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(71) Applicant: MAQUET CRITICAL CARE AB [SE/SE];

P.O. Box 6108, 171 06 Solna (SE).

(72) Inventors: TROILI, Carl-Erik; Kevingeren 83, 182 50

Danderyd (SE). WESTERLUND, Tomas; Kämpevägen 6 B, 191 49 Sollentuna (SE).

(74) Agent: ZACCO SWEDEN AB; P.O. Box 5581, Valhallavägen 117N, 114 85 Stockholm (SE).

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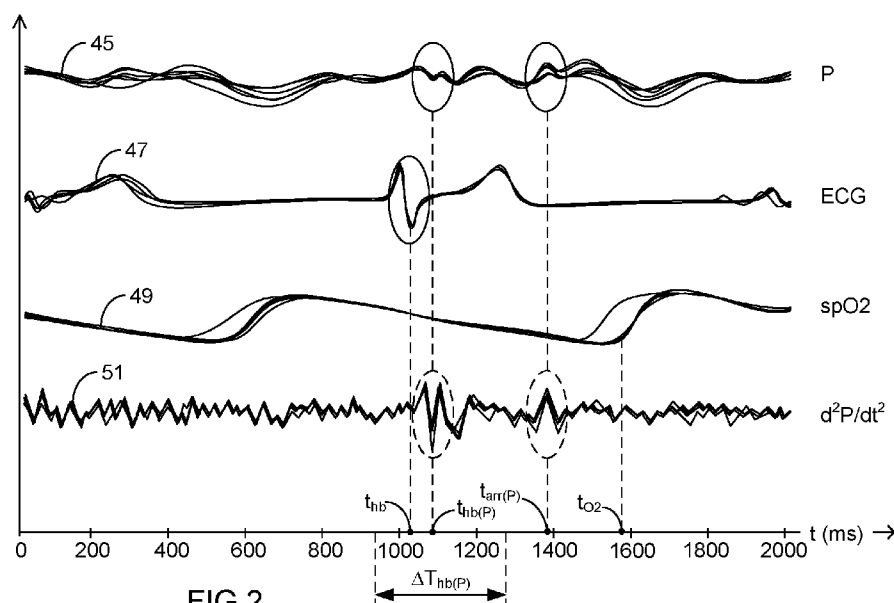


FIG 2

(57) Abstract: A method for non-invasive estimation of a pulmonary blood pressure of a mechanically ventilated subject (3) is disclosed. The method comprises determining a point in time (t_{hb}) of a heartbeat of the ventilated subject; measuring a respiratory gas pressure and/or a respiratory gas flow; obtaining a respiratory pressure curve and/or a respiratory flow curve from said respiratory gas pressure and/or respiratory gas flow measurements; determining an arrival point in time (t_{arr}) at which a blood flow caused by said heartbeat reaches the lungs of the subject (3), and estimating a pulmonary blood pressure of the subject (3) based on the point in time of the heartbeat and said arrival point in time. At least the arrival point in time of the blood flow reaching the lungs of the subject is determined from the respiratory pressure curve and/or the respiratory flow curve.



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Non-Invasive Estimation of Pulmonary Blood Pressure

TECHNICAL FIELD

- 5 The present invention relates to a method, a computer program and an apparatus for estimating a pulmonary blood pressure of a mechanically ventilated subject.

BACKGROUND

- 10 During mechanical ventilation there is a demand for monitoring the physiological state of the ventilated patient. Electrocardiogram (ECG) measurement systems, blood pressure sensors and pulse oximeters are examples of medical devices that are widely known and used to monitor the cardiovascular function of mechanically ventilated patients.

15

- There are two different types of blood pressure that are of importance for the clinician in the assessment of cardiovascular function: the systemic blood pressure and the pulmonary blood pressure. Systemic blood pressure is the pressure of circulating blood on the walls of blood vessels, usually large arteries, of the systemic circulation. Pulmonary blood pressure or pulmonary artery pressure is the pressure of blood on the walls of the pulmonary arteries, i.e., the arteries transporting blood between the heart and the lungs. Increased pulmonary blood pressure may cause pulmonary hypertension, and decreased pulmonary blood pressure may cause pulmonary hypotension, both of which are severe conditions.

25

- Pulmonary blood pressure and ventilation are closely related and the pulmonary blood pressure is highly affected by the level of ventilation provided to the patient during mechanical ventilation. For instance, a high mean lung pressure during mechanical ventilation may cause a decrease in pulmonary circulation due to increased external pressure on pulmonary arteries, typically resulting in increased pulmonary blood pressure.

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There is thus a need for monitoring pulmonary blood pressure during mechanical ventilation of a patient, both for monitoring the cardiovascular function of the patient

and for receiving feedback on potentially adverse effects of the ongoing mechanical ventilation.

There are a few known techniques for measuring pulmonary blood pressure.

5

One known technique is intravascular pressure monitoring by means of a pulmonary artery catheter (PAC) that is inserted into a pulmonary artery of the patient. This enables the pulmonary blood pressure to be measured continuously. However, intravascular monitoring of pulmonary blood pressure is associated with potential severe complications like sepsis, pulmonary infarction, bleeding and arrhythmias, among others. Therefore, it is rarely justified even in most critically ill patients.

An example of a non-invasive technique for pulmonary blood pressure determination is the ultrasound-based technique disclosed by Micah R Fisher et al, "Accuracy of Doppler Echocardiography in the Hemodynamic Assessment of Pulmonary Hypertension", American Journal of Respiratory and Critical Care Medicine, Vol. 179, No. 7 (2009), pp. 615-621. According to this technique, ultrasound is used to compare a flow of blood going in the direction of the lungs of a patient with a blood flow leaking back towards the patient's heart. The comparison may be used to estimate the pulmonary blood flow of the patient. This technique requires additional equipment in form of ultrasound transducers and is dependent on qualified personnel to perform the measurements.

Another known non-invasive technique is the use of Doppler echocardiography to determine the time required (pulse transit time, PTT) for a blood pressure pulse to propagate between two locations along the pulmonary artery. This technique requires Doppler echocardiography equipment and a rather complex setup with at least two points of measurement.

Yet another example of a non-invasive technique for pulmonary blood pressure determination is disclosed in "Non-invasive monitoring of pulmonary artery pressure at the bedside", Conf Proc IEEE Eng Med Biol Soc. 2016 Aug;2016:4236-4239, doi: 10.1109/EMBC.2016.7591662, by Proenca M et al. This technique employs

electrical impedance tomography (EIT), which is another medical imaging technique, in order to monitor the pulmonary blood pressure of a patient continuously.

Non-invasive techniques based on magnetic resonance (MR) imaging techniques
5 have also been proposed for the assessment of pulmonary arterial stiffness or
pulmonary blood pressure estimation. For example, "Assessment of proximal
pulmonary arterial stiffness using magnetic resonance imaging: effects of technique,
age and exercise", BMJ Open Respir Res. 2016 Oct 7;3(1):e000149. eCollection
2016, by Weir-McCall JR et al. discloses an MR-based technique for determining
10 pulmonary pulse wave velocity (PWV).

However, none of the above techniques are suitable for the monitoring of pulmonary
blood pressure of a mechanically ventilated patient due to their complicated nature
and the required use of additional equipment not normally available at the bedside
15 of mechanically ventilated patients.

Consequently, there is a need for a non-invasive technique for estimation of
pulmonary blood pressure, which technique may be readily available at the bedside
of a mechanically ventilated patient.
20

SUMMARY

It is an object of the disclosure to present a technique for non-invasive estimation of
pulmonary blood pressure of a mechanically ventilated patient.
25

It is another object of the disclosure to present a technique for non-invasive
estimation of pulmonary blood pressure of a mechanically ventilated patient, which
solves or at least mitigates one or more of the problems associated with the above
mentioned techniques.

30 It is a particular object of the disclosure to present a technique for non-invasive
estimation of pulmonary blood pressure of a mechanically ventilated patient, which
can be used without the need for additional equipment or medical devices not
normally available at the bedside of a mechanically ventilated patient.

Yet further, it is an object of the disclosure to present a technique for non-invasive estimation of pulmonary blood pressure of a mechanically ventilated patient, which allows the pulmonary blood pressure of the patient to be monitored continuously.

5

These and other objects are achieved in accordance with the present disclosure by a method, a computer program and an apparatus as defined by the appended claims.

- 10 According to an aspect of the disclosure, there is provided a method for non-invasive estimation of a pulmonary blood pressure of a mechanically ventilated subject. The method comprises obtaining a respiratory pressure curve and/or a respiratory flow curve from respiratory gas pressure and/or respiratory gas flow measurements; determining a point in time of a heartbeat of the ventilated subject;
- 15 determining an arrival point in time at which a blood flow caused by said heartbeat reaches the lungs of the subject, and estimating a pulmonary blood pressure of the subject based on the point in time of the heartbeat and said arrival point in time, wherein at least the arrival point in time of the blood flow reaching the lungs of the subject is determined from the respiratory pressure curve and/or the respiratory flow
- 20 curve.

- Consequently, the proposed method suggests the time of transit of a blood pressure pulse from the heart to the lungs of the ventilated subject to be used in the estimation of the pulmonary blood pressure. The use of a blood pressure pulse
- 25 transit time (PTT), sometimes referred to as pulse wave transit time (PWTT), or the use of the closely related quantity pulse wave velocity (PWV), is known in the art of systemic blood pressure determination, where the PTT, PWTT or PWV can be determined by measuring the time required for a blood pressure pulse to propagate between two points of measurements, for instance between two points along the
- 30 arm of the patient. As mentioned in the background, it has also been suggested to derive a blood pressure PTT using Doppler echocardiography, and use the derived PTT in non-invasive determination of pulmonary blood pressure.

In contrast to the Doppler echocardiography approach, the present disclosure suggests the point in time of arrival of the blood pressure pulse at the lungs of the subject to be determined from a respiratory pressure curve and/or a respiratory flow curve. Determining the arrival point in time from a respiratory pressure curve and/or a respiratory flow curve is advantageous in that respiratory pressure and flow curves are readily available from pressure and flow measurements normally obtained by sensors of the breathing apparatus providing the mechanical ventilation to the patient. Consequently, no equipment besides the equipment normally comprised in a breathing apparatus is needed in order to carry out the proposed method.

Furthermore, the method can be performed continuously, e.g. once for each breathing cycle, allowing the pulmonary blood pressure of the mechanically ventilated patient to be continuously monitored.

The arrival time, i.e. the point in time of arrival of the blood pressure pulse at the lungs of the ventilated subject, is typically determined by detecting a change in magnitude or curvature of the respiratory pressure curve and/or the respiratory flow curve.

Fluctuations in respiratory pressure or flow, caused by pulmonary blood flow, are often referred to as cardiogenic oscillations. The proposed method can hence be said to constitute a method for non-invasive estimation of a pulmonary blood pressure from cardiogenic oscillations.

For instance, the arrival time may be determined as the point in time at which the respiratory pressure curve and/or the respiratory flow curve crosses a threshold value. Alternatively, the arrival point in time may be determined from the curvature of the respiratory pressure curve and/or the respiratory flow curve, e.g. through curvature analysis of relevant parts of the respiratory pressure curve and/or the respiratory flow curve. For example, the arrival time may be determined based on a change in a first and/or second order derivative with respect to time of the respiratory pressure curve and/or the respiratory flow curve. This is advantageous in that the first and/or second order derivative of the respiratory pressure curve and/or the respiratory flow curve may be affected to a greater extent than the magnitudes of the respiratory pressure curve and the respiratory flow curve at the time of arrival

of the blood pressure pulse at the lungs of the patient. Consequently, studying changes in the first and/or second order derivative may provide a more precise and/or robust estimation of pulmonary blood pressure.

- 5 According to some aspects, also the point in time of the heartbeat is determined from the respiratory pressure curve and/or the respiratory flow curve. Similar to determination of the arrival time, the point in time of the heartbeat may be determined as the point in time at which the respiratory pressure curve and/or the respiratory flow curve crosses a threshold value. Alternatively, the point in time of
- 10 the heartbeat may be determined from the curvature of the respiratory pressure curve and/or the respiratory flow curve, e.g. through curvature analysis of relevant parts of the respiratory pressure curve and/or the respiratory flow curve. For example, the point in time of the heartbeat may be determined based on a change in a first and/or second order derivative with respect to time of the respiratory pressure
- 15 curve and/or the respiratory flow curve.

- Determining both the point in time of the heartbeat and the point in time of arrival of the blood pressure pulse at the lungs of the ventilated subject from the respiratory pressure curve and/or the respiratory flow curve is advantageous in that no other
- 20 quantities than respiratory pressure and/or respiratory flow and hence no other sensors than pressure and/or flow sensors of the breathing apparatus are required for the determination of the pulmonary blood pressure of the ventilated subject.
- Determining both the point in time of the heartbeat and the point in time of arrival of the blood pressure pulse at the lungs of the ventilated subject from the respiratory
- 25 pressure curve and/or the respiratory flow curve is also advantageous in that the time delay between the point in time of a heartbeat and the point in time of detection of the heartbeat from the respiratory pressure or flow curve substantially corresponds to the time delay between the point in time of arrival of the blood pressure pulse at the lungs of the ventilated subject and the point in time of
- 30 detection of arrival of the blood pressure pulse from the respiratory pressure or flow curve. Therefore, no time delay compensation is needed in the determination of any of the point in time of the heartbeat or the point in time of arrival of the blood pressure pulse.

In order to facilitate detection of the point in time of the heartbeat from the respiratory pressure curve and/or the respiratory flow curve, the method may comprise a step of determining an estimated time window for the heartbeat, and determining the point in time of the heartbeat from the respiratory pressure curve
5 and/or the respiratory flow curve within the estimated time window, e.g. by analysing the magnitude or the curvature of the respiratory pressure curve and/or the respiratory flow curve only within the estimated time window. The time window for the heartbeat may be estimated from available sensor data.

10 The estimated time window for the heartbeat may be determined based on a point in time of a plurality of previously detected heartbeats. For example, the time window may be determined based on the point in time of a preceding heartbeat and a heartrate of the subject, calculated based on the points in time of a plurality of preceding heartbeats. Additionally, a respiration rate of the ventilated subject may
15 be used to more reliably and/or more accurately determine the estimated time window for the heartbeat.

Alternatively or in addition, the estimated time window for the heartbeat may be determined retroactively based on sensor data indicative of the heartbeat itself.

20

For example, the estimated time window for the heartbeat may be determined retroactively based on the arrival point in time of the blood pressure pulse to the lungs of the subject, determined from the respiratory pressure curve and/or the respiratory flow curve. The determined arrival point in time may be used together
25 with an uncertainty associated with the determination of the arrival point in time to set the boundaries of the estimated time window for the heartbeat. This type of retroactive determination of a time window for the heartbeat may be particularly advantageous in situations where the point in time of arrival of the blood pressure pulse to the lungs of the patient is more easily detectable from the respiratory
30 pressure and/or flow curve than the point in time of the heartbeat.

According to another example, the time window for the heartbeat may be determined retroactively based on blood oxygenation measurements. The blood oxygenation measurements may be obtained e.g. by a pulse oximeter attached to a

body part of the ventilated subject, whereby the time window for the heartbeat may be determined based on a point in time of a change in blood oxygenation, registered by the pulse oximeter. The point in time of change in blood oxygenation may, together with an uncertainty associated with the determination thereof, be used to
5 set the boundaries of the estimated time window for the heartbeat. In alternative to a pulse oximeter, a sphygmomanometer (i.e. a cuff-based blood pressure monitor) for measuring systemic blood pressure may be used to determine the point in time at which a systemic blood pressure pulse following a heartbeat reaches the point of measurement. In accordance with the above described principles, the point in time
10 at which the systemic blood pressure pulse reaches the point of measurement can be used to retroactively estimate a time window for the heartbeat.

According to some aspects, the method may comprise the steps of obtaining an electrocardiogram (ECG) of the electrical activity of the heart of the ventilated
15 subject, and using the ECG to determine the point in time of the heartbeat. The ECG may be determined using conventional surface electrodes or an oesophageal ECG catheter. Alternatively, the ECG may be determined from raw signals recorded by an oesophageal catheter for measuring an electric activity of the diaphragm (Edi) of the ventilated subject, which raw signals may also be used to extract an Edi signal for
20 controlling the breathing apparatus when operated in a mode of neurally adjusted ventilatory assist (NAVA).

The pulmonary blood pressure of the ventilated subject may be estimated based on a pulse transit time (PTT), calculated based on a difference between the point in
25 time (t_{hb}) of the heartbeat and the arrival point in time (t_{arr}) of the blood flow to the lungs of the subject (3). Consequently, the PTT may be calculated based on a distance in time between a change in magnitude or curvature of the ECG and/or the respiratory pressure curve and/or the respiratory flow curve, caused by the heartbeat, and a change in magnitude or curvature of the respiratory pressure curve
30 and/or the respiratory flow curve, caused by the arrival of the blood pressure pulse at the lungs of the subject.

In order to more reliably determine the point in time of arrival of the blood pressure pulse to the lungs of the subject from the respiratory pressure and/or flow curve, it

- may be advantageous to study a heartbeat occurring during a final phase of inspiration, when the respiratory flow is relatively low. Therefore, the point in time of arrival of the blood flow to the lungs of the subject is preferably determined for a heartbeat occurring during a final phase of an inspiration. To this end, the method
- 5 may comprise a step of confirming that the determined point in time of the heartbeat of the ventilated subject is within a final phase of inspiration, whereby the step of estimating the pulmonary blood pressure of the subject may be carried out only if it can be confirmed that the heartbeat is within a final phase of inspiration.
- 10 The method may further comprise a step of presenting the estimated pulmonary blood pressure to an operator of the breathing apparatus or other medical personnel. For example, the estimated pulmonary blood pressure may be displayed on a display of the breathing apparatus carrying out the mechanical ventilation of the subject, or on a display of a patient monitor for monitoring the ventilated patient. The
- 15 method may further comprise a step of generating an alarm signal in case the estimated pulmonary blood pressure is outside a predefined range.

According to another aspect of the present disclosure there is provided a ventilation system comprising an apparatus, such as a breathing apparatus or a patient

20 monitor, capable of performing the above described method of non-invasive estimation of pulmonary blood pressure. The proposed method enables the apparatus to determine the pulmonary blood pressure of a subject during ongoing mechanical ventilation.

- 25 The apparatus may comprise at least one computer configured to obtain a respiratory pressure curve and/or a respiratory flow curve from respiratory gas pressure and/or respiratory gas flow measurements. The computer may further be configured to determine a point in time of a heartbeat of the ventilated subject, determine an arrival point in time at which a blood flow caused by said heartbeat
- 30 reaches the lungs of the subject, and estimate a pulmonary blood pressure of the subject based on the point in time of the heartbeat and said arrival point in time, wherein the computer is configured to determine at least said arrival point in time from the respiratory pressure curve and/or the respiratory flow curve.

The ventilation system may comprise at least one pressure sensor and/or at least one flow sensor for obtaining the respiratory gas pressure and/or the respiratory gas flow measurements used by the computer of the apparatus in the estimation of the pulmonary blood pressure of the subject. The apparatus may be, the breathing
5 apparatus itself, a patient monitor for monitoring the ventilated patient, or any other type of apparatus that is devised and configured as set forth above. The at least one pressure sensor and/or the at least one flow sensor may be internal sensors of the breathing apparatus, external sensors connected to the apparatus for transmittal of obtained measurement values to the computer of the apparatus, or both.

10

The computer may be configured to determine the arrival point in time at which the blood flow reaches the lungs in accordance with any of the principles described above, .e.g. by determining when the respiratory pressure curve and/or the respiratory flow curve crosses a threshold value or by analysing the curvature of the
15 respiratory pressure curve and/or the respiratory flow curve. For example, the computer may be configured to determine the arrival point in time based on a change in a first and/or second order derivative with respect to time of the respiratory pressure curve and/or the respiratory flow curve.

20 Likewise, the computer may be configured to determine the point in time of the heartbeat from respiratory pressure curve and/or the respiratory flow curve, in accordance with any of the principles described above.

For example, the computer may be configured to determine an estimated time
25 window for the heartbeat according to the above described principles, and to determine the point in time of the heartbeat from the respiratory pressure curve and/or the respiratory flow curve within the estimated time window for the heartbeat.

As clear from above, the computer may be configured to estimate the time window
30 based on any of, or any combination of:

- the points in time of a plurality of previously detected heartbeats;
- the determined arrival point in time of the blood flow to the lungs of the subject;
- blood oxygenation data relating to oxygenation of blood in a body part at a known or assumable distance from the heart of the subject, and

- systemic blood pressure data relating to a systemic blood pressure measured in a body part at a known or assumable distance from the heart of the subject (3).

The ventilation system may further comprise an ECG sensor for recording an ECG of an electrical activity of the heart of the subject, whereby the computer may be configured to determine the point in time of the heartbeat using the ECG. For example, the ventilation system may comprise an electrode-equipped oesophageal catheter for registration of Edi signals allowing the breathing apparatus to be operated in NAVA mode based on the recorded Edi signals. In this scenario, the ECG of the ventilated subject may be extracted by the computer from recorded raw signals comprising both an Edi component and an ECG component, as well known in the art. Consequently, the ECG sensor of the ventilation system may, in some embodiments, be an oesophageal catheter for measuring an electric activity of a diaphragm of the ventilated subject. In other embodiments, the ECG sensor may comprise a set of surface electrodes. In yet other embodiments, the ECG sensor may be an oesophageal ECG catheter dedicated for registration of ECG signals.

The logic required to enable the proposed apparatus and its components to carry out the steps of the above-described method is preferably implemented by means of software. Thus, according to yet another aspect of the present disclosure there is provided a computer program for non-invasive estimation of a pulmonary blood pressure of a subject being mechanically ventilated by a breathing apparatus. The computer program comprises computer-readable code segments which, when executed by a processor of the proposed apparatus, causes the apparatus to:

- obtain a respiratory pressure curve and/or a respiratory flow curve from respiratory gas pressure and/or respiratory gas flow measurements;
- determine a point in time of a heartbeat of the ventilated subject;
- determine an arrival point in time at which a blood flow caused by said heartbeat reaches the lungs of the subject, and
- estimate a pulmonary blood pressure of the subject based on the point in time of the heartbeat and said arrival point in time,

wherein at least the arrival point in time is determined from the respiratory pressure curve and/or the respiratory flow curve.

The computer program may be stored in a non-volatile memory of the apparatus.

Installation of the computer program on existing apparatuses configured to obtain respiratory gas pressure and/or respiratory gas flow measurements, such as
5 breathing apparatuses and flow-sensor equipped patient monitors, may allow existing apparatuses to carry out the method of the present disclosure without any hardware modification.

More advantageous aspects of the proposed method, apparatus and computer
10 program will be described in the detailed description of embodiments following hereinafter.

BRIEF DESCRIPTION OF THE DRAWINGS

15 The present invention will become more fully understood from the detailed description provided hereinafter and the accompanying drawings which are given by way of illustration only. In the different drawings, same reference numerals correspond to the same element.

20 Fig. 1 illustrates a ventilation system comprising a breathing apparatus capable of non-invasively determining the pulmonary blood pressure of a ventilated patient, according to an exemplary embodiment of the disclosure.

Fig. 2 illustrates curves of measured quantities that may be used by the breathing
25 apparatus in determination of the pulmonary blood pressure.

Fig. 3 is a flowchart illustrating a method for non-invasive determination of the pulmonary blood pressure of a mechanically ventilated patient, according to an
30 exemplary embodiment of the disclosure.

DETAILED DESCRIPTION

Fig. 1 illustrates an exemplary embodiment of a ventilation system 1 comprising a breathing apparatus 2 configured to estimate the pulmonary blood pressure of a

mechanically ventilated subject 3 (hereinafter referred to as the patient) according to the principles disclosed herein. The breathing apparatus may be any type of apparatus capable of providing ventilatory assist to the subject 3 through the supply of pressurised breathing gas to the airways of the subject. Ventilators and anaesthesia
5 machines are non-limiting examples of such breathing apparatuses.

The breathing apparatus 2 is connected to the patient 3 via a patient circuit comprising an inspiratory line 5 for supplying breathing gas to the patient 3, and an expiratory line 7 for conveying expiration gas away from the patient 3. The inspiratory line 5 and the
10 expiratory line 7 are connected to a common line 9, via a so called Y-piece 11, which common line is connected to the patient 3 via a patient connector 13, such as a facemask or an endotracheal tube.

The breathing apparatus 2 comprises a control unit or control computer 15 for
15 controlling the ventilation of the patient 3 based on pre-set parameters and/or measurements obtained by various sensors of the breathing apparatus. The control computer 15 controls the ventilation of the patient 3 by controlling a pneumatic unit 17 of the breathing apparatus 2, which pneumatic unit 17 is connected on one hand to one or more gas sources 19, 21 and on the other hand to the inspiratory line 5 for
20 regulating a flow and/or pressure of breathing gas delivered to the patient 3. The pneumatic unit 17 may comprise various gas mixing and regulating means well known in the art of ventilation, such as gas mixing chambers, controllable gas mixing valves, turbines, controllable inspiration and/or expiration valves, etc. The pneumatic unit 17 is connected to the inspiratory line 5 of the patient circuit via an internal inspiratory
25 flow channel of the breathing apparatus 2, and to the expiratory line 7 of the patient circuit via an internal expiratory flow channel of the breathing apparatus. The gas flow path of the ventilation system 1 that is arranged in fluid communication with the airways of the patient 3 during operation of the breathing apparatus may herein be referred to as the breathing circuit of the ventilation system. The breathing circuit
30 includes at least the patient circuit and the inspiratory and expiratory flow channels of the breathing apparatus 2.

The control computer 15 comprises a processor or processing unit 23, such as a microprocessor, and a non-volatile memory hardware device 25 storing one or more

computer programs for controlling the operation of the breathing apparatus 1 and estimating the pulmonary blood pressure of the patient 3 in accordance with the principles described herein. Unless stated otherwise, actions and method steps described hereinafter are performed by, or caused by, the control computer 15 of the breathing apparatus 1 upon execution by the processing unit 23 of different code segments of a computer program stored in the memory 25.

In accordance with the principles of the present disclosure, the computer program comprises code segments which, when executed, causes the control computer 15 to derive a respiratory pressure curve from respiratory pressure measurements indicative of a respiratory gas pressure in the breathing circuit, and/or to derive a respiratory flow curve from respiratory gas flow measurements indicative of a gas flow in the breathing circuit. The code segments further causes the control computer 15 to determine, from the derived respiratory pressure curve and/or respiratory flow curve, an arrival point in time at which a blood flow caused by a heartbeat of the ventilated patient 3 reaches the patient's lungs, and to estimate the pulmonary blood pressure of the patient using the determined arrival point in time.

To this end, the ventilation system 1 comprises at least one of a flow sensor 33 for measuring a respiratory flow of gas and a pressure sensor 37 for measuring a respiratory gas pressure. In the exemplary embodiment illustrated in Fig. 2, the flow sensor 33 is located in or close to the Y-piece 11 and configured to measure both an inspiratory flow of breathing gas delivered towards the patient 3 during inspiration, and an expiratory flow of gas, exhaled by the patient 3 during expiration. Likewise, the pressure sensor 37 is located in or close to the Y-piece 11 and configured to measure a proximate patient pressure, substantially corresponding to and often referred to as an airway pressure of the patient 3, during both inspiration and expiration. The measurement signals obtained by the flow sensor 33 and the pressure sensor 37 are transmitted to the control computer 15 via a respective signalling line 35, 39, whereby the measurement signals are used by the control computer in the determination of the pulmonary blood pressure of the patient 3. The flow and/or pressure measurements signals received by the control computer 15 from the flow and/or pressure sensors 33, 37 may further be used by the control computer 15 in

automatic feedback control of the operation of the breathing apparatus 2, in accordance with principles well known in the art of ventilation.

Alternatively or in addition to the flow sensor 33 and/or the pressure sensor 37 in the
5 Y-piece 11 of the patient circuit, the breathing apparatus may comprise one or more
internal flow sensors for measuring respiratory gas flow, and/or one or more internal
pressure sensors for measuring respiratory gas pressure. For example, the breathing
apparatus 2 may comprise a flow sensor 33' for measuring a flow of breathing gas in
10 37' for measuring a gas pressure in the inspiratory flow channel of the breathing
apparatus. Alternatively, or in addition, the breathing apparatus 2 may comprise a flow
sensor 33'' for measuring a flow of expiration gas in the expiratory flow channel of the
breathing apparatus 2, and/or a pressure sensor 37'' for measuring a gas pressure in
the expiratory flow channel of the breathing apparatus. The respiratory pressure curve
15 and/or the respiratory flow curve used by the control computer 15 to determine the
arrival point in time at which the blood flow reaches the patient's lungs may be derived
from pressure and/or flow measurements obtained by any of, or any combination of,
the exemplary flow and pressure sensors 33-33'', 37-37'' illustrated in Fig. 1, or by
pressure and/or flow sensors for measuring respiratory flow and/or respiratory
20 pressure disposed elsewhere in the breathing circuit of the ventilation system 1.

According to yet other embodiments (not shown), the respiratory pressure curve
and/or the respiratory flow curve used by the control computer 15 to determine the
pulmonary blood pressure of the ventilated patient 3 may be derived from pressure
25 and/or flow measurements obtained by a pressure and/or a flow sensor inserted into
the trachea of the patient 3. Such a pressure and/or flow sensor may, for instance, be
mounted onto a tracheal tube for intubation of the patient 3 during ventilation. As will
be appreciated from the description following hereinafter, it may be advantageous to
use pressure and/or flow sensors located in the Y-piece 11 or even in the trachea of
30 the patient 3, so as to minimize the distance between the lungs of the patient 3 and
the point of pressure and/or flow measurement.

As also appreciated from the above description, any or both of a respiratory
pressure curve and a respiratory flow curve can be used to identify the points in time

of the heartbeat and the arrival of the blood pressure pulse to the lungs of the patient according to the principles of the present disclosure. Hereinafter, for the sake of conciseness, the term “respiratory curve” may sometimes be used as a general term for any of a respiratory pressure curve and a respiratory flow curve.

5

The ventilation system 1 further comprises an ECG sensor 29 configured to register an ECG or ECG signal indicative of the electrical activity of the heart of the ventilated patient 3. The ECG related signals recorded by the ECG sensor 29 are transmitted to the control computer 15 of the breathing apparatus 2 via a signalling line 30. The ECG
10 signals may then be used by the control computer 15 in the determination of the pulmonary blood pressure of the patient 3, as further described below.

In the illustrated embodiment, the breathing apparatus 2 is a NAVA-enabled ventilator comprising a bioelectric sensor or bioelectric sensor arrangement coupled to the
15 control computer 15 of the breathing apparatus 1. The bioelectric sensor arrangement is an electromyogram (EMG) detector for recording the diaphragm EMG of the patient 3. To this end, the sensor arrangement comprises an oesophageal catheter 29 carrying an array of electrodes 31 for capturing EMG signals from the diaphragm of the patient 3. The electrodes 31 produce a number of subsignals that are processed
20 by the control computer 15 to calculate a signal, the Edi signal, representing the electrical activity of the diaphragm (EAdi). Since the EMG signals captured by the sensor are used to calculate an Edi signal, the oesophageal catheter 29 is often referred to as an Edi catheter within the field of ventilation.

25 Besides the Edi signal, the control computer 15 is configured to derive an ECG or ECG signal from the recorded diaphragm EMG, which ECG signal is indicative of the electrical activity of the patient's heart. How to extract an ECG signal from the diaphragm EMG captured by the electrodes of the oesophageal catheter 29 is well known in the art and disclosed in e.g. US8527036. Consequently, the oesophageal
30 catheter 29 can be said to constitute a combined Edi and ECG sensor.

In other embodiment, other types of sensors may be used to capture the ECG signal of the ventilated patient 3. For example, conventional ECG surface electrodes for placement on the skin of the ventilated patient 3 may be used.

The ventilation system 1 further comprises a blood oxygen sensor 41, such as a pulse oximeter, for obtaining measurements of the oxygen content or concentration in the ventilated patient's blood. The blood oxygen sensor 41 may be attached to a body part of the patient 3, such as a fingertip, an earlobe or a foot, in order to obtain oxygenation data relating to the oxygenation of blood in the body part. The blood oxygenation data may, for instance, comprise data on peripheral oxygen saturation (SpO₂). The blood oxygenation data may be transmitted to the control computer 15 of the breathing apparatus 2 via a signalling line 43, whereby the control computer 15 may use the received blood oxygenation data in the determination of the pulmonary blood pressure of the patient 3, as further described below.

Fig. 2 illustrates a respiratory pressure curve 45, an ECG 47, an SpO₂ curve 49 and a curve 51 representing the second order time derivatives (P'') of the respiratory pressure curve 45. Only to illustrate variations in the respective quantity between different heartbeats, multiple curves obtained during different heartbeats are shown for the respective quantity.

With simultaneous reference now made to Fig. 1, the respiratory pressure curve 45, the ECG 47, the SpO₂ curve 49 and the P'' curve 51 may be derived by the control computer 15 of the breathing apparatus 2 from measurements obtained by the sensors of the ventilation system 1 during a time period including a heartbeat of the patient 3. The respiratory pressure curve 45 is an exemplary respiratory curve that may be derived by the control computer 15 based on measurements received from any of, or any combination of, the pressure sensors 37-37''. For example, the respiratory pressure curve 45 may represent an airway pressure (P_{aw}) of the patient 3. The ECG 47 may be derived by the control computer 15 based on measurements obtained by the ECG sensor 29. The SpO₂ curve may be derived by the control computer 15 based on measurements obtained by the blood oxygen sensor 41. The P'' curve 51 may be derived by the control computer from the respiratory pressure curve 45.

When the heart of the patient 3 beats, a pulse propagates through surrounding tissues to the lungs of the patient and further on into the breathing circuit of the ventilation

system 1 via gas in the lungs and the airways of the patient. This gas pulse, hereinafter referred to as the heartbeat-induced gas pulse, may be detected by studying changes in magnitude or curvature of a respiratory curve derived from sensor measurements in the breathing circuit, such as the respiratory pressure curve 45 in
5 Fig. 2.

The arrival of the heartbeat-induced gas pulse to the point of pressure measurement in the breathing circuit causes a characteristic change in the curvature of the respiratory pressure curve 45. In Fig. 2, the point in time for this characteristic
10 change in curvature of the respiratory pressure curve 45 is denoted $t_{hb(P)}$. The control computer 15 may be configured to detect this change and use it to calculate an actual point in time of the heartbeat, t_{hb} . The actual point in time of the heartbeat, t_{hb} , may be determined by the control computer 15 as the point in time $t_{hb(P)}$ at which the characteristic change in curvature of the respiratory pressure curve 45 occurs,
15 minus a known time delay. The time delay depends, for instance, on pulse propagation velocity and distance in tissue, pulse propagation velocity and distance in gas, and a measurement delay of the sensor system. In other embodiments the control computer 15 may be configured to ignore the time delay and set t_{hb} to equal $t_{hb(P)}$.

20 Furthermore, when the heart of the patient 3 beats, a flow of deoxygenated blood is pumped from the heart towards the lungs of the patient. This flow of blood constitutes a blood pressure pulse that propagates from the heart towards the lungs of the patient, via the pulmonary arteries. Upon arrival of the blood pressure pulse at
25 the lungs of the patient, the expansion of the pulmonary capillaries causes the blood pressure pulse to propagate into the gas of the alveoli. The gas pulse thus created, hereinafter referred to as the blood-pulse induced gas pulse, may also be detected by studying changes in magnitude or curvature of a respiratory curve derived from sensor measurements in the breathing circuit, such as the respiratory pressure
30 curve 45 in Fig. 2.

The arrival of the blood-pulse induced gas pulse to the point of pressure measurement in the breathing circuit causes a characteristic change in the curvature of the respiratory pressure curve 45. In Fig. 2, the point in time for this characteristic

change in curvature of the respiratory pressure curve 45 is denoted $t_{arr(P)}$. The control computer 15 may be configured to detect this change and to use it to determine a point in time of arrival of the blood pressure pulse to the lungs of the patient 3, which point in time will hereinafter be referred to as t_{arr} . In some
5 embodiments, the small time delay between the arrival of the blood pressure pulse to the lungs of the patient 3 and the detection of the blood-pulse induced gas pulse in the breathing circuit may be ignored, whereby t_{arr} can be assumed to correspond to $t_{arr(P)}$. In other embodiments, the time delay may be taken into account, whereby t_{arr} may be calculated by the control computer 15 as $t_{arr(P)}$ minus a certain time delay,
10 which time delay depends on pulse propagation velocity and distance, as well as a measurement delay of the sensor system.

When the control computer 15 has determined the point in time of the heartbeat, t_{hb} , and the point in time of arrival of the blood pressure pulse to the lungs of the patient
15 3, t_{arr} , it calculates a pulse transit time, PTT, as the time elapsed between the heartbeat and the arrival of the blood pressure pulse at the lungs of the patient. The control computer 15 may then calculate a pulse wave velocity, PWV, of the blood pressure pulse based on the PTT and an assumed distance of pulse propagation between the heart and the lungs. The assumed distance of pulse propagation may,
20 for instance, be determined by the control computer 15 based on patient data that are input to the breathing apparatus 2 by an operator, e.g. patient data relating to the height of the ventilated patient 3.

As well known in the art, the PWV of a blood pressure pulse may be expressed as a
25 function of a volumetric elastance of the blood vessel in which the pulse propagates. When the blood pressure rises, the volumetric elastance of the vessel increases, the wall of the vessel becomes hard, and the PWV increases. Therefore, once the PWV of the blood pressure pulse has been determined using the principles of the present disclosure, the control computer 15 may use the PWV to determine the pulmonary
30 blood pressure of the ventilated patient 3 using known principles of pulse propagation-based blood pressure determination. The pulmonary blood pressure is proportional to the PWV of the blood pressure pulse in the pulmonary artery. The constant of proportionality depends on the elastance of the pulmonary artery of the patient. The elastance of the pulmonary artery and hence the constant of

proportionality between the determined PWV and the pulmonary blood pressure of the patient 3 may be set by the control computer 15 based on patient data that are input to the breathing apparatus 2 by an operator, e.g. patient data relating to the age of the ventilated patient. In other embodiments, the constant of proportionality may be determined by the breathing apparatus 2 based on data obtained during a calibration procedure involving systemic blood pressure measurements, e.g. based on data resulting from conventional blood pressure cuff measurements. Such data may be obtained automatically by the breathing apparatus 2 or be manually input to the breathing apparatus 2 by an operator.

10

In an exemplary embodiment, the pulmonary blood pressure of the patient 3 may be calculated from PTT based on the relation:

$$BP_p = -\frac{2}{\alpha} \cdot \ln PTT + \frac{\ln \frac{2r\rho L^2}{hE_0}}{\alpha}, \quad (\text{Eq. 1})$$

where BP_p is the pulmonary blood pressure, α is a constant, r is the inner radius of the blood vessel (i.e. the pulmonary artery), ρ is the blood density, L is the vessel length, h is the vessel wall thickness, and E_0 is the zero-pressure elastic modulus of the vessel wall.

Equation 1 does not take variations in external pressure acting on the blood vessel into account. However, the external pressure of the pulmonary artery may vary quite significantly due to the expansion and contraction of lung tissue during respiration. The external pressure acting on the pulmonary artery is dependent on the current lung pressure of the ventilated patient 3 and, therefore, the control computer 15 may advantageously be configured to take the current lung pressure of the ventilated patient into account in the determination of the pulmonary blood pressure. Variations in external pressure on the pulmonary artery may be regarded as a change in elastance of the pulmonary artery. To account for the variations in lung pressure, the control computer 15 may therefore be configured to determine the elastance of the pulmonary artery as a function of lung pressure. Consequently, according to some embodiments, the constant zero-pressure elastic modulus E_0 in equation 1 may be exchanged for a variable and lung-pressure dependent elastance, $E(P_{lung})$, of the pulmonary artery. The lung pressure of the ventilated patient may be approximated by, or calculated from, the pressure measured by the pressure sensor 37 of the

breathing apparatus, which pressure substantially corresponds to the airway pressure of the patient 3.

To maximize the chance of detection of the heartbeat-induced gas pulse and/or the blood-pulse induced gas pulse from the respiratory curve, such as the respiratory pressure curve 45, the control computer 15 may be configured to perform the determination of the pulmonary blood pressure of the patient 3 based on a heartbeat that occurs during a low flow period of respiration, i.e. a period of low respiratory flow in the breathing circuit, and preferably during a period of substantially constant flow. Alternatively, the control computer 15 may be configured to perform the determination during a period of essentially zero flow in the breathing circuit, e.g. during an inspiratory pause, an expiratory pause or even an occlusion manoeuvre. In the following it will be assumed that determination of the pulmonary blood pressure is made based on a heartbeat that occurs during a final phase of inspiration. At the end of inspiration, the flow of respiratory gases in the breathing circuit is low and the lung pressure of the patient 2 is substantially constant, thereby facilitating detection of the heartbeat-induced gas pulse and the blood-pulse induced gas pulse from a respiratory pressure or flow curve derived by the control computer 15. To this end, the control computer 15 may be configured to analyse the respiratory curve only within an end-inspiratory time window in order to identify the point in time of the heartbeat, t_{hb} , and/or the point in time of arrival of the blood pressure pulse to the lungs of the patient, t_{arr} .

The control computer 15 may be configured to determine any one or both of the point in time of the heartbeat, t_{hb} , and the point in time of arrival of the blood pressure pulse to the lungs of the patient 3, t_{arr} , by analysing the magnitude of the respiratory curve. For example, the point in time of the heartbeat, t_{hb} , and/or the point in time of arrival of the blood pressure pulse to the lungs of the patient 3, t_{arr} , may be determined by the control computer 15 based on the crossing of the respiratory curve of one or more predetermined threshold values. However, measurement noise and natural pressure and flow fluctuations in the breathing circuit may, in this instance, cause "false triggering" and thus render detection of the pulses difficult. Therefore, to improve the robustness of the method, the control

computer 15 may be configured to analyse the curvature of the respiratory curve, instead or in addition to the magnitude thereof.

For example, the control computer 15 may be configured to study a first and/or
5 second order time derivative of the respiratory curve, and preferably a second order time derivative of the respiratory curve. As illustrated by the P'' curve 51 in Fig. 2, the characteristic changes in the respiratory pressure curve 45 caused by the arrival of the heartbeat- and blood-pulse induced gas pulses to the sensor becomes even more distinct when studying the second order derivative, thereby facilitating
10 determination of t_{hb} and t_{arr} . As discussed above, to facilitate determination of t_{hb} and/or t_{arr} , the control computer 15 may be configured to analyse the P'' curve only within an end-inspiratory time window.

In some embodiments, the control computer 15 may be configured to use blood
15 oxygenation data relating to the oxygenation of blood in a body part of the ventilated patient 3 to further facilitate determination of t_{hb} . According to one example, the control computer 15 may use the SpO2 curve 49 registered by the blood oxygen sensor 41, illustrated in Fig. 2. By analysing the obtained blood oxygenation data, the control computer 15 can determine an approximate time for the heartbeat based
20 on a change (increase) in measured blood oxygenation. By first determining an approximate time for the heartbeat, detection of the heartbeat-induced gas pulse in the respiratory curve is facilitated. The approximate time of the heartbeat may be determined by the control computer 15 based on the time of detection of the change in oxygenation (denoted t_{o2} in Fig. 2) and an estimated PTT for a systemic blood
25 pressure pulse propagating from the patient's heart to the point of blood oxygen measurement. The PTT of the systemic blood pressure pulse may be estimated based on a measured or assumed distance between the patient's heart and the point of measurement (typically estimated as $0.5 \times$ patient length for fingertip measurements), a measured or assumed systemic blood pressure of the patient,
30 and an assumed compliance of the systemic arteries of the patient. Typically, the PTT of the systemic blood pressure pulse is estimated by the control computer 15 based on body measures of the ventilated patient 3 alone. For example, the control computer 15 may be configured to estimate the PTT based on patient data that are

input to the breathing apparatus 2 by an operator, e.g. patient data relating to the height of the ventilated patient 3

The above described functionality may, for example, be implemented by having the control computer 15 determine a time window for the heartbeat, denoted $\Delta T_{hb(P)}$ in Fig. 2, within which the heartbeat-induced gas pulse can be assumed to cause a detectable change in the respiratory curve. The boundaries of the time window $\Delta T_{hb(P)}$ may be set by the control computer 15 based on an uncertainty in the determination of the approximate time of the heartbeat. The control computer 15 may then be configured to analyse the magnitude and/or curvature of the respiratory curve only within the determined time window $\Delta T_{hb(P)}$ for the heartbeat.

In other embodiments, the control computer 15 may use data other than blood oxygenation data in order to estimate an approximate time for the heartbeat. For instance, the control computer 15 may be configured to estimate a heart rate of the ventilated patient 3, and use the estimated heart rate to estimate an approximate time for the heartbeat. For example, the estimated heart rate may be used together with a determined point in time for at least one preceding heartbeat in order to calculate an approximate time for the heartbeat. The heart rate of the patient 3 may be estimated by the control computer 15 based on a plurality of previously determined points in time for a heartbeat, determined from a respiratory curve in accordance with the above described principles. Furthermore, the control computer 15 may utilize knowledge related to the ongoing respiratory treatment of the patient 3 in order to more accurately estimate an approximate time for the heartbeat. The heart rate and the timing of heartbeats of a subject are highly affected by the respiratory rate and the timing of respiration of the subject. Therefore, the control computer 15 may be configured to use sensor data indicative of the respiratory phases of the patient 3 to further improve estimation of the approximate time for the heartbeat. Such sensor data may relate to a respiratory gas pressure, a respiratory gas flow, and/or a bioelectric signal indicative of breathing efforts by the patient 3, such as an Edi signal. In accordance with the above described example, the control computer 15 may, after having estimated the approximate time for the heartbeat, define a time window for the heartbeat in which the respiratory curve is analysed in order to determine a more exact time for the heartbeat.

Furthermore, the control computer 15 may be configured to calculate an approximate time for the heartbeat retroactively based on the determined point in time, t_{arr} , of arrival of the blood pressure pulse to the lungs of the patient 3. There may be circumstances in which the heartbeat-induced gas pulse is weak and difficult to identify in the respiratory curve, whereas the blood-pulse induced gas pulse is strong enough to be detected. In such situations, the time of detection of the blood-pulse induced gas pulse may give valuable information on the approximate time of the heartbeat. Once the arrival time, t_{arr} , has been determined, the control computer 15 may calculate an approximate time of the heartbeat based on an assumed approximate PTT for propagation of the blood pressure pulse from the heart to the lungs of the patient 3. In accordance with the above described examples, the control computer 15 may then use the approximate time of the heartbeat to define a time window in which the respiratory curve is further analysed to identify the actual point in time of the heartbeat (or the point in time $t_{b(P)}$ from which the point in time t_{hb} of the actual heartbeat may be determined).

Above, it has been described how the control computer 15 may determine both the point in time of the heartbeat and the point in time of arrival of the blood pressure pulse to the lungs of the patient 3 from a respiratory curve derived from respiratory pressure and/or flow measurements in the breathing circuit. However, in scenarios where an ECG of the patient 3 is available, such as the scenario illustrated in the drawings, the control computer 15 may advantageously be configured to use the ECG signal to determine the point in time of the heartbeat, t_{hb} . For example, the control computer 15 may be configured to analyse the ECG and to determine the point in time of the heartbeat, t_{hb} , as the location of the R wave in the ECG QRS complex.

Furthermore, the steps involved in determination of the point in time of the heartbeat, t_{hb} , and the point in time of arrival of the blood pressure pulse to the lungs of the patient, t_{arr} , have been described above with reference to the respiratory pressure curve 45 in Fig. 2. It should be noted, however, that the same or similar steps may be taken in order to determine the points in time of the heartbeat and arrival of the blood pressure pulse to the lungs of the patient from a respiratory flow curve obtained from respiratory gas flow measurements. In a breathing apparatus having zero breathing

circuit resistance and ideal control of applied airway pressure, the measured pressure (also used for controlling the supply of breathing gas to the patient in a pressure controlled mode of ventilation) would typically be fixed during a main part of inspiration and a final phase of expiration, and any pressure fluctuations would be compensated for immediately. For such an ideal ventilator, during these periods of respiration, there would not be any pressure changes (and hence no detectable heartbeat or blood-pulse induced pressure changes) and changes in flow would be the only indicator of the heartbeat and the arrival of the blood pressure pulse to the lungs of the patient. For a typical breathing apparatus with non-zero patient circuit resistance and non-ideal control of applied airway pressure, however, heartbeat and blood-pulse induced pressure changes may be more easily detectable than heartbeat and blood-pulse induced flow changes. Therefore, depending on the characteristics of the breathing apparatus, it may be advantageous to use either a respiratory pressure curve or a respiratory flow curve in the determination of the points in time of the heartbeat and the arrival of the blood pressure pulse to the lungs of the patient. Of course, although not disclosed in any detail, it is possible to obtain and use both a respiratory pressure curve and a respiratory flow curve in the determination of the point in time of the heartbeat and/or the point in time of arrival of the blood pressure pulse to the lungs of the patient. For example, the control computer 15 may be configured to obtain both a respiratory pressure curve and a respiratory flow curve, and to compare the curves with each other in order to increase robustness and/or improve accuracy in the determination of the point in time of the heartbeat and/or the point in time of arrival of the blood pressure pulse to the lungs of the patient

Fig. 3 is a flowchart illustrating a method for non-invasive estimation of a pulmonary blood pressure of a mechanically ventilated subject. When describing the method, simultaneous reference will be made to the ventilation system 1 in Fig. 1 as well as the diagrams in Fig. 2.

In a first step, S31, at least one respiratory curve is obtained. The at least one respiratory curve may be a respiratory pressure curve obtained from respiratory gas pressure measurements and/or a respiratory flow curve obtained from respiratory gas flow measurements. The at least one respiratory curve is derived by the control computer 15 of the breathing apparatus 2 from pressure and/or flow measurements

obtained by the one or more pressure sensors 37-37'' and/or the one or more flow sensors 33-33''.

5 In a second step, S32, a point in time, t_{hb} , of a heartbeat of the ventilated subject is determined. The determination is made by the control computer 15 of the breathing apparatus and may be made from the at least one respiratory curve or an ECG signal captured by an ECG sensor 29 of the ventilation system 1, optionally by utilizing blood oxygenation data, as further described above.

10 In a third step, S33, an arrival point in time, t_{arr} , at which a blood flow (blood pressure pulse) caused by the heartbeat reaches the lungs of the ventilated subject is determined from the at least one respiratory curve. The determination is made by the control computer 15 of the breathing apparatus 2 and may be made by detecting a change in magnitude or curvature of the at least one respiratory curve, indicative
15 of the arrival of a blood-pulse induced gas pulse at a point of measurement of respiratory gas pressure or respiratory gas flow, as further described above.

In a fourth step, S34, a pulmonary blood pressure of the ventilated subject is estimated based on the determined point in time, t_{hb} , of the heartbeat and the
20 determined point in time, t_{arr} , of arrival of the blood pressure pulse to the lungs of the subject. The estimation may be made by the control computer 15 of the breathing apparatus 2.

Although the proposed method of non-invasive pulmonary blood pressure estimation
25 has been described above as being performed by the breathing apparatus 2 providing the mechanical ventilation to the patient 3, it should be appreciated that the method may just as well be performed by any other apparatus capable of obtaining any or both of respiratory gas pressure measurements and respiratory gas flow measurements. For example, the method may be performed by a patient
30 monitor comprising an external flow sensor for obtaining respiratory gas flow measurements during ongoing ventilatory treatment of the monitored patient. Such a flow-sensor equipped patient monitor may store the computer program described above, and be caused to perform the proposed method upon execution of the computer program by a computer of the patient monitor.

CLAIMS

1. A method for non-invasive estimation of a pulmonary blood pressure of a mechanically ventilated subject (3), comprising the steps of:
 - 5 - obtaining a respiratory pressure curve and/or a respiratory flow curve from respiratory gas pressure and/or respiratory gas flow measurements;
 - determining a point in time (t_{hb}) of a heartbeat of the ventilated subject;
 - determining an arrival point in time (t_{arr}) at which a blood flow caused by said heartbeat reaches the lungs of the subject (3), and
 - 10 - estimating a pulmonary blood pressure of the subject (3) based on the point in time (t_{hb}) of the heartbeat and said arrival point in time (t_{arr}),
wherein at least the arrival point in time (t_{arr}) is determined from the respiratory pressure curve and/or the respiratory flow curve.
- 15 2. The method of claim 1, wherein the arrival point in time (t_{arr}) is determined from a curvature of the respiratory pressure curve and/or the respiratory flow curve.
3. The method of claim 1 or 2, wherein the arrival point in time (t_{arr}) is determined based on a change in a first and/or second order derivative of the respiratory
20 pressure curve and/or the respiratory flow curve.
4. The method of any of the preceding claims, wherein also the point in time (t_{hb}) of the heartbeat is determined from the respiratory pressure curve and/or the respiratory flow curve.
- 25 5. The method of claim 4, further comprising the steps of estimating a time window for the heartbeat ($\Delta T_{hb(P)}$) based on available sensor data, and analysing the respiratory pressure curve and/or the respiratory flow curve within said time window in order to detect the point in time of the heartbeat.
- 30 6. The method of claim 5, wherein the time window ($\Delta T_{hb(P)}$) is estimated based on any of, or any combination of:
 - the points in time of a plurality of previously detected heartbeats;

- the determined arrival point in time (t_{arr}) of the blood flow to the lungs of the subject (3);
 - blood oxygenation data relating to oxygenation of blood in a body part at a known or assumable distance from the heart of the subject (3), and
 - 5 - systemic blood pressure data relating to a systemic blood pressure measured in a body part at a known or assumable distance from the heart of the subject (3).
7. The method of any of the claims 1-3, further comprising a step of obtaining an
10 electrocardiogram, ECG, of the electrical activity of the heart of the subject (3), the point in time (t_{hb}) of the heartbeat being determined using the ECG.
8. The method of claim 7, wherein the ECG is determined from signals recorded by
an oesophageal catheter (29) for measuring an electric activity of a diaphragm of
15 the subject (3).
9. The method of any of the preceding claims, wherein the pulmonary blood pressure of the subject (3) is estimated based on a pulse transit time, PTT, calculated based on a difference between the point in time (t_{hb}) of the heartbeat
20 and the arrival point in time (t_{arr}) of the blood flow to the lungs of the subject (3).
10. A computer program for non-invasive estimation of a pulmonary blood pressure of a subject (3) being mechanically ventilated by a breathing apparatus (2), the computer program comprising computer-readable code segments which, when
25 executed by a processor (23) of the breathing apparatus (2), causes the breathing apparatus to carry out the method according to any of the preceding claims.
11. An apparatus (2) for non-invasive estimation of a pulmonary blood pressure of a
30 subject (3) being mechanically ventilated by the breathing apparatus (2), comprising at least one computer (15) configured to obtain a respiratory pressure curve and/or a respiratory flow curve from respiratory gas pressure measurements and/or respiratory gas flow measurements, the computer (15) further being configured to:
- 35 - determine a point in time (t_{hb}) of a heartbeat of the ventilated subject (3);

- determine an arrival point in time (t_{arr}) at which a blood flow caused by said heartbeat reaches the lungs of the subject (3), and
 - estimate a pulmonary blood pressure of the subject (3) based on the point in time (t_{hb}) of the heartbeat and said arrival point in time (t_{arr}),
- 5 the computer (15) being configured to determine at least said arrival point in time (t_{arr}) from the respiratory pressure curve and/or the respiratory flow curve.

12. The apparatus (2) of claim 11, the computer (15) being configured to determine the arrival point in time (t_{arr}) from a curvature of the respiratory pressure curve and/or the respiratory flow curve.

10

13. The apparatus (2) of claim 11 or 12, the computer (15) being configured to determine the arrival point in time (t_{arr}) based on a change in a first and/or second order derivative of the respiratory pressure curve and/or the respiratory flow curve.

15

14. The apparatus (2) of any of the claims 11-13, the computer (15) being configured to determine also the point in time (t_{hb}) of the heartbeat from the respiratory pressure curve and/or the respiratory flow curve.

20

15. The apparatus (2) of claim 14, the computer (15) being configured to estimate a time window for the heartbeat ($\Delta T_{hb(P)}$) based on available sensor data, and to analyse the respiratory pressure curve and/or the respiratory flow curve within said time window in order to detect the point in time of the heartbeat.

25

16. The apparatus (2) of claim 15, the computer (15) being configured to estimate the time window ($\Delta T_{hb(P)}$) based on any of, or any combination of:

- the points in time of a plurality of previously detected heartbeats;
- the determined arrival point in time (t_{arr}) of the blood flow to the lungs of the subject (3), and
- blood oxygenation data relating to oxygenation of blood in a body part at a known or assumable distance from the heart of the subject (3).

30

17. The apparatus (2) of any of the claims 11-13, the computer (15) being configured to obtain an ECG of an electrical activity of the heart of the subject (3) from signals recorded by an ECG sensor (29), and to determine the point in time (t_{hb}) of the heartbeat using the obtained ECG.

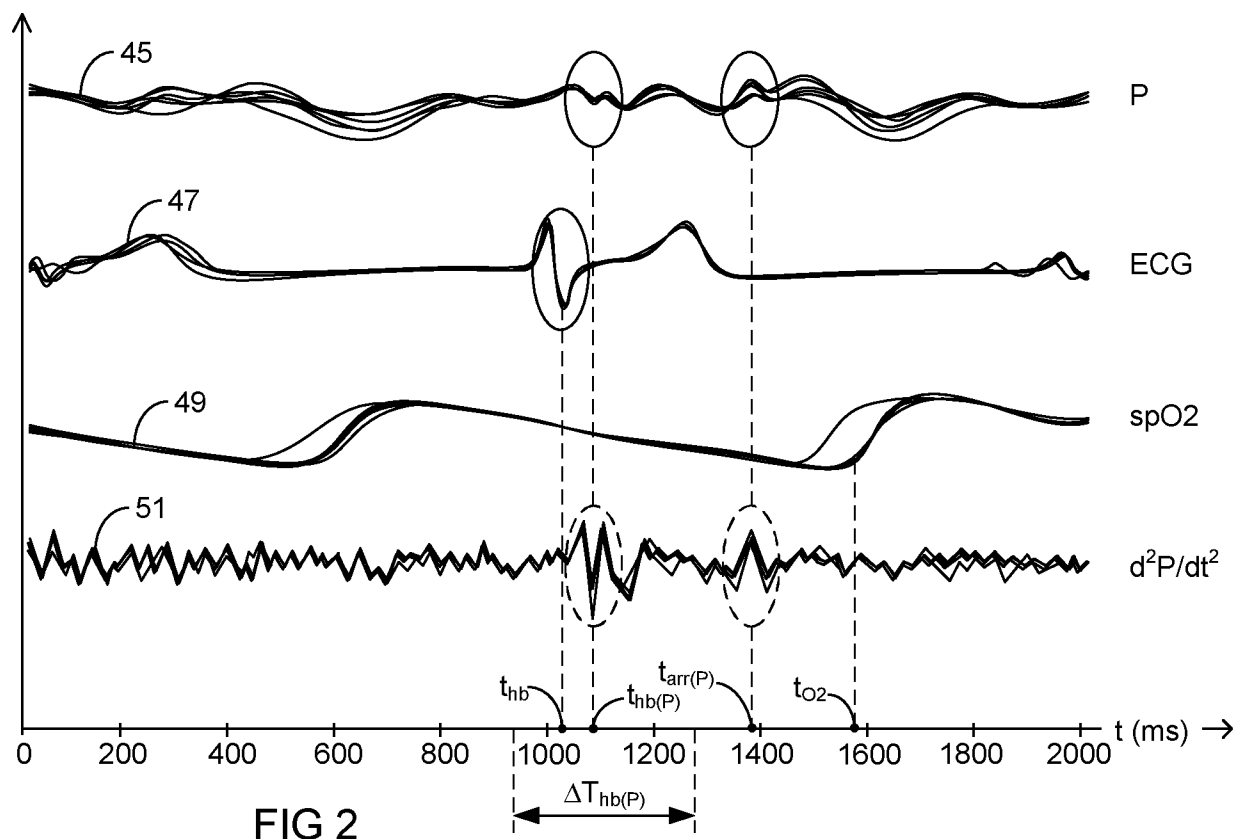
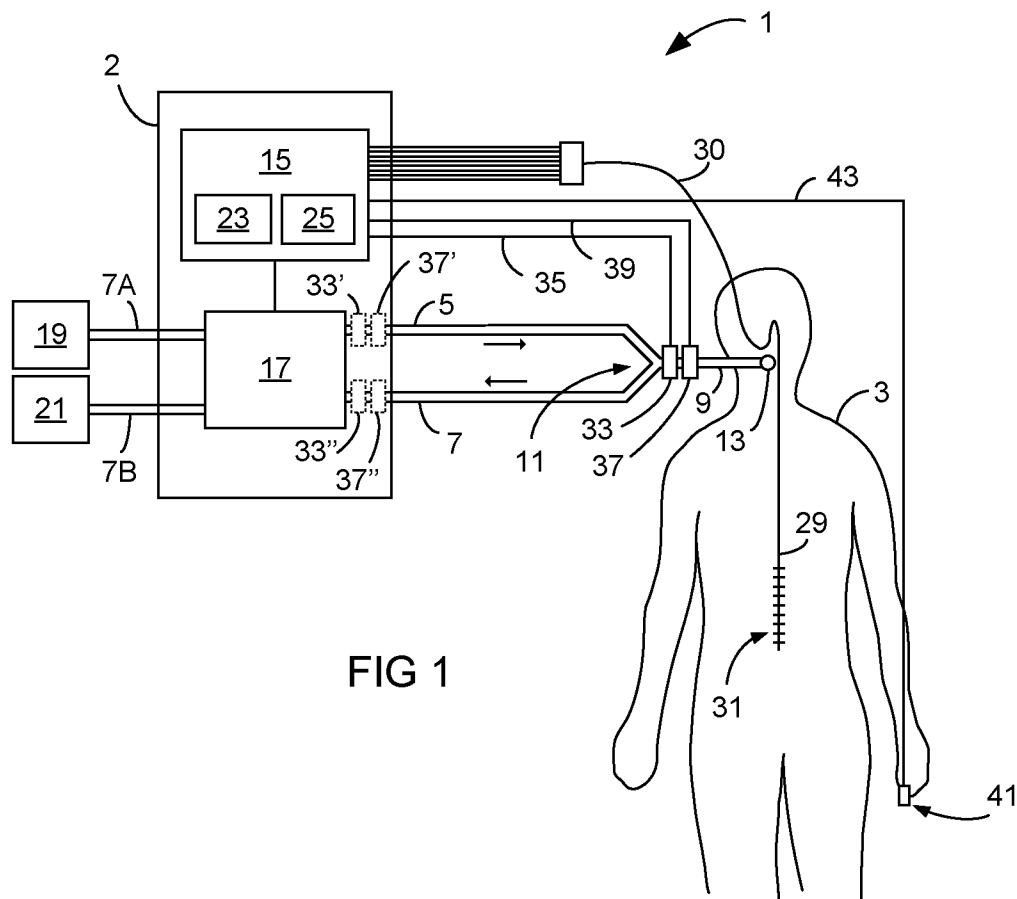
5

18. The apparatus (2) of claim 17, wherein the ECG sensor is an oesophageal catheter for recording an electric activity of a diaphragm of the subject (3), the computer (15) being configured to obtain the ECG from signals recorded by the oesophageal catheter.

10

19. The apparatus (2) of any of the claims 11-18, the computer (15) being configured to estimate the pulmonary blood pressure of the subject (3) based on a pulse transit time, PTT, calculated based on a difference between the point in time (t_{hb}) of the heartbeat and the arrival point in time (t_{arr}) of the blood flow to the lungs of the subject.

15



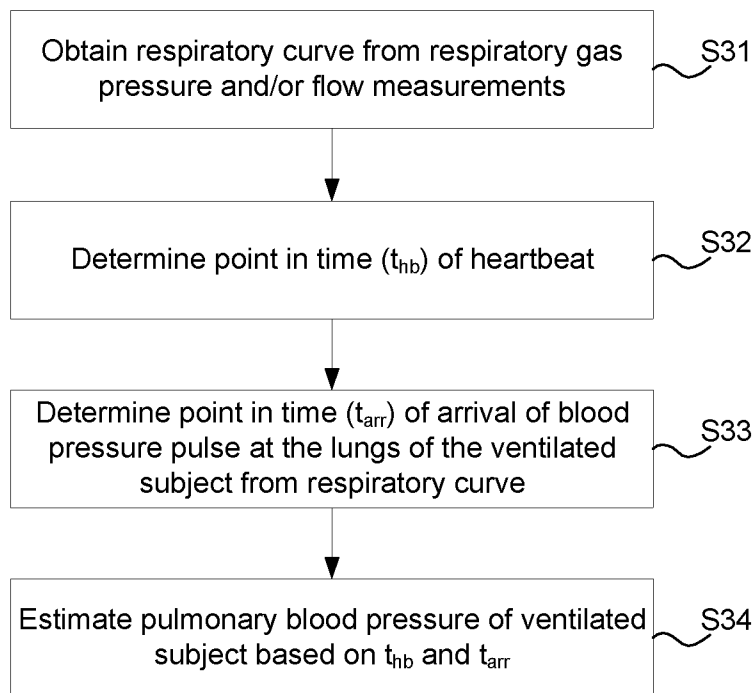


FIG 3

INTERNATIONAL SEARCH REPORT

International application No
PCT/SE2018/050748

A. CLASSIFICATION OF SUBJECT MATTER INV. A61B5/0205 A61B5/087 A61B5/02 A61B5/021 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		
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 2016/066801 A1 (KAHLERT JOACHIM [DE] ET AL) 10 March 2016 (2016-03-10) paragraphs [0011], [0014], [0017], [0028], [0031] - [0033] -----	1-19
A	US 2017/238815 A1 (LUXON EVAN S [US] ET AL) 24 August 2017 (2017-08-24) paragraphs [0007], [0008], [0010] -----	1-19
A	WO 2016/153406 A1 (MAQUET CRITICAL CARE AB [SE]) 29 September 2016 (2016-09-29) page 7, line 2 - line 16 -----	1-19
A	US 2016/345844 A1 (MCCOMBIE DEVIN [US] ET AL) 1 December 2016 (2016-12-01) paragraph [0010] -----	1-19
☐ 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 "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 12 November 2018		Date of mailing of the international search report 19/11/2018
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 Chau, Thoi Dai

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/SE2018/050748

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