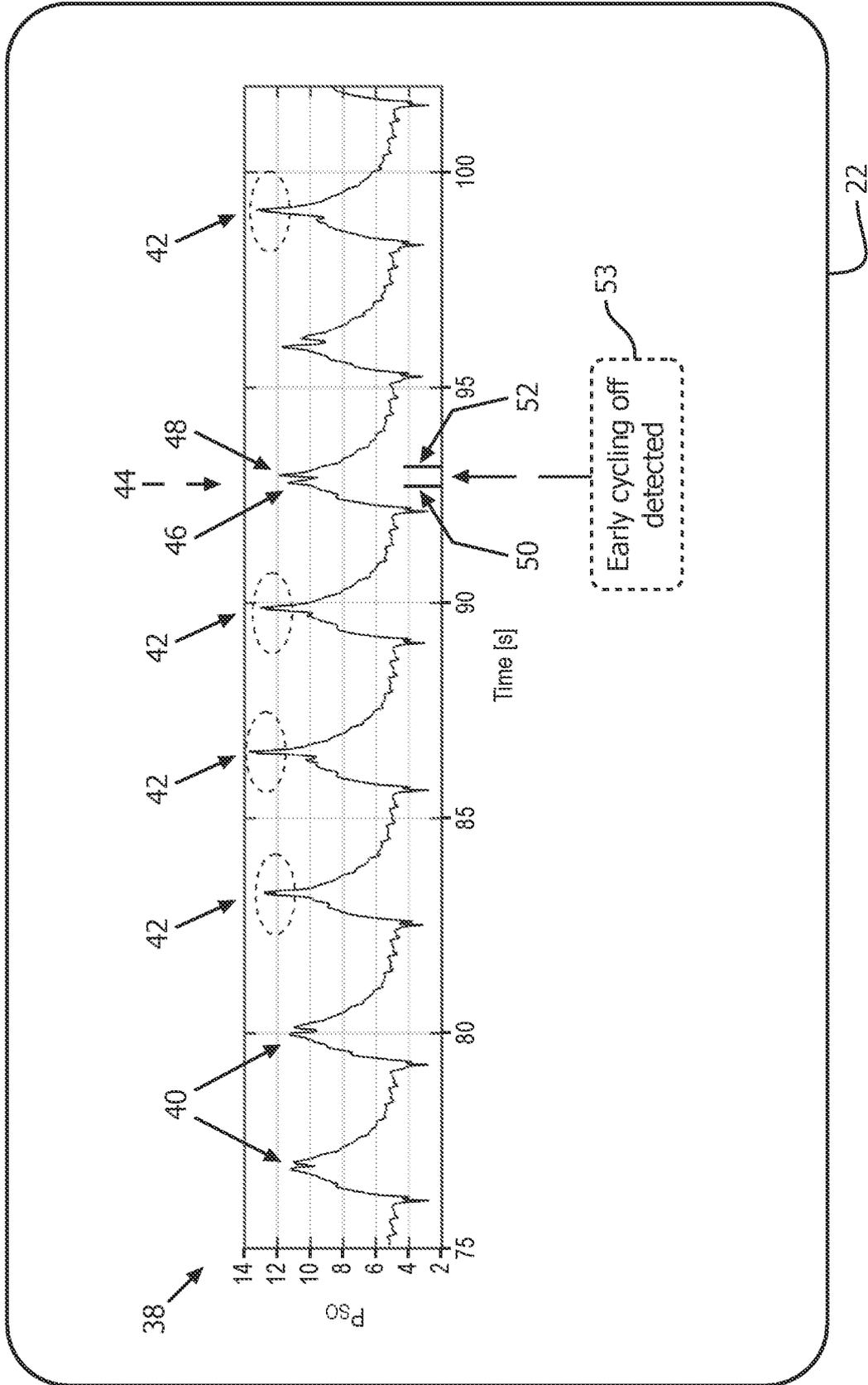
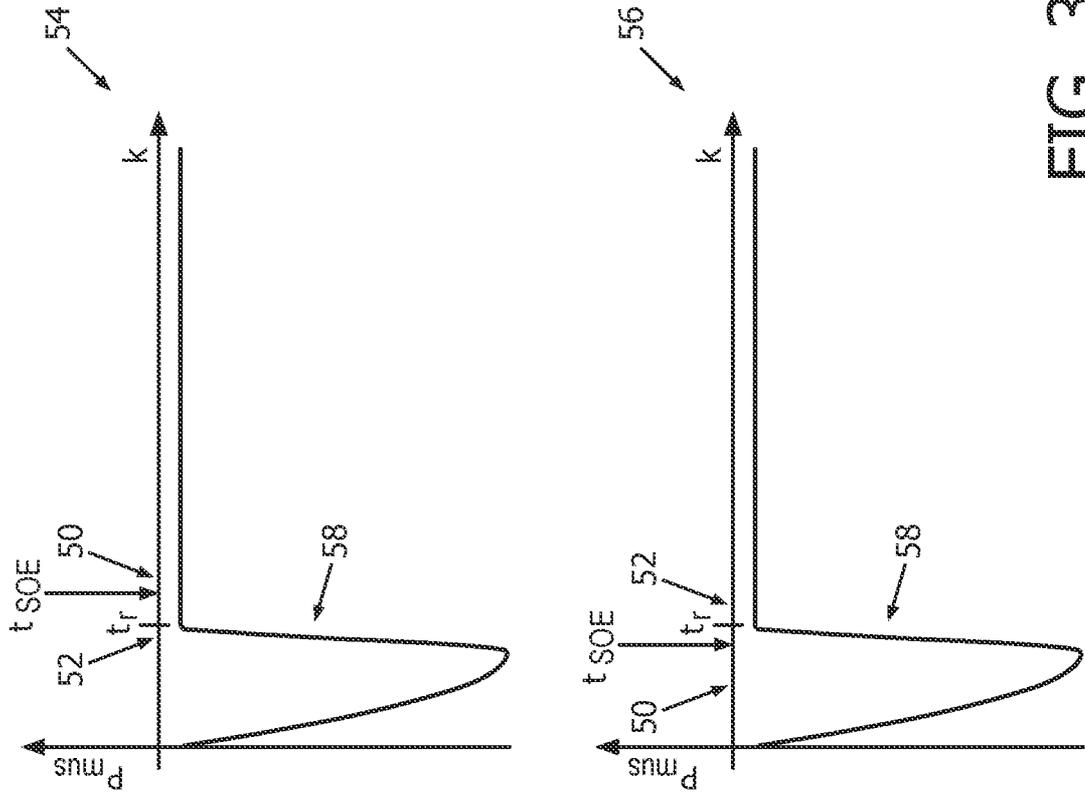


FIG. 2



E <sub>cycle</sub>	t <sub>SOE</sub>	t <sub>SOE</sub> -t <sub>r</sub>	R <sub>est</sub>	E <sub>est</sub>
0.15	1.72	0.72	7.0000	10.0000
0.20	1.50	0.50	7.0000	10.0000
0.23	1.39	0.39	7.0000	10.0000
0.25	1.32	0.32	7.0000	10.0000
0.27	1.25	0.25	7.0000	10.0000
0.29	1.19	0.19	7.0000	10.0000
0.30	1.16	0.16	7.0000	10.0000
0.31	1.13	0.13	7.0000	10.0000
0.32	1.10	0.10	7.0000	10.0000
0.33	1.06	0.06	7.0000	10.0000
0.34	1.03	0.03	7.0000	10.0000
0.35	1.00	0.00	8.6354	11.8171
0.36	0.99	-0.01	6.9866	9.9851
0.37	0.98	-0.02	6.9602	9.9558
0.38	0.97	-0.03	6.9351	9.9279
0.39	0.97	-0.03	6.9351	9.9279
0.40	0.96	-0.04	17.0663	21.1848
0.41	0.96	-0.04	17.0663	21.1848
0.43	0.95	-0.05	17.0661	21.1846
0.45	0.94	-0.06	17.0663	21.1848
0.47	0.94	-0.06	17.0663	21.1848
0.50	0.93	-0.07	17.0663	21.1848
0.55	0.91	-0.09	8.5974	11.7749

FIG. 3

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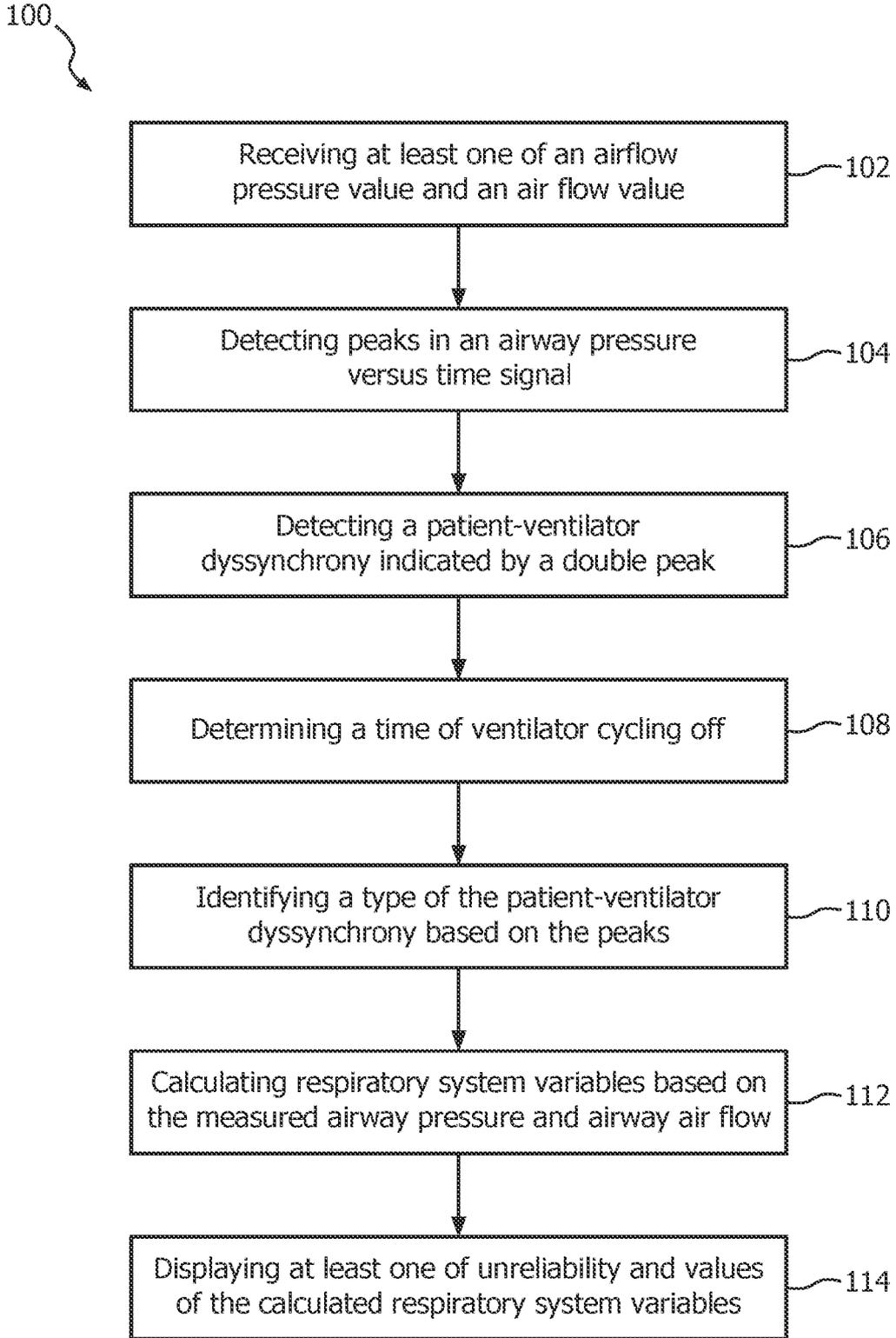


FIG. 4

INTERNATIONAL SEARCH REPORT

International application No  
PCT/IB2016/056115

A. CLASSIFICATION OF SUBJECT MATTER  
INV. A61B5/00  
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)  
A61B A61M

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 2012/037159 A1 (MULQUEENY QESTRA CAMILLE [AU] ET AL) 16 February 2012 (2012-02-16)	1-11, 14-16,20
A	abstract paragraph [0052] - paragraph [0299] figures 3-19 ----- -/--	12,13, 17-19

Further documents are listed in the continuation of Box C.

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
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- "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  20 January 2017	Date of mailing of the international search report  26/01/2017
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer  Marteau, Frédéric
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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/IB2016/056115

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>VICARIO FRANCESCO ET AL: "Noninvasive Estimation of Respiratory Mechanics in Spontaneously Breathing Ventilated Patients: A Constrained Optimization Approach", IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, IEEE SERVICE CENTER, PISCATAWAY, NJ, USA, vol. 63, no. 4, 20 August 2015 (2015-08-20), pages 775-787, XP011603486, ISSN: 0018-9294, DOI: 10.1109/TBME.2015.2470641 [retrieved on 2016-03-17] section 'III. Method'</p> <p style="text-align: center;">-----</p>	1-20
A	<p>MAGDY YOUNES ET AL: "A method for monitoring and improving patient: ventilator interaction", INTENSIVE CARE MEDICINE, SPRINGER, BERLIN, DE, vol. 33, no. 8, 31 May 2007 (2007-05-31), pages 1337-1346, XP019536326, ISSN: 1432-1238, DOI: 10.1007/S00134-007-0681-4 abstract section 'Methods' section 'Discussion' figures 1,5</p> <p style="text-align: center;">-----</p>	1-20

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2016/056115

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		US 2016279361 A1	29-09-2016
		WO 2010121313 A1	28-10-2010
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