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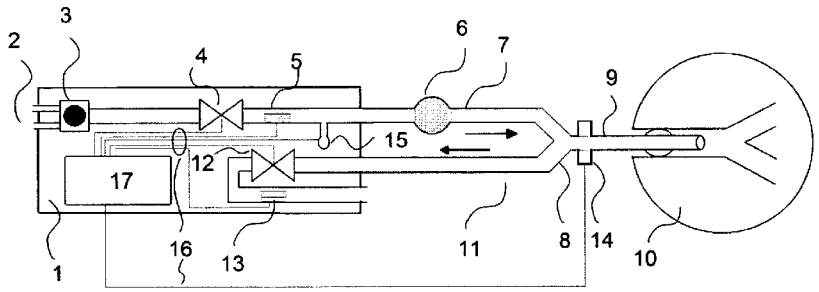
Fig. 1



(57) Abstract: The invention relates to an apparatus for monitoring of physiological parameters at mechanical ventilation. The objective is to identify beneficial and injurious effects of ventilator resetting within few breaths while the operator remains at bedside. Monitored parameters include e.g. tidal volume, airway pressures, end tidal CO_2, haemodynamics and volume of CO_2 eliminated per minute, $V_{MIN}CO_2$. Data sets of each signal before and after resetting are statistically analyzed to reduce noise and to allow accurate presentation of changes in conjunction with resetting. The quotient between $V_{MIN}CO_2$ after and before resetting is used to illustrate the effect on alveolar ventilation and thereby effects on arterial partial pressure of CO_2. The course of $V_{MIN}CO_2$ after resetting is analyzed to get an accurate value of $V_{MIN}CO_2$ after resetting. The invention can be used at different modes of ventilation because of noise reducing strategies, which are of particular importance at supported and irregular ventilation.

WO 2013/137797 A1

APPARATUS AND METHOD FOR MONITORING OF MECHANICAL VENTILATION

Description of the invention

Field of the invention

The present invention relates to an apparatus used at mechanical ventilation of man or animal, hereafter referred to as "the patient", for follow up of physiological effects of a change of ventilator setting, allowing the operator to nearly immediately evaluate effects of ventilator resetting according to the preamble of claim 1. Thereby the operator timely receives information allowing judgement of physiological effects of the new setting with regards to therapeutic and physiological goals.

Description of the Prior Art

The properties of the respiratory system comprising airways, lung parenchyma, alveoli, pulmonary blood vessels, heart and thoracic cage are complex, particularly so in disease. The operator of a ventilator, usually a physician or a respiratory therapist, frequently changes the setting of a ventilator. The purpose behind resetting is to reach desired goals of mechanical ventilation. Due to the complexity of physiology, it is in general not possible to foresee which effects a certain resetting will have on respiratory mechanics, gas exchange and circulation. Therefore, the effects need to be evaluated by measuring the physiological status before and after resetting. A particularly important parameter is arterial partial pressure of carbon dioxide, P_aCO_2, that reflects alveolar ventilation and influences arterial pH. The body contains large amounts of exchangeable carbon dioxide, CO_2. This implies that a change of alveolar ventilation leads to a slow change in P_aCO_2. It takes more than 20 minutes to reach a new steady state with regards to P_aCO_2 and arterial pH after resetting. Accordingly, an arterial sample does not properly indicate the effect on P_aCO_2 until long after resetting. During that interval other physiological events may obscure the effect of resetting. Therefore, there is a need for faster feedback to the operator than that obtained with conventional monitoring methods.

CO_2 exchange is only one phenomenon that needs to be monitored during mechanical ventilation, particularly in conjunction with ventilator resetting. High tidal volumes and high airway pressures are injurious to the lung and must be controlled to avoid ventilation induced lung injury, VILI. In the acute respiratory distress syndrome repetitive lung collapse and re-expansion of lung units, RECOREX, is a particularly injurious process that must be avoided. To get an overview of the ventilation process with respect to goals which should be reached and risks for VILI a number of parameters need to be monitored. These parameters refer to oxygen and carbon dioxide exchange, volumes and pressures associated with the ventilation process. High intrapulmonary pressures may perturb circulation. Therefore also parameters relating to circulation need to be monitored. A large variety of physiological parameters are indeed monitored with several systems on the market, but not in a comprehensive way, easy to survey with relation to goals and dangers of the ventilation process. Delays of the physiological response to resetting and noise in the recorded signals are factors which make it difficult to survey physiological effects of resetting in prior art systems.

A method that may alleviate problems to foresee effects of resetting a ventilator is computer simulation of potential effects of ventilator resetting. Such simulation is based upon a physiological profile of the respiratory system and a mathematical description of the function of a ventilator at different settings. Such a method is described in U.S. patent 6,578,575 B1. The accuracy of the prediction based upon computer simulation is limited by the non-exactness of the physiological profile and by such changes in physiology, which may be the results of the resetting. Accordingly, there is always a need to follow up effects of ventilator

resetting.

The invention

The objective of the present invention is to make possible evaluation of physiological effects following ventilator resetting within a limited number of breaths after resetting, preferably while the operator performing the resetting is present at bedside. The physiological effects in question include effects on airway pressure, for example mean airway pressure, peak airway pressure, postinspiratory plateau pressure, and positive end-expiratory pressure, PEEP. Other physiological effects are end tidal concentration of CO_2, volume of CO_2 eliminated by ventilation per minute, $V_{MIN}CO_2$, and change of P_aCO_2 and pH in blood imposed by resetting at a new steady state. Oxygen saturation in blood studied in the periphery, S_PO_2, is an important parameter. Physiological effects are measured with sensors providing signals, which are analyzed using a computer. The sensors and the computer may be integrated with the ventilator into one single apparatus. An alternative is that the sensors are the same as those of the ventilator and that a separate computer receives the signals from those sensors and performs the analysis. Signals representing circulation, such as arterial pressure, are commonly recorded by special monitoring equipment, the information from which may be entered to the system according to a preferred embodiment of the invention. Another alternative according to an embodiment of the invention is that both sensors and the computer are separate from the ventilator. This form of embodiment can be used in combination with different kinds of ventilators. Recording and analysis of signals are started before resetting is performed and continue through the resetting and during a period after resetting. Within a number of breaths, or within few minutes after resetting, the computer reports how selected physiological parameters changed allowing the operator to judge if the changes are in line with expectations and accord with the objectives behind resetting. According to a preferred embodiment of the invention the signals are analyzed with respect to noise and to trends caused by physiological phenomena related to non-instant establishment of a steady state. Thereby effects on for example $V_{MIN}CO_2$ and $PaCO_2$ caused by resetting are exposed.

Description of the drawings

Figure 1

Figure 1 illustrates an apparatus that accords with a preferred embodiment of the invention. The apparatus is only schematically depicted, since configuration options are virtually unlimited with modern technology.

A pneumatic inspiratory system of the ventilator comprises inlets for gases like air and oxygen 2, a blender for the gases 3 and a flow controller in the inspiratory line 4. In an alternative embodiment of the invention the blender 3 and the controller 4 are integrated into a single unit. The inspiratory line is equipped with a flow meter 5. Outside the ventilator or integrated into the ventilator the inspiratory line is often equipped with a humidifier 6 and continues in the form of a flexible inspiratory tube 7 that leads to the Y-piece 8. The ventilator is connected to the patient 10 with a tracheal tube 9 but can be connected by other means. Expiration occurs through a pneumatic expiratory system of the ventilator starting at the Y-piece 8 and further through a flexible expiratory tube 11, an expiratory valve 12 and an expiratory flow meter 13. The order of 12 and 13 may be the opposite. A CO_2 analyzer 14 measures fraction of CO_2 at the Y-piece. A pressure transducer 15 measures airway pressure. It can alternatively be connected to the expiratory line 11 or be duplicated in both inspiratory line and in expiratory line.

The function of the ventilator is controlled by an electronic control unit 17 that may be an analogue or digital device. In a preferred embodiment of the invention the control unit comprises at least one computer that records and analyzes the signals from flow, pressure and CO_2 transducers 5, 13, 15 and 14. This computer can also receive signals from systems for monitoring of circulation such as arterial pressure. The control unit is able to communicate with the user through a keyboard, by touch controls or by other means. Communication is also

possible from distance, e.g. from a central system in a critical care unit. All the stipulated parts can be integrated into a single apparatus or functionally distributed among different apparatuses. The latter option could mean that e.g. the function serving to control the pneumatic systems is located within the ventilator, whereas e.g. calculation and monitoring functions are physically located in another apparatus such as an external computer.

The control unit receives analogue or digital signals representing flow rate, pressure and CO_2 and sends signals to the inspiratory and expiratory valves 4 and 12 through means for electronic communication 16. The control unit may apart from components within the ventilator itself comprise components and systems outside the ventilator. The technique of today offers virtually limitless possibilities to embody the invention with respect to technical solutions of electronic components and their communication with each other by wired or wireless means. Monitoring of the ventilation process may be achieved by a system incorporated in the ventilator or by a system outside the ventilator but communicating with the control unit inside the ventilator. The control unit 17 is in a preferred embodiment of the invention equipped with a visual screen for monitoring of flow and pressure signals and for display of other information.

Figure 2

Figure 2 illustrates an alternative preferred embodiment of the invention in which the numbers 1-17 indicate the same structures as in Figure 1. The system used for monitoring according to the present invention is embodied with an apparatus that is separate from the ventilator 1. The monitoring apparatus comprises a computer 20 and transducers for CO_2 14 flow rate 18 and airway pressure 19, which through wired or wireless means of communication 21 send signals to the computer 20. According to the embodiment illustrated in Figure 2 the invention can be applied to any type of ventilator.

According to a further embodiment of the invention the computer 20 may receive signals for one or more of the parameters flow rate, airway pressure and CO_2 from transducers integrated in the ventilator thus avoiding duplication of transducer equipment. The computer 20 may also have access to other information from the ventilator 1 such as ventilator setting, respiratory rate and information about timing of partitions of the respiratory cycle through a digital or analogue, wired or wireless communication link. Likewise, the computer 20 may receive information from other sources such as those used for monitoring of circulation like arterial pressure.

Figure 3

Figure 3 illustrates a monitoring screen in conjunction with ventilator resetting in a patient with ARDS that was performed at the time 2 minutes. The upper panel A shows Respiratory rate, tidal volume, V_T, and Positive End Expiratory Pressure, PEEP. V_T is obtained by integration of the flow signal over each breath. PEEP is measured by the transducer 15 or 19. Panel B shows post inspiratory plateau pressure, P_{PLAT}, and the difference between P_{PLAT} and PEEP denoted delta-P. Ideally, delta-P should represent the true difference of the elastic recoil pressure of the respiratory system after and before inspiration. To measure these values exactly, the patient needs to be passive and airway flow rate zero at these moments. Zero flow rate can be achieved with some modern ventilators by closing the valves 4 and 12. Under circumstances this is not achievable or desirable. Then, P_{PLAT} can be determined at minimal inspiratory flow rate towards the end of inspiration. PEEP can be determined at minimal expiratory flow rate towards the end of expiration. These PEEP values can be corrected for flow and resistance dependent pressure gradients in the airways according to principles described by Jonson et al. (Bull. Physiopath. Resp. 1975, v 11, pp 729-743)

Panel C illustrates the volume of CO_2 eliminated per minute through ventilation, $V_{MIN}CO_2$. $V_{MIN}CO_2$ is calculated from the volume of CO_2 eliminated during each breath divided by the duration of the breath. $V_{MIN}CO_2$ is derived from integration of the product between flow rate and fraction of CO_2 measured at airway opening. Panel D is a recording of peripheral saturation of oxygen, S_PO_2, measured by conventional means and Panel E shows end tidal CO_2, E_TCO_2.

In the example,at the initial ventilator setting, monitoring showed that V_T, P_{PLAT} and delta-P were higher than conventionally recommended. $PaCO_2$ was also high, 62 mmHg. In order to comply with recommendations, at 2 minutes RR was increased from 25 to 33 breaths per minute, V_T was reduced from 6.9 to 5.8 ml per kg body weight and PEEP reduced from 12 to 8 cmH_2O. Immediately after resetting, pressures fell to within recommended values. The immediate increase in $V_{MIN}CO_2$ was followed by a slow decline towards initial level. S_PO_2 and E_TCO_2 fell slightly with some delay.

Figure 4

Figure 4 Panel A illustrates how different kind of noise can affect the signals, e.g. the one representing $V_{MIN}CO_2$. Such noise will negatively affect the precision in determination of the change in $V_{MIN}CO_2$ that occurs after ventilator resetting, in this example at 2 minutes. A slow drift is common in $V_{MIN}CO_2$ that may reflect changing metabolic rate due to variation in body temperature or varying inflammatory activity in the body as well as other reasons for changing homeostasis. In the example in Figure 4 there is a trend towards increasing $V_{MIN}CO_2$. A second type of noise is caused by breath by breath variation in volume of CO_2 eliminated. This variation has several causes such as measurement errors, breath by breath variation in tidal volume and varying pulmonary perfusion at heart arrhythmia.

The slow drift was in the example in Figure 4 mathematically characterized during the 2 minutes before resetting. The heavy straight line in Panel A shows this trend extrapolated to 11 minutes. After setting the trend value at 2 minutes to zero the trend was subtracted from the signal as shown in Panel B. After ventilator resetting, determination of the immediate change in $V_{MIN}CO_2$, $\Delta V_{MIN}CO_2$, is an important aspect of the invention. It is therefore important to minimize the influence of breath by breath noise on $\Delta V_{MIN}CO_2$. This must be done without applying conventional filtering of the signal over the resetting period.

Before resetting, breath by breath noise in $V_{MIN}CO_2$ is reduced by statistical analysis of values before resetting, as illustrated by the solid line during the initial 2 minutes. The value of $V_{MIN}CO_2$ before resetting is denoted $V_{MIN}CO_2$baseline. At resetting, $V_{MIN}CO_2$ will immediately increase or decrease to a new value $V_{MIN}CO_2$reset. The change will be indirectly proportional to the change in effective alveolar ventilation. During the following period of 15-30 minutes $V_{MIN}CO_2$ will slowly return towards the value that represents current metabolic CO_2 production following an exponential course. To reduce breath by breath noise in $V_{MIN}CO_2$ after resetting, $V_{MIN}CO_2$ data after resetting are used to analyze this course by statistical means as further described below and in Figure 4 shown by a heavy line representing decline towards baseline. The immediate change of $V_{MIN}CO_2$ after resetting, $\Delta V_{MIN}CO_2$, is determined from the difference between the $V_{MIN}CO_2$reset and $V_{MIN}CO_2$baseline as illustrated by interrupted vertical line in Figure 4.

Figure 5

Figure 5 shows a numerical display of the same parameters as depicted in figure 3 based on data during 2 minutes before ventilator resetting and 15 s to 2 minutes after resetting. A change is according to a preferred embodiment of the invention accompanied by information about its statistical significance. In this example significant changes ($p<0.05$) are highlighted in bold characters. SE is standard error of the estimation.

Description of preferred embodiments

The system is based upon sensors for airway flow rate, airway pressure and CO_2 as illustrated in Figure 1 and 2. Flow rate and airway pressure may be measured within the ventilator 5, 13 and 15 in Figure 1 or at the airway opening of the patient 18, 19 in Figure 2. According to preferred embodiments, CO_2 is measured at the airway opening 14. In an alternative embodiment of the invention, CO_2 is measured somewhere along the expiratory pneumatic system. Then, the small volume of CO_2 re-inspired at the start of inspiration from the Y-piece 8 and the inspiratory and expiratory lines 7 and 11 will not be measured. This limitation may be balanced by technical advantages of this alternative embodiment. For all embodiments of the invention, signals for flow rate, airway pressure and CO_2 should have an adequate frequency response and be adequately in synchrony with each other so that events during breaths representing each signal or combinations of signals can be accurately recorded and monitored. Optional transducers for S_PO_2, arterial pressure and other signals are foreseen to be incorporated in alternative preferred embodiments of the invention.

A computer that may be integrated into the ventilator 17 or be a separate computer 20 samples the signals for CO_2, airway pressure and flow at an adequate rate. These signals, together with data calculated from the signals and other information may be displayed and stored by the computer in accordance with conventional monitoring systems. Accordingly, volumes are calculated by integration of flow rate over time. Respiratory rate in breaths per minute may be derived from signals controlling the valves of the ventilator 4, 12 or from analysis of pressure and flow signals by the computer 17 or 20.

The objective of the present invention is to monitor parameters providing the most essential information with respect to goal achievement of mechanical ventilation and risks associated with mechanical ventilation and particularly how ventilator resetting affects these parameters. Figure 3 illustrates an example of combinations of such parameters. The combination of parameters may be varied for example with the nature of the disease of the patient and availability of optional transducer signals. The traced parameters are accompanied by numeric information. An example is given in Figure 5. Figure 3 Panel A shows respiratory rate, PEEP and V_T, all of which at controlled ventilation are parameters directly related to ventilator setting. Panel B shows the end expiratory plateau pressure, P_{PLAT}, that is the pressure at zero of very low flow rate at the end of an inspiration. P_{PLAT} is the commonly used parameter that indicates the degree of lung distension that when too high will cause lung damage related to hyperdistension. delta-P is the difference between P_{PLAT} and PEEP and is a recommended parameter to estimate risks for VILI. Panel C describes the elimination of CO_2 eliminated per minute, $V_{MIN}CO_2$. The value is in a preferred embodiment of the invention calculated breath by breath from the integral of the product of flow rate and CO_2 determined at airway opening with the transducers 5, 13, 14 and 18. Panels D and E show tracings of peripheral oxygen saturation and end tidal CO_2 concentration.

The primary objective of ventilation, mechanical or spontaneous, is exchange of O_2 and CO_2 so that arterial blood will acquire adequate properties with respect to these gases. For oxygen, focus is often on saturation of haemoglobin that can easily be measured in the periphery, S_PO_2. For CO_2, the arterial partial pressure of CO_2, $PaCO_2$, is the parameter of primary interest. $PaCO_2$ cannot be accurately estimated without analysis of arterial blood samples. Then, apart from blood sampling and costs, a further problem is that the change in $PaCO_2$ occurs slowly after a change of alveolar ventilation caused by ventilator resetting. This is due to large CO_2 stores in body fluids. It may take 30 minutes or more before a new steady state is reached after a change of alveolar ventilation. An alternative to $PaCO_2$ is to measure end tidal partial pressure of CO_2, E_TCO_2. E_TCO_2 is easily obtained from the transducer 14. However, in lung disease E_TCO_2 often differs greatly from $PaCO_2$. Furthermore, a change of E_TCO_2 occurs after a similar delay as $PaCO_2$ and is influenced by several physiological effects which change with time and with ventilator setting. There is no available method to directly measure or accurately estimate $PaCO_2$ at bedside in conjunction with ventilator resetting. However, a

change in $PaCO_2$ in conjunction with ventilator resetting, $\Delta PaCO_2$, can according to the invention be estimated within short after resetting as explained below.

$V_{MIN}CO_2$ averaged over so long time that body stores of CO_2 may be regarded as constant represents the rate of CO_2 production that is proportional to aerobic metabolic rate. A change of $V_{MIN}CO_2$ observed after ventilator resetting over such a short time that metabolic rate and body stores of CO_2 can be regarded as constant reflects a change of efficient alveolar ventilation, which equals total ventilation minus physiological dead space ventilation. Therefore, the determination of the change in $V_{MIN}CO_2$ occurring immediately after resetting, $\Delta V_{MIN}CO_2$, is of particular interest. In stable conditions, such as in controlled ventilation of a sedated patient, $\Delta V_{MIN}CO_2$ can often be roughly estimated from observation of the recorded signal Figure 3, Panel C. Very commonly the signal representing $V_{MIN}CO_2$ is affected by noise from many sources. Then, an accurate estimation of $\Delta V_{MIN}CO_2$ cannot be made from visual analysis of the $V_{MIN}CO_2$ signal.

Figure 4 with associated text illustrates how the influence of noise on measured $\Delta V_{MIN}CO_2$ according to a preferred embodiment of the invention is reduced to a level that under most circumstances is adequately low. $V_{MIN}CO_2$baseline is calculated from statistical analysis of values during a period preceding ventilator resetting. This analysis not only minimizes breath by breath variation but also allows determination of slow drift. Values after ventilator resetting are corrected for the slow drift characterized before resetting. $V_{MIN}CO_2$reset is according to preferred embodiments of the invention obtained by statistical analysis of data after resetting. This analysis serves to characterize the slow asymptotic return towards steady state corresponding to the metabolic production of CO_2. According to a preferred embodiment of the invention an exponential return is anticipated, but similar results may be obtained using alternative mathematical expressions.

Ventilator resetting does not always occur at a specific moment, e.g. when more than one parameter is changed as in the example behind Figure 3. Furthermore, a feature of some ventilators is that ventilator setting is not immediately executed at the moment of resetting but implemented over some breaths. Accordingly, the first breaths following the initiation of resetting must pass before data defining the course of $V_{MIN}CO_2$ after resetting is characterized. 5 breaths or 15 s after the last resetting is according to a preferred embodiment of the invention the default for delay of analysis, which by the operator can be prolonged but preferably not to more than about 30 s after last resetting. If longer, the accuracy may decline because of changing CO_2 stores in body fluids and because data which could lessen the influence of noise are lost. When the course of $V_{MIN}CO_2$ after resetting has been characterized, the equation is extrapolated backwards to the time of resetting to obtain $V_{MIN}CO_2$reset representing the time of resetting and to calculate $\Delta V_{MIN}CO_2$ as the difference between $V_{MIN}CO_2$reset and $V_{MIN}CO_2$baseline. $\Delta V_{MIN}CO_2$ denotes the change of CO_2 elimination at the time of ventilator resetting.

The accuracy of $\Delta V_{MIN}CO_2$ is reduced by noise of the $V_{MIN}CO_2$ signal. The level of noise is according to a preferred embodiment of the invention statistically analyzed. Thereby the influence of noise on the determination of $\Delta V_{MIN}CO_2$ can be estimated by applying ordinary statistical methods. The fraction $\Delta V_{MIN}CO_2$reset/$V_{MIN}CO_2$baseline shows to what extent alveolar ventilation changed in conjunction with ventilator resetting and can be expressed in percent, $\Delta V_{MIN}CO_2$%. In the example given in Figure 4, data sets for $V_{MIN}CO_2$ 2 minutes before and 15 s to 2 minutes after resetting were analyzed. Two minutes may be a suitable default value for those periods. In the presence of heavy noise in the tracing of $V_{MIN}CO_2$ longer periods may be automatically or manually instituted in order to increase the accuracy of $\Delta V_{MIN}CO_2$ determination. At controlled ventilation respiratory rate is usually constant. Then, values of eliminated volumes of CO_2 per breath may be used instead of values for $V_{MIN}CO_2$ for calculation of the change of CO_2 elimination in conjunction with ventilator resetting.

$PaCO_2$ is proportional to metabolic CO_2 production and indirectly proportional to efficient alveolar ventilation. As a consequence, the change of $PaCO_2$ that will follow resetting after equilibration of body fluid stores of CO_2 is according to a preferred embodiment of the

invention estimated from $\Delta V_{MIN}CO_2\%$. In the example in Figure 4, $\Delta V_{MIN}CO_2\%$ was +7% with an estimated range between +6 and +8%. The values for range were estimated using ordinary statistical methods as the 95% confidence interval. This interval serves as default according to a preferred embodiment of the invention. Accordingly, the expected relative change of $PaCO_2$ after equilibration was -7%, range -8 to -6%. An alternative to range is to report standard error of the estimated change of $PaCO_2$ as illustrated in Figure 5. If information of the $PaCO_2$ value before resetting is available in the system, the estimated $PaCO_2$ value after resetting will according to a preferred embodiment of the invention be presented to the operator. If the computer 17 or 20 also has access to present pH value and the acid base status for example expressed as Base excess, the computer can also calculate the expected change in pH by using standard well known equations. The following serves as an example:

Present $PaCO_2$ 8.3 kPa. Estimated $PaCO_2$ after resetting 7.7 kPa (range 7.6-7.8).

Present pH 7.28. Estimated pH after resetting 7.32

It is worth noting that few studies have been published about relationships between observed change of $V_{MIN}CO_2$ and change of PaO_2 in various patient populations. Secondary feedback reactions in the body may under some circumstances lead to complementary mechanisms which to marginal extent may offset the calculation of $PaCO_2$ after ventilator resetting. It is therefore expected that refined algorithms used to predict a change of $PaCO_2$ and pH on the basis of $\Delta V_{MIN}CO_2$ will be developed for different patient populations.

In Figure 3 and 4 each data point represent a single breath. This is at controlled ventilation a preferred embodiment of the invention. At very irregular breathing $V_{MIN}CO_2$ and other parameters like tidal volume may vary much between breaths. An alternative embodiment of the invention is to measure parameters over longer periods of time rather than per breath.

Determination of volumes of e.g. CO_2 on the basis of gas flow rate and fraction of CO_2 are affected by conditions at which flow rate and CO_2 are measured. Conditions may vary before and after ventilator resetting, particularly with respect to pressure. According to a preferred embodiment of the invention, corrections are made to standardized conditions, for example BTPS (body temperature, atmospheric pressure and saturated with water vapour) or STPD (standard temperature and pressure, saturated). Which standard is chosen does not matter with respect to the present invention. Corrections to a standard is performed according to well known physics utilising information from the airway pressure transducer 15,19. The signal from the CO_2 transducer may be slightly affected by the oxygen concentration in respired air. When oxygen concentration is changed in association with ventilator resetting, the accuracy of $\Delta V_{MIN}CO_2$ determination is according to a preferred embodiment of the invention increased by correction of the CO_2 signal for variation in oxygen concentration. A signal for oxygen concentration in respired air is available in current advanced ventilators.

The analysis of other physiological parameters than $V_{MIN}CO_2$ before and after resetting is made by statistical analysis of data sets for each signal sampled before and after resetting. For most parameters, a steady state is to be expected already within a few breaths after resetting. Accordingly, the level of a particular physiological parameter after resetting is determined on the basis of data during a period that according to default setting starts 5 breaths or 15 s after the last resetting and ends 2 minutes later, as for the analysis of $V_{MIN}CO_2$. During that period the mean value, range or standard error of the parameter in question is reported. For parameters which attain a steady state after a few breaths, analysis of trends before and after resetting is in contrast to $\Delta V_{MIN}CO_2$ not necessary. As ventilator resetting does not occur at an exactly defined moment a change due to ventilator resetting is referred to as a "change in conjunction with ventilator resetting".

End tidal CO_2, E_TCO_2, has its own particular behaviour after ventilator resetting. As a first approximation it will fall at a rate and to a degree similar to that of $PaCO_2$, following an exponential course. However, E_TCO_2 is affected by more physiological factors than $PaCO_2$. When for example the respiratory rate is increased and tidal volume decreased, the difference

between E_TCO_2 and $PaCO_2$ will under most circumstances increase. E_TCO_2 is also affected by the cardiac output and intrapulmonary shunt fraction, which are often affected after ventilator resetting. As variation of E_TCO_2 is complexly affected by both slow and fast phenomena it is in general not useful to predict its upcoming steady state value after ventilator resetting but rather to trace its variation with time as in Figure 3. In spite of the complexity of E_TCO_2 changes it is of value to display this parameter. E_TCO_2 may suddenly fall at an important suppression of pulmonary perfusion that may happen after unsuitable ventilator resetting. At such an event, also $V_{MIN}CO_2$ falls suddenly. A sudden fall of both E_TCO_2 and $V_{MIN}CO_2$ warns against suppressed circulation.

Examples given in Figure 3 and Figure 4 refer to controlled ventilation in a sedated patient. Under such circumstances noise in the signals is in general low. The signal for Respiratory rate and Tidal volume are virtually free from noise. The invention can be applied for other modes of ventilation, for example different types of supported ventilation. Then, the variability of parameters leading to noise in the observations is often much more important. The observation periods over which calculations are performed should then be adapted to the noise level. When the noise becomes so high that values of $\Delta V_{MIN}CO_2\%$ cannot be statistically determined, the prediction of change in $PaCO_2$ is according to a preferred embodiment of the invention suppressed.

Apart from a graphical presentation such as that in Figure 3, data before and after ventilator resetting are presented in a numerical format. Figure 5 shows an example based upon the data in Figure 3. According to a preferred embodiment of the invention, the parameters displayed graphically and numerically can be selected in a set up procedure of systems like those in Figure 1 and 2. This option includes parameters not shown in Figure 3. Examples are mean airway pressure and total PEEP. Total PEEP is the pressure in alveoli at the end of expiration that can be measured during a post-expiratory pause or estimated according to principles described by Jonson et al. (Bull. Physiopath. Resp. 1975, v 11, pp 729-743). According to a preferred embodiment of the invention, signals from haemodynamic monitoring systems and meters for S_PO_2 are transmitted to the computer 17, 20. Such parameters are monitored and analyzed in analogy with parameters from inherent transducers.

Both graphically and numerically presented information are according to a preferred embodiment of the invention stored and may be retrieved for documentation of treatment and for research.

Claims

1. A monitoring apparatus for mechanical ventilation comprising transducers for measurement of at least airway flow rate (5, 13, 18) and CO_2 (14) and a computer (17, 20) that monitors physiological parameters derived from the transducers such as CO_2 elimination per unit time calculated by integration of the product between flow rate and CO_2 concentration in expired air, **characterized in that** the relative change of arterial partial pressure of CO_2, which after ventilator resetting will occur during establishment of steady state, is estimated on the basis of the relationship between measured value of CO_2 elimination and the change of CO_2 elimination measured at the time of ventilator resetting.

2. A monitoring apparatus according to claim 1 **characterized in that** the relative change of arterial partial pressure of CO_2, which after ventilator resetting will occur during establishment of steady state, is estimated on the basis of the quotient between the change of CO_2 elimination measured at the time of ventilator resetting and a measured value of CO_2 elimination.

3. A monitoring apparatus according to claim 1 or 2 **characterized in that** the value of arterial PCO_2, which ventilator resetting will lead to after establishment of steady state, is estimated on the basis of the relationship between the change of CO_2 elimination measured at the time of ventilator resetting and measured value of CO_2 elimination compiled with a value of arterial PCO_2.

4. A monitoring apparatus according to claim 3, **characterized in that** arterial PCO_2 combined with other acid/base data measured before resetting are compiled with estimated value of arterial PCO_2 following the resetting for calculation of arterial pH after establishment of steady state.

5. A monitoring apparatus according to any of claim 1-4, **characterized in that** the change in CO_2 elimination per unit time occurring at ventilator resetting is calculated by statistical analysis of separate data volumes of CO_2 elimination observed before and after the resetting.

6. A monitoring apparatus according to claim 4, **characterized in that** the change in CO_2 elimination per unit time occurring at ventilator resetting is based upon an equation describing a slow trend of changing CO_2 elimination per unit time statistically characterised from data measured before ventilator resetting.

7. A monitoring apparatus according to claim 4, **characterized in that** the change in CO_2 elimination per unit time occurring at ventilator resetting is based upon an equation describing a course towards a value that represents steady state, which course is statistically characterised from data measured after ventilator resetting.

8. A monitoring apparatus according to claim 1, **characterized in** a transducer for measurement of airway pressure (15, 19) and in that changes of parameters related to lung mechanics such as postinspiratory plateau pressure and end-expiratory pressure are calculated by statistical analysis of separate data volumes of each parameter before and after the resetting.

9. A monitoring apparatus according to any of claim 1 to 7, **characterized in** complementary monitoring equipment transmitting signals to the computer (17, 20), which signals in conjunction with ventilator resetting are monitored on the basis of statistical analysis of separate data volumes of each parameter before and after the resetting, in analogy with parameters from transducers incorporated in the apparatus.

10. A method for monitoring of mechanical ventilation based on measurement of at least airway flow rate (5, 13, 18) and CO_2 (14) and a computer (17, 20) that monitors physiological parameters derived from the transducers such as CO_2 elimination per unit time calculated by integration of the product between flow rate and CO_2 concentration in expired air, **characterized in that** the relative change of arterial partial pressure of CO_2, which after ventilator resetting will occur during establishment of steady state, is estimated on the basis of the relationship between measured value of CO_2 elimination and the change of CO_2 elimination measured at the time of ventilator resetting.

11. A method for monitoring of mechanical ventilation according to claim 10 **characterized in that** the relative change of arterial partial pressure of CO_2, which after ventilator resetting will occur during establishment of steady state, is estimated on the basis of the quotient between the change of CO_2 elimination measured at the time of ventilator resetting and a measured value of CO_2 elimination.

12. A method for monitoring of mechanical ventilation according to claim 10 or 11 **characterized in that** the value of arterial PCO_2, which ventilator resetting will lead to after establishment of steady state, is estimated on the basis of the relationship between the change of CO_2 elimination measured at the time of ventilator resetting and measured value of CO_2 elimination compiled with a value of arterial PCO_2.

13. A method for monitoring of mechanical ventilation according to claim 12, **characterized in that** arterial PCO_2 combined with other acid/base data measured before resetting are compiled with estimated value of arterial PCO_2 following the resetting for calculation of arterial pH after establishment of steady state.

14. A method for monitoring of mechanical ventilation according to any of claim 10-13, **characterized in that** the change in CO_2 elimination per unit time occurring at ventilator resetting is calculated by statistical analysis of separate data volumes of CO_2 elimination observed before and after the resetting.

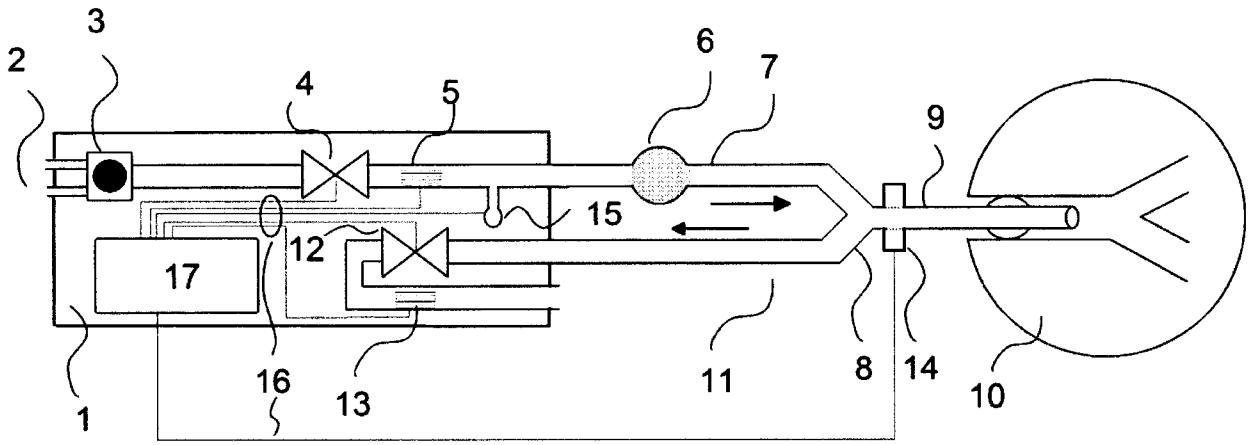
15. A method for monitoring of mechanical ventilation according to claim 14, **characterized in that** the change in CO_2 elimination per unit time occurring at ventilator resetting is based upon an equation describing a slow trend of changing CO_2 elimination per unit time statistically characterised from data measured before ventilator resetting.

16. A method for monitoring of mechanical ventilation according to claim 14, **characterized in that** the change in CO_2 elimination per unit time occurring at ventilator resetting is based upon an equation describing a course towards a value that represents steady state, which course is statistically characterised from data measured after ventilator resetting.

17. A method for monitoring of mechanical ventilation according to claim 10, **characterized in** a transducer for measurement of airway pressure (15, 19) and in that changes of parameters related to lung mechanics such as postinspiratory plateau pressure and end-expiratory pressure are calculated by statistical analysis of separate data volumes of each parameter before and after the resetting.

18. A method for monitoring of mechanical ventilation according to any of claim 10 to 17, **characterized in** complementary monitoring equipment transmitting signals to the computer (17, 20), which signals in conjunction with ventilator resetting are monitored on the basis of statistical analysis of separate data volumes of each parameter before and after the resetting, in analogy with parameters from transducers incorporated in the apparatus.

Fig. 1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4
5
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9
15
12
17
16
13
11
8
14
10
1

Fig. 2

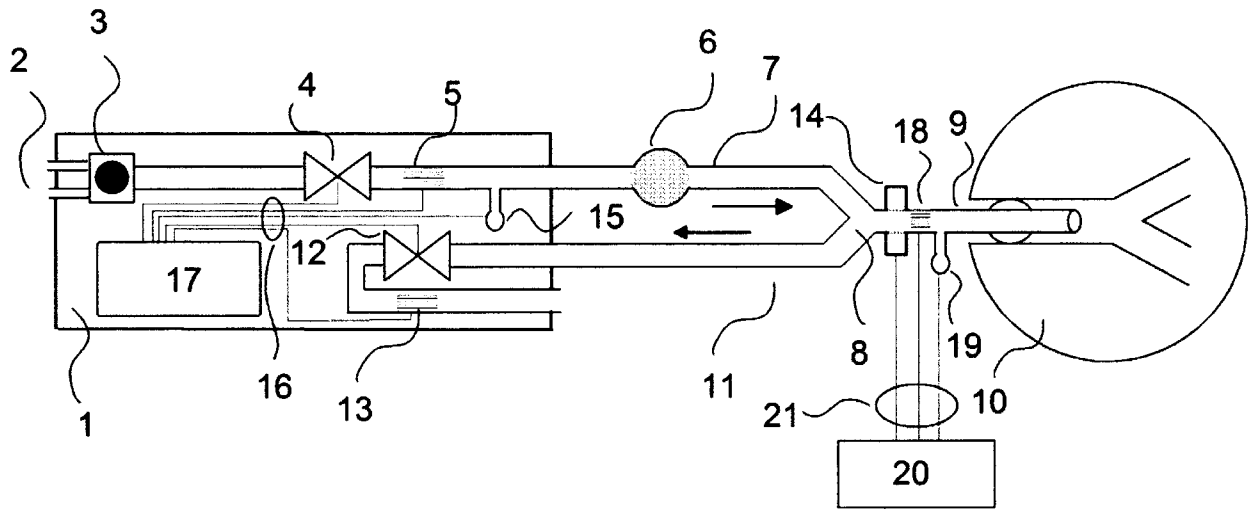
3
2
4
5
6
7
14
18
9
15
12
17
16
13
11
8
19
10
21
20
1

Fig. 3

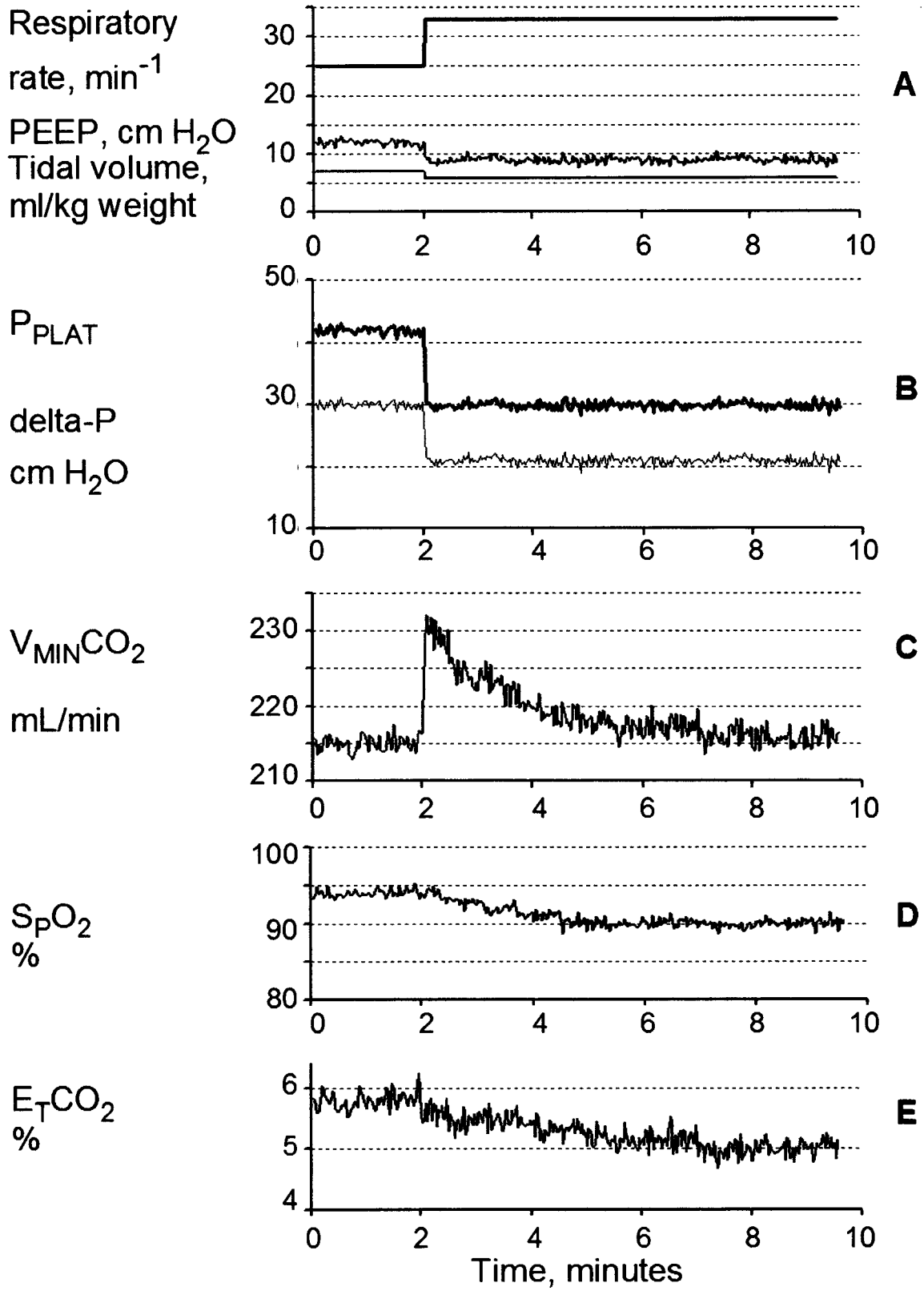
Respiratory rate, min-1
PEEP, cm H2O
Tidal volume, ml/kg weight
30
20
10
0
0 2 4 6 8 10
A
PPLAT
delta-P
cm H2O
50
30
10
0 2 4 6 8 10
B
VMINCO2
mL/min
230
220
210
0 2 4 6 8 10
C
SPO2
%
100
90
80
0 2 4 6 8 10
D
ETCO2
%
6
5
4
0 2 4 6 8 10
E
Time, minutes

Fig. 4

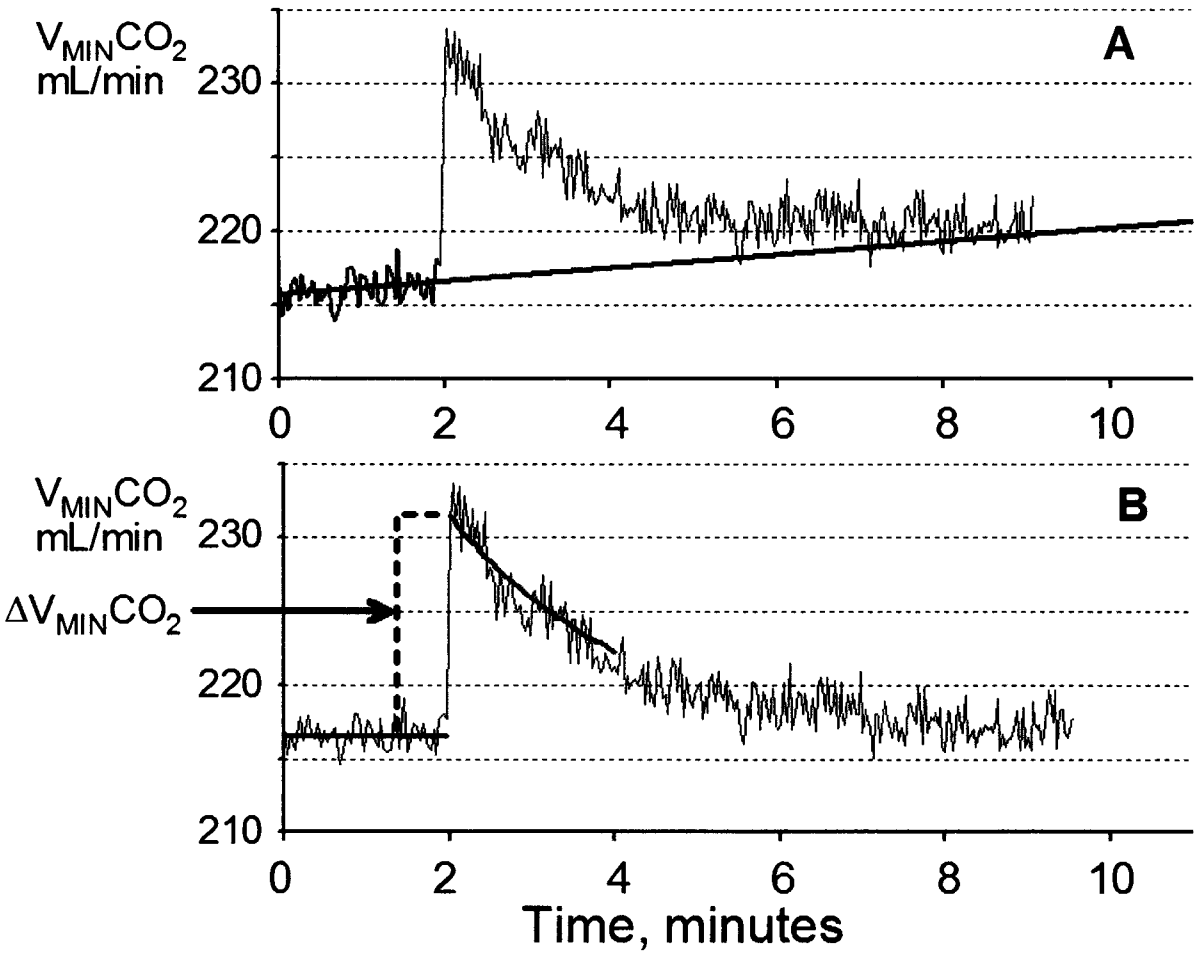
$V_{MIN}CO_2$ mL/min
230
220
210
0
2
4
6
8
10
A
$V_{MIN}CO_2$ mL/min
$\Delta V_{MIN}CO_2$
230
220
210
0
2
4
6
8
10
B
Time, minutes

Fig. 5

	Before ventilator resetting	After ventilator resetting	Change at ventilator resetting	SE of change
Respiratory rate breaths/minute	25	33	**8**	0.0
Tidal volume ml/kg body weight	6.9	5.8	**-1.2**	0.1
PEEP cmH_2O	12	9.1	**-2.9**	0.0
P_{PLAT} cmH_2O	42	30	**-12**	0.4
delta-P cmH_2O	30	21	**-9.1**	0.4
E_TCO_2 %	5.7	5.5	**-0.2**	0.07
S_PO_2 %	94	92.4	-1.5	1.1
$V_{MIN}CO_2$ mL/min	217	232	**15**	0.2
$\Delta PaCO_2$ %			**-7**	0.05
$PaCO_2$ kPa	8.3	7.7	**0.6**	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2013/000035

A. CLASSIFICATION OF SUBJECT MATTER

IPC: see extra sheet

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)

IPC: A61B, A61M

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

SE, DK, FI, NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, PAJ, WPI data, BIOSIS, COMPENDEX, EMBASE, INSPEC, MEDLINE, IBM-TDB

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 20080230065 A1 (HEINONEN ERKKI PAAVO), 25 September 2008 (2008-09-25); paragraphs [0001], [0019]-[0020], [0024], [0047], [0054]-[0055], [0057], [0061], [0063], [0074]	1-18
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X	US 6578575 B1 (JONSON BJOERN), 17 June 2003 (2003-06-17); column 1, line 46 - column 4, line 26; column 7, line 1 - column 10, line 7	1-18
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X	Taskar et al: "Dynamics of carbon dioxide elimination following ventilator resetting", Chest, US, 1995-07, vol.108, nr.1, pg.196-202; whole document	1-18
	--	

☒ 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	Date of mailing of the international search report
31-07-2013	01-08-2013
Name and mailing address of the ISA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. + 46 8 666 02 86	Authorized officer Gordana Ninkovic Telephone No. + 46 8 782 25 00

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2013/000035

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

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

1. ☒ Claims Nos.: 10-18
because they relate to subject matter not required to be searched by this Authority, namely:

Claims 10-18 relate to a method for treatment of the human or animal body by surgery or by therapy, as well as diagnostic methods, see PCT rule 39.1(iv). Nevertheless, a search has been made for these claims. The search has been directed to the technical content of the claims.

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

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

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

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

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

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

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

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

Remark on Protest

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

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

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2013/000035

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Uttman et al: "Computer-aided ventilator resetting is feasible on the basis of a physiological profile", Acta anaesthesiologica Scandinavica, Denmark, 2002-03, vol.46, nr.3, pg.289-296; whole document --	1-18
A	Uttman et al: "Computer simulation allows goal-oriented mechanical ventilation in acute respiratory distress syndrome", Critical care, UK, 2007, vol.11, nr.2, pg.R36; whole document --	1-18
A	Uttman et al: "A prolonged postinspiratory pause enhances CO2 elimination by reducing airway dead space", Clinical physiology and functional imaging, UK, 2003-09, vol.23, nr.5, pg.252-256; whole document --	1-18
A	Devaquet et al: "Effects of inspiratory pause on CO2 elimination and arterial PCO2 in acute lung injury", Journal of applied physiology, US, 2008-12, vol.105, nr.6, pg.1944-1949; whole document --	1-18
A	Uttman et al: "Effects of positive end-expiratory pressure increments can be predicted by computer simulation based on a physiological profile in acute respiratory failure", Intensive Care Medicine, DE, 2003-02, vol.29, nr.2, pg.226-232; whole document --	1-18
A	US 5931160 A1 (GILMORE DON ET AL), 3 August 1999 (1999-08-03); abstract --	1-18
A	US 20100037895 A1 (BERTHON-JONES MICHAEL ET AL), 18 February 2010 (2010-02-18); paragraphs [0029]-[0031], [0041]-[0042] --	1-18
A	US 20090107498 A1 (PLATTNER DIANA ET AL), 30 April 2009 (2009-04-30); abstract --	1-18
A	US 20110213215 A1 (DOYLE PETER ET AL), 1 September 2011 (2011-09-01); paragraphs [0031]-[0037]; claims 14-18 --	1-18

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2013/000035

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 20110277765 A1 (CHRISTOPHER KENT L ET AL), 17 November 2011 (2011-11-17); abstract --	1-18
A	US 20040003813 A1 (BANNER MICHAEL J ET AL), 8 January 2004 (2004-01-08); paragraphs [0046]-[0050] --	1-18
A	US 20100275920 A1 (THAM ROBERT ET AL), 4 November 2010 (2010-11-04); abstract; paragraph [0033] -- --------	1-18

International application No.
PCT/SE2013/000035

Continuation of: second sheet

International Patent Classification (IPC)

A61M 16/00 (2006.01)
A61B 5/08 (2006.01)

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				US	8020558	B2 20/09/2011
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