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(54) Title: SYSTEM AND PROCESS FOR DETERMINING A POSITIVE END-EXPIRATORY PRESSURE FOR A MECHANICAL VENTILATION SYSTEM

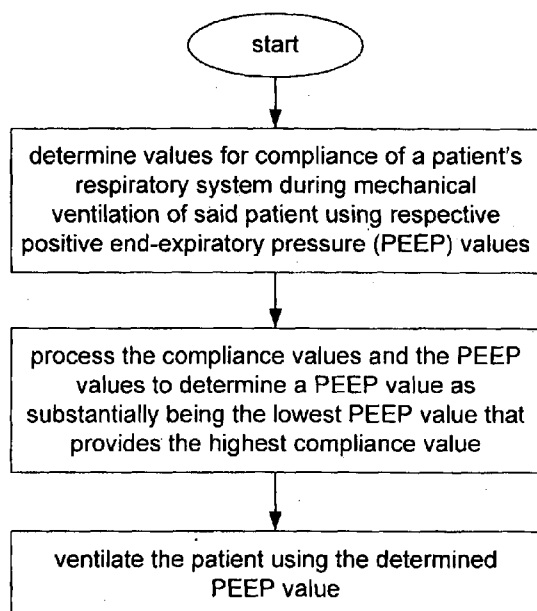


Figure 1

(57) Abstract: A process for determining a positive end-expiratory pressure for a mechanical ventilation system, including: determining values for compliance of a patient's respiratory system during mechanical ventilation of the patient using respective positive end-expiratory pressure (PEEP) values; and processing the compliance values and the PEEP values to determine a PEEP value as substantially being a lowest PEEP value that provides a highest compliance value.



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**SYSTEM AND PROCESS FOR DETERMINING
A POSITIVE END-EXPIRATORY PRESSURE
FOR A MECHANICAL VENTILATION SYSTEM**

TECHNICAL FIELD

- 5 The present invention relates to a system and process for determining a positive end-expiratory pressure for a mechanical ventilation system and use of the mechanical ventilation system in therapeutic protocols.

BACKGROUND

- Many patients who are admitted to intensive care units require some form of ventilatory
10 (breathing) assistance via a mechanical ventilator, either to support and treat a diseased lung, or to assist ventilation whilst the patient recovers from another problem. Mechanical ventilators provide ventilatory support via positive pressure, which means that these machines move the lungs by blowing gas into the lungs under pressure. The amount of pressure applied to the lung is directly proportional to the resultant volume of gas in the
15 lung. The clinician needs to set the ventilator to deliver the correct pressure to inflate the lung during each 'breath' (positive inspiratory pressure, or PIP), and also to deliver the correct pressure between inflations to prevent the lung totally collapsing or being too distended (positive end-expiratory pressure, or PEEP).

- 20 When done properly, mechanical ventilation is life saving and safe, but when applied poorly the lung is at risk of injury from either inadequate or excessive applied pressure for both PIP and PEEP.

- Modern ventilators are now very complex devices with internal central processing units
25 able to perform and apply intricate mathematical algorithms. Nearly all modern ventilators have in built safety modes that try to avoid the inadvertent delivery of excessive PIP. Each manufacturer has a different proprietary name for these modes, but all are based on a volume-targeted algorithm whereby the clinician sets the amount of gas (volume) that is believed to be needed to adequately inflate the lung (referred to as the tidal volume), and

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the ventilator applies an algorithm to determine what PIP will achieve this. Modern ventilators can do this as they are able to measure the volume of gas that goes into and out of the lung. The resultant tidal volume is dependent on the PIP and PEEP the ventilator applies to the lung and the compliance of the patient's respiratory system (C_{rs}).
5 Compliance is a mechanical term that refers to the ability of the patient's lungs and chest wall to move when a pressure is applied. A very sick lung has a low C_{rs} and a normal lung a relatively high C_{rs} , explaining why patients with severe lung disease require higher pressures during mechanical ventilation. Volume targeted modalities are now commonly used during mechanical ventilation in an ICU, especially in the treatment of lung disease in
10 the preterm infant, whose lungs are especially vulnerable to injury from inappropriate pressures.

Current volume targeted modalities simply focus on the PIP, and ignore the importance of optimising the PEEP during mechanical ventilation, yet there is now evidence in all age
15 groups that inappropriate PEEP results in greater lung injury and mortality. The problem has been how to determine the optimal PEEP. Although methods to determine the optimal PEEP exist, most of them use oxygenation as a measure of lung volume or other techniques that claim to measure end expiratory lung volume (for example, gas wash-out techniques). Thus, the clinician determines the PEEP that results in the best oxygen levels
20 for that patient at that time during a procedure that is referred to as a 'lung volume optimisation' manoeuvre or LVO manoeuvre. During an LVO manoeuvre, the clinician applies a series of step-wise increases in PEEP to determine the PEEP that recruits lung volume (increases lung volume) and/or overdistension of the lung (defined as a reduction in oxygenation). Then the PEEP is reduced in a step-wise manner until lung collapse
25 (inadequate pressure and volume) occur, again defined by a fall in oxygen. The optimal PEEP is then defined as the lowest PEEP that maintained the best oxygenation during the LVO manoeuvre.

The inventors have identified a fundamental problem with an oxygen-based approach to
30 LVO, namely that oxygen levels in the blood are affected by many parameters and organs, including the heart and the pulmonary blood vessels. Thus, the response seen by the

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clinician may not accurately reflect lung volume at any given PEEP. Additionally, only one commercially available ventilator has an in-built system to monitor oxygen levels and, thus, is able to apply a closed loop feedback system to the ventilator. This means that LVO manoeuvres cannot be readily automated in most cases, yet an automated LVO technique
5 would be quicker and more attractive to clinicians.

It is desired to provide a process for determining a positive end-expiratory pressure for a mechanical ventilation system, a mechanical ventilation system, and a method of treating a subject with a pathological lung disease or who is at risk of developing same that alleviate
10 one or more difficulties of the prior art, or that at least provide a useful alternative.

SUMMARY

Some embodiments of the present invention provide a process for determining a positive end-expiratory pressure for a mechanical ventilation system, including:

15 determining values for compliance of a patient's respiratory system during mechanical ventilation of said patient using respective positive end-expiratory pressure (PEEP) values; and
processing the compliance values and the PEEP values to determine a PEEP value as substantially being a lowest PEEP value that provides a highest compliance value.

20

In some embodiments, the quasi-optimal PEEP value is determined by selecting from the PEEP values the lowest PEEP value whose corresponding compliance value is substantially equal to the highest compliance value of the determined compliance values. In other embodiments, the PEEP value can be determined from the PEEP values and their
25 associated respective compliance values, but need not be equal to one of those PEEP values.

In some embodiments, the step of determining includes:

30 applying mechanical ventilation to lungs of said patient in a volume targeted mode to inflate said lungs by delivering a predetermined tidal volume of gas to said lungs

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adequate for CO₂ removal, and to deflate said lungs to a positive end-expiratory pressure (PEEP) value;

determining a value for compliance of the patient's respiratory system during said mechanical ventilation and corresponding to the PEEP value;

5 repeatedly increasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the patient's respiratory system for each increased PEEP value until the compliance of the patient's respiratory system has not increased for at least two consecutive PEEP increment steps, thereby providing a maximum PEEP value and a corresponding maximum compliance
10 value; and

repeatedly decreasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the patient's respiratory system for each decreased PEEP value until the compliance of the patient's respiratory system has decreased over at least two consecutive PEEP decrement steps.

15

It will be apparent those skilled in the art that the conditions of the process that the compliance of the patient's respiratory system (i) has not increased and (ii) has decreased need to be understood as being subject to the accuracy of the determined compliance values. In general, these are determined in modern ventilators based on gas flow sensors
20 whose relative accuracy is typically about $\pm 6\%$, and consequently any comparison of the determined compliance values need to be evaluated within these constraints. Accordingly, in respective embodiments, compliance values are taken to be equal if they differ by 0.1, 0.2, 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12%, respectively, corresponding to the estimated relative accuracies of the determined compliance values in those embodiments.

25

In some embodiments, the step of processing includes selecting from the determined PEEP values a PEEP value whose value is the lowest of the determined PEEP values whose corresponding compliance value is substantially equal to the maximum compliance value.

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In some embodiments, the process includes:

increasing the PEEP value of the mechanical ventilation to a PEEP value substantially equal to the maximum PEEP value;

5 decreasing the PEEP value of the mechanical ventilation to the selected PEEP value; and

applying mechanical ventilation to said lungs of said patient in said volume targeted mode using the selected PEEP value.

Some embodiments of the present invention provide a process for determining a positive
10 end-expiratory pressure for a mechanical ventilation system, including:

applying mechanical ventilation to lungs of a patient in a volume targeted mode to inflate said lungs by delivering a predetermined tidal volume of gas to said lungs adequate for CO₂ removal, and to deflate said lungs to a positive end-expiratory pressure (PEEP) value;

15 determining a value for compliance of the patient's respiratory system during said mechanical ventilation and corresponding to the PEEP value;

repeatedly increasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the patient's respiratory system for each increased PEEP value until the compliance of the patient's
20 respiratory system has not increased for at least two consecutive PEEP increment steps, thereby providing a maximum PEEP value and a corresponding maximum compliance value;

repeatedly decreasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the patient's
25 respiratory system for each decreased PEEP value until the compliance of the patient's respiratory system has decreased over at least two consecutive PEEP decrement steps;

increasing the PEEP value of the mechanical ventilation to a PEEP value substantially equal to the maximum PEEP value;

30 selecting from the determined PEEP values a PEEP value whose value is the lowest of the determined PEEP values whose corresponding compliance value is substantially equal to the maximum compliance value;

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decreasing the PEEP value of the mechanical ventilation to the selected PEEP value; and

applying mechanical ventilation to said lungs of said patient in said volume targeted mode using the selected PEEP value.

5

In some embodiments, the mechanical ventilation for each PEEP value is maintained for a predetermined number of inflation and deflation cycles. However, this is not typically the case. In most cases, the mechanical ventilation for each PEEP value is maintained for a period of time sufficient for the patient's respiratory system to have substantially stabilised,
10 as set by the clinician based on the patient's lung pathology and the quasi-static or static time constant of the patient's lung. The times required for stabilisation typically range from about 10 seconds to about 20 minutes for infants, and from about 2 minutes to about 20 minutes for adults.

15 In some embodiments, said repeatedly increasing is performed until the compliance of the patient's respiratory system has not increased for two consecutive PEEP increment steps.

In some embodiments, said repeatedly decreasing is performed until the compliance of the patient's respiratory system has decreased for two consecutive PEEP decrement steps.

20

Some embodiments of the present invention provide a process to determine a positive end-expiratory pressure for mechanical ventilation of a newborn infant, including:

determining values for compliance of the newborn infant's respiratory system during mechanical ventilation of said newborn infant using respective positive end-expiratory pressure (PEEP) values;
25

processing the compliance values and the PEEP values to determine a PEEP value as substantially being a lowest PEEP value that provides a highest compliance value.

30 The process may include applying mechanical ventilation to said lungs of said newborn infant using the determined PEEP value.

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Some embodiments of the present invention provide a process to determine a positive end-expiratory pressure for mechanical ventilation of a patient having a pathological lung disease, including:

- 5 determining values for compliance of the patient's respiratory system during mechanical ventilation of said patient using respective positive end-expiratory pressure (PEEP) values;
- processing the compliance values and the PEEP values to determine a PEEP value as substantially being a lowest PEEP value that provides a highest compliance
- 10 value.

The present invention also provides a mechanical ventilation system configured to execute any one of the above processes.

- 15 The present invention also provides a mechanical ventilation system including one or more data processing components programmed to execute any one of the above processes.

The present invention also provides a computer-readable storage medium having stored thereon processor-executable instructions that, when executed by a processor of a

20 processor-controlled mechanical ventilation system, cause the mechanical ventilation system to execute any one of the above processes.

The computer-readable storage medium may be in the form of an integrated circuit or memory chip, a CD-ROM, DVD-ROM, hard disk or solid state drive, or other form of

25 non-volatile storage.

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Some embodiments of the present invention provide a mechanical ventilation system, including:

- at least one gas inlet to receive at least one gas to be supplied to lungs of a patient;
- 5 a gas outlet to be coupled to lungs of said patient;
- user interface components configured to display ventilation data to a user of the system and to receive ventilation control inputs from said user;
- one or more data processing components configured to receive data representing the supply of gas to the patient and to receive control data representing said ventilation control inputs, and to control the supply of said gas to said patient
- 10 in accordance with said ventilation control inputs;
- mechanical ventilation components configured to supply said gas to said patient under control of said data processing components;
- wherein the data processing components are configured to determine values for
- 15 compliance of the patient's respiratory system for respective values for positive end-expiratory pressure (PEEP) for ventilating said patient, and to determine a quasi-optimal PEEP value as being a lowest PEEP value that provides a highest compliance value.

Some embodiments of the present invention provide a mechanical ventilation system, including:

- at least one gas inlet to receive at least one gas to be supplied to lungs of a patient;
- a gas outlet to be coupled to lungs of said patient;
- user interface components configured to display ventilation data to a user of
- 25 the system and to receive ventilation control inputs from said user;
- one or more data processing components configured to receive data representing the supply of gas to the patient and to receive control data representing said ventilation control inputs, and to control the supply of said gas to said patient in accordance with said ventilation control inputs;
- 30 mechanical ventilation components configured to supply said gas to said patient under control of said data processing components;

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wherein the data processing components are configured to cause the mechanical ventilation system to:

5 apply mechanical ventilation to lungs of a patient in a volume targeted mode to inflate said lungs by delivering a predetermined tidal volume of gas to said lungs adequate for CO₂ removal, and to deflate said lungs to a positive end-expiratory pressure (PEEP) value;

 determine a value for compliance of the patient's respiratory system during said mechanical ventilation and corresponding to the PEEP value;

10 repeatedly increase the PEEP value of the mechanical ventilation in a stepwise manner and determine a corresponding value for the compliance of the patient's respiratory system for each increased PEEP value until the compliance of the patient's respiratory system has not increased for at least two consecutive PEEP increment steps, thereby providing a maximum PEEP value and a corresponding maximum compliance value;

15 repeatedly decrease the PEEP value of the mechanical ventilation in a stepwise manner and determine a corresponding value for the compliance of the patient's respiratory system for each decreased PEEP value until the compliance of the patient's respiratory system has decreased over at least two consecutive PEEP decrement steps;

20 increase the PEEP value of the mechanical ventilation to a PEEP value substantially equal to the maximum PEEP value;

 select from the determined PEEP values a PEEP value whose value is the lowest of the determined PEEP values whose corresponding compliance value is substantially equal to the maximum compliance value;

25 decrease the PEEP value of the mechanical ventilation to the selected PEEP value; and

 apply mechanical ventilation to said lungs of said patient in said volume targeted mode using the selected PEEP value.

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The mechanical ventilation system of the present invention is useful in therapeutic protocols including for treating a subject with pathological lung disease.

The present invention contemplates a method of treating a subject with a pathological lung disease or who is at risk of developing same, said method comprising administering to said
5 subject open lung ventilation (OLV) with a mechanical ventilator wherein a positive end-expiratory pressure (PEEP) for the mechanical ventilator is determined by:

determining values for compliance of the subject's respiratory system during the mechanical ventilation of said subject using respective PEEP values; and

10 processing the compliance values and the PEEP values to determine a PEEP value as substantially being a lowest PEEP value that provides a highest compliance value.

BRIEF DESCRIPTION OF THE DRAWINGS

15 Some embodiments of the present invention are hereinafter described, by way of example only, with reference to the accompanying drawings, wherein:

Figure 1 is a flow diagram of an embodiment of a process for determining a positive end-expiratory pressure for a mechanical ventilation system;

Figure 2 is a block diagram of an embodiment of a system for determining a
20 positive end-expiratory pressure for a mechanical ventilation system;

Figures 3 to 6 are graphs of end-expiratory lung volume (EELV), the pressure differential $\Delta P = PIP - PEEP$, the alveolar-arterial oxygen partial pressure difference ($AaDO_2$), and respiratory system compliance (C_{rs}), respectively, as a function of time after initiation of a recruitment manoeuvre in accordance with an embodiment of the present
25 invention.

DETAILED DESCRIPTION**Abbreviations**

	AaDO ₂	Alveolar-arterial oxygen partial pressure difference
	CPAP	Continuous positive applied pressure
5	C _{rs}	Respiratory System Compliance
	EELV	End-expiratory Lung Volume
	F _I O ₂	Fraction of inspired oxygen
	P _a CO ₂	Partial arterial pressure of CO ₂
	PEEP	Positive End-expiratory Pressure
10	PEEP _o	Opening PEEP (maximum PEEP obtained during the OLV strategy)
	PEEP _{opt}	Optimum PEEP as determine by the specific OLV strategy
	PPV	Positive Pressure Ventilation
	SI	Sustained Inflation
	SIPPV	Synchronised Intermittent Positive Pressure Ventilation
15	SpO ₂	Peripheral oxygen saturation
	TTV	Targeted Tidal Volume
	V _T	Tidal Volume

Over 7000 newborn infants develop respiratory failure in Australasia annually. The majority are born prematurely with surfactant-deficient lungs. Those infants born at 29 weeks or earlier are at the greatest risk of severe short and long-term complications and constitute a major health-care burden. Due to their respiratory and neurological immaturity, many need prolonged respiratory support (mechanical ventilation) to survive, at a cost of more than A\$2000 per infant per day. However, ventilation of these immature lungs can lead to damage and the development of chronic lung disease, which is associated with prolonged hospital stay and long-term morbidity. Evidence of this ventilator-induced lung injury can be found even after the first few supported inflations in the delivery room. Thus, the inventors have identified that more refined strategies of ventilation, applicable from these very first inflations, are required to minimise the damage caused to the preterm lung, and believe that the mechanical ventilation strategies used at birth can be improved to

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optimise regional aeration, lung mechanics and pulmonary blood flow and, thus, minimise lung injury in a preterm lung model.

To this end, the inventors have determined that there is a relationship between the compliance of a patient's respiratory system C_{rs} and lung volume during mechanical ventilation that is similar to that of oxygenation. Hence, when the lung is overdistended or collapsed, C_{rs} deteriorates, irrespective of the degree of lung disease. Similarly, the inventors have determined that the optimal PEEP provides the best (maximum) C_{rs} during an LVO manoeuvre in a preterm lamb model and a small series of ventilated infants at the Royal Children's Hospital.

Based on these insights, the inventors have developed processes for determining an optimal or at least quasi-optimal PEEP value based on using the compliance values C_{rs} measured and displayed by modern ventilators.

15

In some embodiments of the present invention, a process for determining a positive end-expiratory pressure for a mechanical ventilation system includes

determining values for compliance of a patient's respiratory system during mechanical ventilation of said patient using respective positive end-expiratory pressure (PEEP) values; and
processing the compliance values and the PEEP values to determine a PEEP value as substantially being a lowest PEEP value that provides a highest compliance value.

20

25 In some embodiments, the quasi-optimal PEEP value is determined by selecting from the PEEP values the lowest PEEP value whose corresponding compliance value is substantially equal to the highest compliance value of the determined compliance values. In other embodiments, the PEEP value can be determined from the PEEP values and their associated respective compliance values, but need not be equal to one of those PEEP values.
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In some embodiments, the step of determining includes:

5 applying mechanical ventilation to lungs of said patient in a volume targeted mode to inflate said lungs by delivering a predetermined tidal volume of gas to said lungs adequate for CO₂ removal, and to deflate said lungs to a positive end-expiratory pressure (PEEP) value;

 determining a value for compliance of the patient's respiratory system during said mechanical ventilation and corresponding to the PEEP value;

10 repeatedly increasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the patient's respiratory system for each increased PEEP value until the compliance of the patient's respiratory system has not increased for at least two consecutive PEEP increment steps, thereby providing a maximum PEEP value and a corresponding maximum compliance value; and

15 repeatedly decreasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the patient's respiratory system for each decreased PEEP value until the compliance of the patient's respiratory system has decreased over at least two consecutive PEEP decrement steps.

20 It will be apparent those skilled in the art that the conditions of the process that the compliance of the patient's respiratory system (i) has not increased and (ii) has decreased need to be understood as being subject to the accuracy of the determined compliance values. In general, these are determined in modern ventilators based on gas flow sensors whose relative accuracy is typically about $\pm 6\%$, and consequently any comparison of the determined compliance values need to be evaluated within these constraints. Accordingly, 25 in respective embodiments, compliance values are taken to be equal if they differ by 0.1, 0.2, 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12%, respectively, corresponding to the estimated relative accuracies of the determined compliance values in those embodiments.

30 In some embodiments, the step of processing includes selecting from the determined PEEP values a PEEP value whose value is the lowest of the determined PEEP values whose corresponding compliance value is substantially equal to the maximum compliance value.

In some embodiments, the process includes:

increasing the PEEP value of the mechanical ventilation to a PEEP value substantially equal to the maximum PEEP value;

5 decreasing the PEEP value of the mechanical ventilation to the selected PEEP value; and

applying mechanical ventilation to said lungs of said patient in said volume targeted mode using the selected PEEP value.

10 In some embodiments of the present invention, a process for determining a positive end-expiratory pressure for a mechanical ventilation system includes:

applying mechanical ventilation to lungs of a patient in a volume targeted mode to inflate said lungs by delivering a predetermined tidal volume of gas to said lungs adequate for CO₂ removal, and to deflate said lungs to a positive end-expiratory pressure (PEEP) value;

15 determining a value for compliance of the patient's respiratory system during said mechanical ventilation and corresponding to the PEEP value;

repeatedly increasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the patient's respiratory system for each increased PEEP value until the compliance of the patient's respiratory system has not increased for at least two consecutive PEEP increment steps, thereby providing a maximum PEEP value and a corresponding maximum compliance value;

20 repeatedly decreasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the patient's respiratory system for each decreased PEEP value until the compliance of the patient's respiratory system has decreased over at least two consecutive PEEP decrement steps;

25 increasing the PEEP value of the mechanical ventilation to a PEEP value substantially equal to the maximum PEEP value;

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selecting from the determined PEEP values a PEEP value whose value is the lowest of the determined PEEP values whose corresponding compliance value is substantially equal to the maximum compliance value;

5 decreasing the PEEP value of the mechanical ventilation to the selected PEEP value; and

applying mechanical ventilation to said lungs of said patient in said volume targeted mode using the selected PEEP value.

10 In some embodiments, the mechanical ventilation for each PEEP value is maintained for a predetermined number of inflation and deflation cycles. However, this is not typically the case. In most cases, the mechanical ventilation for each PEEP value is maintained for a period of time sufficient for the patient's respiratory system to have substantially stabilised, as dictated by the patient's lung pathology and the quasi-static or static time constant of the patient's lung. The times required for stabilisation typically range from about 10 seconds
15 to about 20 minutes for infants, and from about 2 minutes to about 20 minutes for adults.

In some embodiments, said repeatedly increasing is performed until the compliance of the patient's respiratory system has not increased for two consecutive PEEP increment steps.

20 In some embodiments, said repeatedly decreasing is performed until the compliance of the patient's respiratory system has decreased for two consecutive PEEP decrement steps.

In some embodiments of the present invention, a process to determine a positive end-expiratory pressure for mechanical ventilation of a newborn infant includes:

25 determining values for compliance of the newborn infant's respiratory system during mechanical ventilation of said newborn infant using respective positive end-expiratory pressure (PEEP) values;

processing the compliance values and the PEEP values to determine a PEEP value as substantially being a lowest PEEP value that provides a highest compliance
30 value.

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The process may include applying mechanical ventilation to said lungs of said newborn infant using the determined PEEP value.

In some embodiments of the present invention, a process to determine a positive end-
5 expiratory pressure for mechanical ventilation of a patient having a pathological lung disease includes:

- determining values for compliance of the patient's respiratory system during mechanical ventilation of said patient using respective positive end-expiratory pressure (PEEP) values;
- 10 processing the compliance values and the PEEP values to determine a PEEP value as substantially being a lowest PEEP value that provides a highest compliance value.

The processes first determine values for the compliance of a patient's respiratory system
15 during mechanical ventilation using respective PEEP values. The compliance and PEEP values are then used to determine an optimal or at least quasi-optimal PEEP value as the lowest of the PEEP values that provides the highest compliance value. Typically, the optimal PEEP value is determined by selecting the lowest PEEP value whose corresponding compliance value is substantially equal to the highest of the determined
20 compliance values, although it will be apparent to those skilled in the art that this need not be the case if, for example, interpolation or other estimation methods are used to determine a PEEP value that might be between two of the PEEP values that were used to determine the compliance values.

25 The processes can be performed manually by an operator of a standard mechanical ventilator using the compliance values determined and displayed by the ventilator, or can be performed in an automated manner by a modified mechanical ventilator. Given that modern mechanical ventilators are controlled by one or microprocessors and associated software and use feedback processes to control the ventilation of a patient, and moreover
30 that such ventilators already determine compliance values during ventilation, it will be

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apparent that the processes described herein can be implemented in existing mechanical ventilation systems by modifying only the software of such ventilation systems.

In some embodiments, the process consists of the following:

- 5 1. Applying mechanical ventilation in a volume targeted mode to deliver a tidal volume adequate for CO₂ removal. If the patient is spontaneously breathing, a synchronised mode is also set.
2. Setting the maximum PIP to the highest value the clinician believes is acceptable.
3. repeatedly increasing the PEEP in 2 cm H₂O increments until no further
10 improvement in the C_{rs} (as displayed on the ventilator) is observed over two consecutive PEEP increment steps. The lung is then said to have been recruited. The fact that no further improvement in C_{rs} is demonstrated indicates that overdistension is likely to occur with further increases in PEEP. In some embodiments, the PEEP is increased every 10-15 inflations, but it will be understood by those
15 skilled in the art that other values can be used. Indeed, the time needed at each PEEP value depends on the patient's size and lung disease. A preterm infant will likely only need 10-15 inflations, but an adult will require longer.
4. Repeatedly decreasing the PEEP in 2 cm H₂O decrements until C_{rs} has fallen over
20 two consecutive PEEP decrements, thus indicating that the previously recruited lung is now collapsing or under-inflated.
5. The PEEP is then increased to the highest PEEP achieved, and maintained at that value for the same number of inflations used during every PEEP step previously.
6. Finally, the PEEP is then reduced to the lowest PEEP value that nevertheless
25 resulted in the best C_{rs} during the procedure.

The advantages of this process include:

1. It is individualised to each patient.
2. It is based solely on a parameter that is only influenced by the lung.
3. It is independent of oxygenation.
- 5 4. The use of a volume targeted modality minimises the risk of inadvertently high PIP being applied during the procedure, as the ventilator will automatically adjust PIP with PEEP changes. Also, when performed manually, the clinician only has to adjust one knob/dial (*i.e.*, the PEEP setting).
- 10 5. It uses a parameter already measured by modern ventilators and used in other ventilator modes (volume targeted modes). The advantages of this include
 - a. It is relatively easy to integrate into current ventilator software processes based on closed-loop feedback of measured C_{rs} .
 - b. A ventilator could have a 'LVO' button which the clinician could press and the ventilator will automatically find the correct PEEP, in a similar fashion to how they currently determine the correct PIP.
 - 15 c. Similarly, the ventilator could be programmed to automatically repeat the LVO if it determines a significant deviation in the C_{rs} after an LVO optimisation. In volume targeted modalities, the only reason why a C_{rs} would change at a constant PEEP would be a change in the patient's lung disease, in which case the optimal PEEP for that patient at that point in time
20 may be different.

Another potential advantage of the ventilator processes described herein are that they are patient adaptive, and thus may result in less time on a ventilator and less lung injury.

25

The processes described herein are suitable for use on neonatal, paediatric, and adult patients, including patients with various lung pathologies, including lung (alveolar) collapse (atelectasis) and atelectatic lung disease such as adult respiratory distress syndrome (ARDS), for example, and newborn respiratory distress syndrome (RDS) or
30 hyaline membrane disease (HMD), for which the processes described herein would be preferred methods of treatment. The processes can be used with non-invasive ventilation

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systems such as in-home use ventilators with leak-proof face masks. The processes can be used with human or animal patients.

Hence, enabled herein is a method of treating a subject with a pathological lung disease or who is at risk of developing same, said method comprising administering to said subject open lung ventilation (OLV) with a mechanical ventilator wherein a positive end-expiratory pressure (PEEP) for the mechanical ventilator is determined by:

- determining values for compliance of the subject's respiratory system during the mechanical ventilation of said subject using respective PEEP values; and
- processing the compliance values and the PEEP values to determine a PEEP value as substantially being a lowest PEEP value that provides a highest compliance value.

The ventilator inflations are synchronised to the subject's positive inflationary pressure (PIP) and wherein the delivered inflation pressure is adjusted to maintain a constant tidal volume (V_T).

In use, the method includes:

- applying mechanical ventilation to lungs of the subject in a volume targeted mode to inflate said lungs by delivering a predetermined V_T of gas to said lungs adequate for CO_2 removal, and to deflate said lungs to a positive end-expiratory pressure (PEEP) value;

- determining a value for compliance of the subject's respiratory system during said mechanical ventilation and corresponding to the PEEP value;

- repeatedly increasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the subject's respiratory system for each increased PEEP value until the compliance of the subject's respiratory system has not increased for at least two consecutive PEEP increment steps, thereby providing a maximum PEEP value and a corresponding maximum compliance value;

- repeatedly decreasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the

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subject's respiratory system for each decreased PEEP value until the compliance of the subject's respiratory system has decreased over at least two consecutive PEEP decrement steps;

5 increasing the PEEP value of the mechanical ventilation to a PEEP value substantially equal to the maximum PEEP value;

 selecting from the determined PEEP values a PEEP value whose value is the lowest of the determined PEEP values whose corresponding compliance value is substantially equal to the maximum compliance value;

10 decreasing the PEEP value of the mechanical ventilation to the selected PEEP value; and

 applying mechanical ventilation to said lungs of said subject in said volume targeted mode using the selected PEEP value.

15 Some embodiments of the present invention provide a mechanical ventilation system configured to execute any one of the above processes.

20 Some embodiments of the present invention provide a mechanical ventilation system including one or more data processing components programmed to execute any one of the above processes.

25 Some embodiments of the present invention provide a computer-readable storage medium having stored thereon processor-executable instructions that, when executed by a processor of a processor-controlled mechanical ventilation system, cause the mechanical ventilation system to execute any one of the above processes.

 The computer-readable storage medium may be in the form of an integrated circuit or memory chip, a CD-ROM, DVD-ROM, hard disk or solid state drive, or other form of non-volatile storage.

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Some embodiments of the present invention provide a mechanical ventilation system, including:

- at least one gas inlet to receive at least one gas to be supplied to lungs of a patient;
- 5 a gas outlet to be coupled to lungs of said patient;
- user interface components configured to display ventilation data to a user of the system and to receive ventilation control inputs from said user;
- one or more data processing components configured to receive data representing the supply of gas to the patient and to receive control data representing said ventilation control inputs, and to control the supply of said gas to said patient
- 10 in accordance with said ventilation control inputs;
- mechanical ventilation components configured to supply said gas to said patient under control of said data processing components;
- wherein the data processing components are configured to determine values for
- 15 compliance of the patient's respiratory system for respective values for positive end-expiratory pressure (PEEP) for ventilating said patient, and to determine a quasi-optimal PEEP value as being a lowest PEEP value that provides a highest compliance value.

Figure 2 is a block diagram of an embodiment of a processor-controlled mechanical ventilation system or ventilator 200. The ventilator 200 includes at least one gas inlet 202 for receiving at least one gas, and a gas outlet 204 to be coupled to lungs of a patient. Mechanical ventilation components 206 pressurise the gas to supply the gas through the outlet 204 at a positive pressure to ventilate the patient. The mechanical ventilation components 206 are controlled by a data processing subsystem 208 based on ventilation

20 data representing the supply of gas to the patient received from one or more sensors 210 and also ventilation control inputs entered by an operator of the ventilator using user input controls 212. Thus the ventilation of the patient is performed in accordance with the ventilation control inputs and using feedback from the sensors 210.

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The data processing subsystem 208 includes standard computer components, and the processes described herein as implemented as programming instructions of one or more software modules 214 stored on at least one non-volatile storage medium 216 (e.g., hard disk, solid-state drive, PROM, EPROM, and the like). However, it will be apparent that at least parts of the processes could alternatively be implemented as one or more dedicated hardware components, such as application-specific integrated circuits (ASICs) and/or field programmable gate arrays (FPGAs), for example.

The data processing subsystem 208 also includes random access memory (RAM) 218, at least one processor 220, and external interfaces 222, 224, 226, 228, all interconnected by a bus 230. One of the external interfaces 222 is connected to user input controls 212, which may be in the form of a standard keyboard, buttons, or touchscreen, for example. A display adapter 228 is connected to a display device such as an LCD panel display 232 to display input and output parameters to the operator.

In use, the data processing subsystem 208 controls the mechanical ventilation components 206 to ventilate the patient in a volume targeted mode using an initial (PEEP) value, and then repeatedly increases the PEEP value in a stepwise manner as described above to determine compliance values corresponding to the PEEP values, all of which are stored in the RAM 218. The data processing subsystem 208 then controls the mechanical ventilation components 206 to decrease the PEEP values as described above and determine corresponding compliance values, all of which are also stored in RAM 218.

The data processing subsystem 208 then processes the stored PEEP values and associated compliance values as described above to determine a PEEP value that is or approximates the lowest PEEP value that provides a compliance value equal to or substantially equal to the maximum compliance value determined for all of the PEEP values used to ventilate the patient. The data processing subsystem 208 then controls the mechanical ventilation components 206 to ventilate the patient in a volume targeted mode using the determined (PEEP) value.

EXAMPLE 1

127d GA lambs (n=8/group, mean weight 2.97kg) were ventilated for 70 min and randomly divided into three groups with respective ventilation strategies from delivery, as follows:

- 5 1. **Sustained Inflation (SI):** the lambs in this group were mechanically ventilated by initially applying sustained ventilation for a period of 20 sec at a PIP pressure of 35cm H₂O, followed by cyclic deflation and inflation and introduction of a surfactant into the lungs at 10 min; the gas for tidal inflation was nominally 21% O₂ (FiO₂=0.21) using a Targeted Tidal Volume (TTV) of 7mL/kg, and a PEEP value
10 of 6cm H₂O, but during the ventilation both FiO₂ and TTV were adjusted to maintain SpO₂ (peripheral oxygen saturation) at 88–92% and PaCO₂ (partial pressure of arterial CO₂) at 45–55mmHg;
2. **SurfSI:** in this strategy, the surfactant was administered prior to delivery, but otherwise the strategy was as described above for SI; and
- 15 3. **Stepwise PEEP recruitment (SPR):** in this group, PEEP was increased by 2cm H₂O every 10 inflations from 4 to 20cm H₂O using PPV+TTV, and was then decreased in decrements of 2 cm H₂O every 10 inflations until the corresponding C_{rs} values decreased over two consecutive PEEP decrement steps. In this process,
20 the lung is transiently exposed to a lower PEEP than that resulting in the best C_{rs} to identify an optimal or quasi-optimal PEEP value that does provide the highest C_{rs}. The PEEP was then transiently increased to 20 cm H₂O for ten inflations to re-recruit the lung, and then returned to the PEEP value (Mean (SD) PEEP 7.9(1.6)cmH₂O) resulting in the best value of C_{rs}. The surfactant was administered at 10 min.
- 25 For each group, regular arterial gas analysis was performed from 8 to 70 min. SpO₂, pressure, C_{rs}, total and regional tidal volume (V_T) and end-expiratory lung volume (EELV). Respiratory inductive plethysmography and electrical impedance tomography were recorded for the first 15 min, and with arterial gases. The results from the lambs in each group were subjected to statistical analysis using 2-way ANOVA to provide a single result
30 for each group.

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Figures 3 to 6 are graphs of end-expiratory lung volume (EELV), the pressure differential $\Delta P = PIP - PEEP$, the alveolar-arterial oxygen partial pressure difference ($AaDO_2$), and respiratory system compliance (C_{rs}), respectively, as a function of time after initiation of the recruitment manoeuvre.

- 5 From Figures 3 to 6, it is apparent that the SPR and SurfSI strategies resulted in better EELV, C_{rs} and $AaDO_2$ compared to SI, with EELV being 18(SD 9)mL/kg after SPR vs 4(6)mL/kg after SI ($p < 0.0001$). C_{rs} was 0.22 (0.1)mL/cmH₂O greater than SI for both SurfSI and SPR ($p < 0.05$). Surfactant administration generally negated these differences, but by 70 min SPR again resulted in better $AaDO_2$, C_{rs} and EELV compared to SI. The SI
- 10 group required a higher TTV ($p = 0.0017$; ANOVA) to maintain the desired PaCO₂ range. SI resulted in the least uniform distribution of ventilation.

- The results demonstrate that a stepwise PEEP strategy applied at birth emphasizing time and pressure-based recruitment, and titratable to patients' lung mechanics, is practical and demonstrates short-term results similar to a surfactant-replete lung. The strategy applied at
- 15 birth results in better short-term respiratory outcomes than a sustained inflation in a preterm lamb model.

Example 2

This study investigates the safety and feasibility of two strategies of recruiting end-expiratory lung volume, and determines the optimal positive end-expiratory pressure (PEEP) setting, in premature infants with acute respiratory failure, requiring conventional
5 mechanical ventilation at the time of exogenous surfactant therapy.

It is proposed that in a subject such as a preterm infant requiring conventional mechanical ventilation for acute respiratory failure:

1. The use of a ventilation strategy that identifies an optimal PEEP results in better
10 gas exchange in the short term.
2. There is a relationship between the timing of such a ventilation strategy and the administration of exogenous surfactant therapy

This study compares an OLV strategy using synchronised (SIPPV) and volume targeted
15 (TTV) conventional mode of PPV with the current PEEP strategy in preterm infants at the time of surfactant administration. Furthermore, this study investigates the influence of using oxygenation or C_{RS} or both to determine the optimal PEEP during an OLV strategy. An OLV strategy is developed that uses a mode of PPV called SIPPV+TTV to provide feedback to the clinician regarding PEEP and lung volume. This mode synchronises the
20 ventilators inflations to the patients' spontaneous effort (SIPPV) and automatically adjusts the delivered inflation pressure (PIP) to maintain a constant, clinician-set tidal volume (TTV), thus minimising inadvertent over-distension. The PIP is controlled by the patients own lung compliance (C_{RS}); C_{RS} is known to be influenced by lung volume and thus PEEP, and is displayed on all modern ventilators. Practically, this strategy uses the TTV mode to
25 avoid exposure to high inflating pressures during a positive end-expiratory pressure (PEEP) recruitment phase. The clinician also gets two forms of feedback, oxygenation and C_{RS} , to define overdistension and collapse. In addition, as the ventilator adjusts most of the settings automatically, the clinician only needs to adjust PEEP and oxygen. In lamb models, this approach results in better lung volume, oxygenation and lung mechanics than
30 SIPPV+TTV with the standard PEEP of 6 cm H_2O .

Methods

Study population

Preterm infants between 24-29 weeks' completed gestation are selected if they:

1. Are requiring intubation and conventional mechanical ventilation with
5 SIPPV+TTV from no later than 24 hours of age.
2. Meet the criteria for exogenous surfactant administration (clinical evidence of increased work of breathing and need for more than 30% inspired oxygen).
3. TTV is set at ≥ 4 mL/kg to maintain a P_{aCO_2} of at least 45 mmHg on an arterial or capillary blood gas (if available).

10

Infants are not selected if they are:

1. Likely to be extubated to CPAP within 2 hours
2. Requiring $<30\%$ inspired oxygen at time of randomisation
3. Had previous surfactant therapy
- 15 4. Known to have a significant congenital, chromosomal and/or cardiac anomalies
5. Have profound bradycardia.

Enrolled infants who meet the study criteria are randomised to one of three treatment arms prior to surfactant therapy. Randomisation is via a block randomisation code managed by
20 CEBU designed to maximise the chance of matching known confounding factors, such as gender and maternal antenatal corticosteroid therapy. Once randomised the infant receives one of three ventilation strategies at the time of surfactant administration. Infants enrolled prior to birth are randomised on admission to the NICU, so as not to delay surfactant administration.

25

This strategy compares an OLV PEEP strategy using SIPPV+TTV immediately prior to or immediately after exogenous surfactant administration with a control ventilation group of preterm infants <24 hours old. The definition of opening $PEEP_o$ (maximum PEEP) and optimal PEEP ($PEEP_{opt}$) is defined by oxygenation.

30

Ventilation Strategy Groups

A) Control Group: This group receives standard care, consisting of SIPPV at a PEEP 6 cm H₂O and TTV at 4-6 mL/kg (PIP maximum set at 25 cm H₂O). Infants then receive
 5 exogenous surfactant therapy (2.5mL/kgCurosurf™) *via* a pre-measured feeding catheter through the ETT using a closed-circuit system. Post-surfactant therapy ventilation management is provided as required.

B) Pre-surfactant OLV: Infants randomised to this group receive an OLV manoeuvre
 10 using SIPPV+TTV immediately prior to surfactant therapy. This consists of the following:

- a. Starting at a PEEP of 6 cm H₂O, TTV set at that required at the time of implementation (4-6 mL/kg) and PIP maximum set at 25 cm H₂O, the PEEP is increased by 1 cm H₂O. SpO₂ and FiO₂ is continually observed.
- b. The PEEP is further increased by 1 cm H₂O if there is an improvement in
 15 oxygenation or no change in oxygenation. An improvement in oxygenation is defined as an improvement in SpO₂ such that FiO₂ needs to be reduced to maintain target SpO₂ range. PEEP is held at each step for a minimum of 2 mins and a maximum of 5 mins, unless acute desaturation (defined as SpO₂<85% and an increase in FiO₂ of at least 0.1).
- c. At each PEEP step, FiO₂ is adjusted to maintain a SpO₂ between 88 – 94% (preferably pre-ductal). PEEP is increased to a maximum of 10 cm H₂O or the
 20 PEEP in which the following occur:
 - i. There is no further benefit in either oxygenation after two increases in PEEP
or
 - 25 ii. FiO₂ needs to be increased by at least 0.1 to maintain SpO₂ range
 This resultant PEEP will be defined the opening pressure (PEEP_o).
- d. PEEP is then be decreased by 1 cm H₂O every 2-5 mins until either:
 - i. PEEP of 5 cm H₂O or
 - ii. PEEP in which the there is an increase in FiO₂ by 0.1 to maintain SpO₂
 30 range.

This PEEP represents the closing pressure of the lung.

- e. If the lowest PEEP is associated with deoxygenation, then the PEEP is increased to the highest that was obtained during the incremental phase for 2 mins before being decreased to either 5 cm H₂O or 1 cm H₂O above that which resulted in deterioration during the decremental phase. This is defined as the optimal pressure (PEEP_{opt})
- f. Surfactant is then administered as per the control group.

C) Post-surfactant OLV: Infants in this group receive exogenous surfactant as per the Control group. Immediately after surfactant therapy, an OLV strategy is performed using steps a) – d) of the pre-surfactant OLV group. Animal data strongly suggest that an OLV manoeuvre immediately before surfactant is better than after but some practitioners consider that a post-surfactant OLV manoeuvre is safer in human infants.

Ventilation strategy post surfactant administration:

- 15 All groups have the following standardised approach to ventilation after surfactant:
 - 1) FiO₂ set to maintain an oxygen saturation of 88-94% (ideally pre-ductal).
 - 2) TTV range of 4.0-6.0 mL/kg to maintain an arterial or capillary blood PaCO₂ of 45-55 mmHg and/or pH >7.25.
 - 3) Second dose of surfactant permitted if the infant requires a FiO₂>0.3 and has increased work of breathing.
 - 4) PEEP to remain at that set during the surfactant period unless:
 - a. FiO₂ has increased by >0.2 and a second dose of surfactant has already been administered
 - b. The infant is in air and weaning towards extubation likely in the next 6 hours.
 - 5) Infants should be considered for extubation to CPAP if:
 - a. They are able to maintain adequate CO₂ removal and work of breathing in a TTV 3.5 – 4.0 mL/kg
 - b. Are in air if < 72 hours old or the best FiO₂ obtainable for at least 24 hours, at the discretion of the treating clinician.

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- 6) Use of other therapies, including high-frequency ventilation and intotropes, is at the discretion of the treating clinical team.

Measurements

- 5 For the 20-mins before surfactant, and any OLV manoeuvre, and for 60-mins after SpO₂, HR, BP, FiO₂ and C_{RS} at minutely intervals. Ventilator settings are recorded at each PEEP step or every 5-minutes.

- 10 Thereafter, required inspired oxygen concentration (and modified Oxygenation Index), ventilation settings, CO₂ and heart rate are measured hourly for the first 72 hours (*primary outcomes*).

The need for a second dose of exogenous surfactant, complications, age at extubation and duration of all respiratory support (*secondary outcomes*) are also recorded.

15

Adverse events, including pneumothorax, other airleak syndromes, intra-cranial haemorrhages and inadvertent or failed extubation, are assessed after recruitment of the first five, and then ten infants in the OLV groups and protocol refinements made as needed.

20

Outcome

The purpose of this study is to determine the benefit and safety of the OLV strategies.

- 25 Hence, a method for treating a subject is contemplated herein with a pathological lung disease or who is at risk of developing same, said method comprising administering to said subject open lung ventilation (OLV) with a mechanical ventilator wherein a positive end-expiratory pressure (PEEP) for the mechanical ventilator is determined by:

determining values for compliance of the subject's respiratory system during the mechanical ventilation of said subject using respective PEEP values; and

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processing the compliance values and the PEEP values to determine a PEEP value as substantially being a lowest PEEP value that provides a highest compliance value.

- 5 The ventilator inflations are synchronised to the subject's positive inflationary pressure (PIP) and wherein the delivered inflation pressure is adjusted to maintain a constant tidal volume (V_T).

Many modifications will be apparent to those skilled in the art without departing from the
10 scope of the present invention.

CLAIMS:

1. A process for determining a positive end-expiratory pressure for a mechanical ventilation system, including:

determining values for compliance of a patient's respiratory system during mechanical ventilation of said patient using respective positive end-expiratory pressure (PEEP) values; and

processing the compliance values and the PEEP values to determine a PEEP value as substantially being a lowest PEEP value that provides a highest compliance value.

2. The process of claim 1, wherein the processing includes determining the PEEP value by selecting from the PEEP values the lowest PEEP value whose corresponding compliance value is substantially equal to the highest compliance value of the determined compliance values.

3. The process of claim 1, wherein the processing includes determining the PEEP value from the PEEP values and their associated respective compliance values, but wherein the determined PEEP value is not equal to one of those PEEP values.

4. The process of any one of claims 1 to 3, wherein the determining includes:

applying mechanical ventilation to lungs of said patient in a volume targeted mode to inflate said lungs by delivering a predetermined tidal volume of gas to said lungs adequate for CO₂ removal, and to deflate said lungs to a positive end-expiratory pressure (PEEP) value;

determining a value for compliance of the patient's respiratory system during said mechanical ventilation and corresponding to the PEEP value;

repeatedly increasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the patient's respiratory system for each increased PEEP value until the compliance of the patient's respiratory system has not increased for at least two consecutive PEEP

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increment steps, thereby providing a maximum PEEP value and a corresponding maximum compliance value; and

repeatedly decreasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the patient's respiratory system for each decreased PEEP value until the compliance of the patient's respiratory system has decreased over at least two consecutive PEEP decrement steps.

5. The process of any one of claims 1 to 4, wherein the processing includes selecting from the determined PEEP values a PEEP value whose value is the lowest of the determined PEEP values whose corresponding compliance value is substantially equal to the maximum compliance value.

6. The process of claim 5, further including:

increasing the PEEP value of the mechanical ventilation to a PEEP value substantially equal to the maximum PEEP value;

decreasing the PEEP value of the mechanical ventilation to the selected PEEP value; and

applying mechanical ventilation to said lungs of said patient in said volume targeted mode using the selected PEEP value.

7. The process of any one of claims 1 to 6, wherein the mechanical ventilation for each PEEP value is maintained for a period of time sufficient for the patient's respiratory system to have substantially stabilised, as dictated by the patient's lung pathology.

8. The process of any one of claims 1 to 7, including applying mechanical ventilation to said lungs of said patient using the determined PEEP value.

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9. A process for determining a positive end-expiratory pressure for a mechanical ventilation system, including:

applying mechanical ventilation to lungs of a patient in a volume targeted mode to inflate said lungs by delivering a predetermined tidal volume of gas to said lungs adequate for CO₂ removal, and to deflate said lungs to a positive end-expiratory pressure (PEEP) value;

determining a value for compliance of the patient's respiratory system during said mechanical ventilation and corresponding to the PEEP value;

repeatedly increasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the patient's respiratory system for each increased PEEP value until the compliance of the patient's respiratory system has not increased for at least two consecutive PEEP increment steps, thereby providing a maximum PEEP value and a corresponding maximum compliance value;

repeatedly decreasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the patient's respiratory system for each decreased PEEP value until the compliance of the patient's respiratory system has decreased over at least two consecutive PEEP decrement steps;

increasing the PEEP value of the mechanical ventilation to a PEEP value substantially equal to the maximum PEEP value;

selecting from the determined PEEP values a PEEP value whose value is the lowest of the determined PEEP values whose corresponding compliance value is substantially equal to the maximum compliance value;

decreasing the PEEP value of the mechanical ventilation to the selected PEEP value; and

applying mechanical ventilation to said lungs of said patient in said volume targeted mode using the selected PEEP value.

10. The process of any one of claims 1 to 9, wherein the patient is a newborn infant.

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11. The process of any one of claims 1 to 9, wherein the patient is an adult having a pathological lung disease.
- 5 12. A mechanical ventilation system configured to execute any one of the above processes.
13. A mechanical ventilation system including one or more data processing components programmed to execute any one of the above processes.
- 10 14. A computer-readable storage medium having stored thereon processor-executable instructions that, when executed by a processor of a processor-controlled mechanical ventilation system, cause the mechanical ventilation system to execute the process of any one of claims 1 to 11.
- 15 15. A mechanical ventilation system, including:
- at least one gas inlet to receive at least one gas to be supplied to lungs of a patient;
 - a gas outlet to be coupled to lungs of said patient;
 - 20 user interface components configured to display ventilation data to a user of the system and to receive ventilation control inputs from said user;
 - one or more data processing components configured to receive data representing the supply of gas to the patient and to receive control data representing said ventilation control inputs, and to control the supply of said gas to said patient
 - 25 in accordance with said ventilation control inputs;
 - mechanical ventilation components configured to supply said gas to said patient under control of said data processing components;
 - wherein the data processing components are configured to determine values for compliance of the patient's respiratory system for respective values for positive
 - 30 end-expiratory pressure (PEEP) for ventilating said patient, and to determine a

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quasi-optimal PEEP value as being a lowest PEEP value that provides a highest compliance value.

- 5 16. The mechanical ventilation system of claim 15, wherein the data processing components are configured to determine the quasi-optimal PEEP value by selecting from the PEEP values the lowest PEEP value whose corresponding compliance value is substantially equal to the highest compliance value of the determined compliance values.
- 10 17. The mechanical ventilation system of claim 15, wherein the data processing components are configured to determine the quasi-optimal PEEP value from the PEEP values and their associated respective compliance values, but wherein the determined PEEP value is not equal to one of those PEEP values.
- 15 18. The mechanical ventilation system of any one of claims claim 15 to 17, wherein the data processing components are configured to determine the quasi-optimal PEEP value by:
- applying mechanical ventilation to lungs of said patient in a volume targeted mode to inflate said lungs by delivering a predetermined tidal volume of gas to said
- 20 lungs adequate for CO₂ removal, and to deflate said lungs to a positive end-expiratory pressure (PEEP) value;
- determining a value for compliance of the patient's respiratory system during said mechanical ventilation and corresponding to the PEEP value;
- repeatedly increasing the PEEP value of the mechanical ventilation in a
- 25 stepwise manner and determining a corresponding value for the compliance of the patient's respiratory system for each increased PEEP value until the compliance of the patient's respiratory system has not increased for at least two consecutive PEEP increment steps, thereby providing a maximum PEEP value and a corresponding maximum compliance value; and

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repeatedly decreasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the patient's respiratory system for each decreased PEEP value until the compliance of the patient's respiratory system has decreased over at least two consecutive PEEP decrement steps.

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19. The mechanical ventilation system of any one of claims claim 15 to 18, wherein the data processing components are configured to determine the quasi-optimal PEEP value by selecting from the determined PEEP values a PEEP value whose value is the lowest of the determined PEEP values whose corresponding compliance value is substantially equal to the maximum compliance value.

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20. The mechanical ventilation system of claim 19, wherein the data processing components are further configured to:

15

increase the PEEP value of the mechanical ventilation to a PEEP value substantially equal to the maximum PEEP value;

decrease the PEEP value of the mechanical ventilation to the selected PEEP value; and

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apply mechanical ventilation to said lungs of said patient in said volume targeted mode using the selected PEEP value.

21. The mechanical ventilation system of any one of claims claim 15 to 20, wherein the data processing components are further configured to maintain the mechanical ventilation for each PEEP value for a period of time sufficient for the patient's respiratory system to have substantially stabilised, as dictated by the patient's lung pathology.

25

22. The mechanical ventilation system of any one of claims claim 15 to 21, wherein the data processing components are further configured to apply mechanical ventilation to said lungs of said patient using the determined PEEP value.

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23. A mechanical ventilation system, including:

at least one gas inlet to receive at least one gas to be supplied to lungs of a patient;

5 a gas outlet to be coupled to lungs of said patient;

user interface components configured to display ventilation data to a user of the system and to receive ventilation control inputs from said user;

one or more data processing components configured to receive data representing the supply of gas to the patient and to receive control data representing said ventilation control inputs, and to control the supply of said gas to said patient in accordance with said ventilation control inputs;

10 mechanical ventilation components configured to supply said gas to said patient under control of said data processing components;

wherein the data processing components are configured to cause the mechanical ventilation system to:

15 apply mechanical ventilation to lungs of a patient in a volume targeted mode to inflate said lungs by delivering a predetermined tidal volume of gas to said lungs adequate for CO₂ removal, and to deflate said lungs to a positive end-expiratory pressure (PEEP) value;

20 determine a value for compliance of the patient's respiratory system during said mechanical ventilation and corresponding to the PEEP value;

repeatedly increase the PEEP value of the mechanical ventilation in a stepwise manner and determine a corresponding value for the compliance of the patient's respiratory system for each increased PEEP value until the compliance of the patient's respiratory system has not increased for at least two consecutive PEEP increment steps, thereby providing a maximum PEEP value and a corresponding maximum compliance value;

25 repeatedly decrease the PEEP value of the mechanical ventilation in a stepwise manner and determine a corresponding value for the compliance of the patient's respiratory system for each decreased PEEP value until the compliance of the

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patient's respiratory system has decreased over at least two consecutive PEEP decrement steps;

increase the PEEP value of the mechanical ventilation to a PEEP value substantially equal to the maximum PEEP value;

5 select from the determined PEEP values a PEEP value whose value is the lowest of the determined PEEP values whose corresponding compliance value is substantially equal to the maximum compliance value;

decrease the PEEP value of the mechanical ventilation to the selected PEEP value; and

10 apply mechanical ventilation to said lungs of said patient in said volume targeted mode using the selected PEEP value.

24. A method of treating a subject with a pathological lung disease or who is at risk of developing same, said method comprising administering to said subject open lung ventilation (OLV) with a mechanical ventilator wherein a positive end-expiratory pressure (PEEP) for the mechanical ventilator is determined by:

15 determining values for compliance of the subject's respiratory system during the mechanical ventilation of said subject using respective PEEP values; and
 processing the compliance values and the PEEP values to determine a PEEP
20 value as substantially being a lowest PEEP value that provides a highest compliance value.

25 25. The method of claim 24 wherein the ventilator inflations are synchronised to the subject's positive inflationary pressure (PIP) and wherein the delivered inflation pressure is adjusted to maintain a constant tidal volume (V_T).

26. The method of claim 24 or 25, including:

applying mechanical ventilation to lungs of the subject in a volume targeted mode to inflate said lungs by delivering a predetermined V_T of gas to said lungs

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adequate for CO₂ removal, and to deflate said lungs to a positive end-expiratory pressure (PEEP) value;

determining a value for compliance of the subject's respiratory system during said mechanical ventilation and corresponding to the PEEP value;

5 repeatedly increasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the subject's respiratory system for each increased PEEP value until the compliance of the subject's respiratory system has not increased for at least two consecutive PEEP increment steps, thereby providing a maximum PEEP value and a corresponding maximum compliance value;

10 repeatedly decreasing the PEEP value of the mechanical ventilation in a stepwise manner and determining a corresponding value for the compliance of the subject's respiratory system for each decreased PEEP value until the compliance of the subject's respiratory system has decreased over at least two consecutive PEEP decrement steps;

15 increasing the PEEP value of the mechanical ventilation to a PEEP value substantially equal to the maximum PEEP value;

20 selecting from the determined PEEP values a PEEP value whose value is the lowest of the determined PEEP values whose corresponding compliance value is substantially equal to the maximum compliance value;

decreasing the PEEP value of the mechanical ventilation to the selected PEEP value; and

applying mechanical ventilation to said lungs of said subject in said volume targeted mode using the selected PEEP value.

25

27. The method of any one of claims 24 to 26, wherein the subject is a human newborn infant.

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28. The method of any one of claims 24 to 27, wherein the pathological lung disease is selected from lung collapse, atelactic lung disease, and respiratory distress syndrome.
- 5 29. The method of any one of claims 24 to 27 wherein the pathological lung disease is acute respiratory failure.

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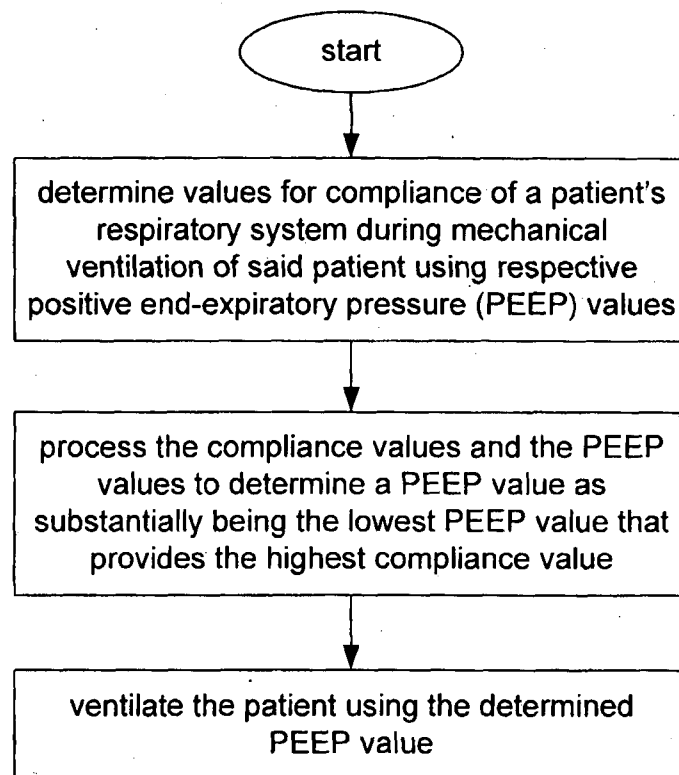


Figure 1

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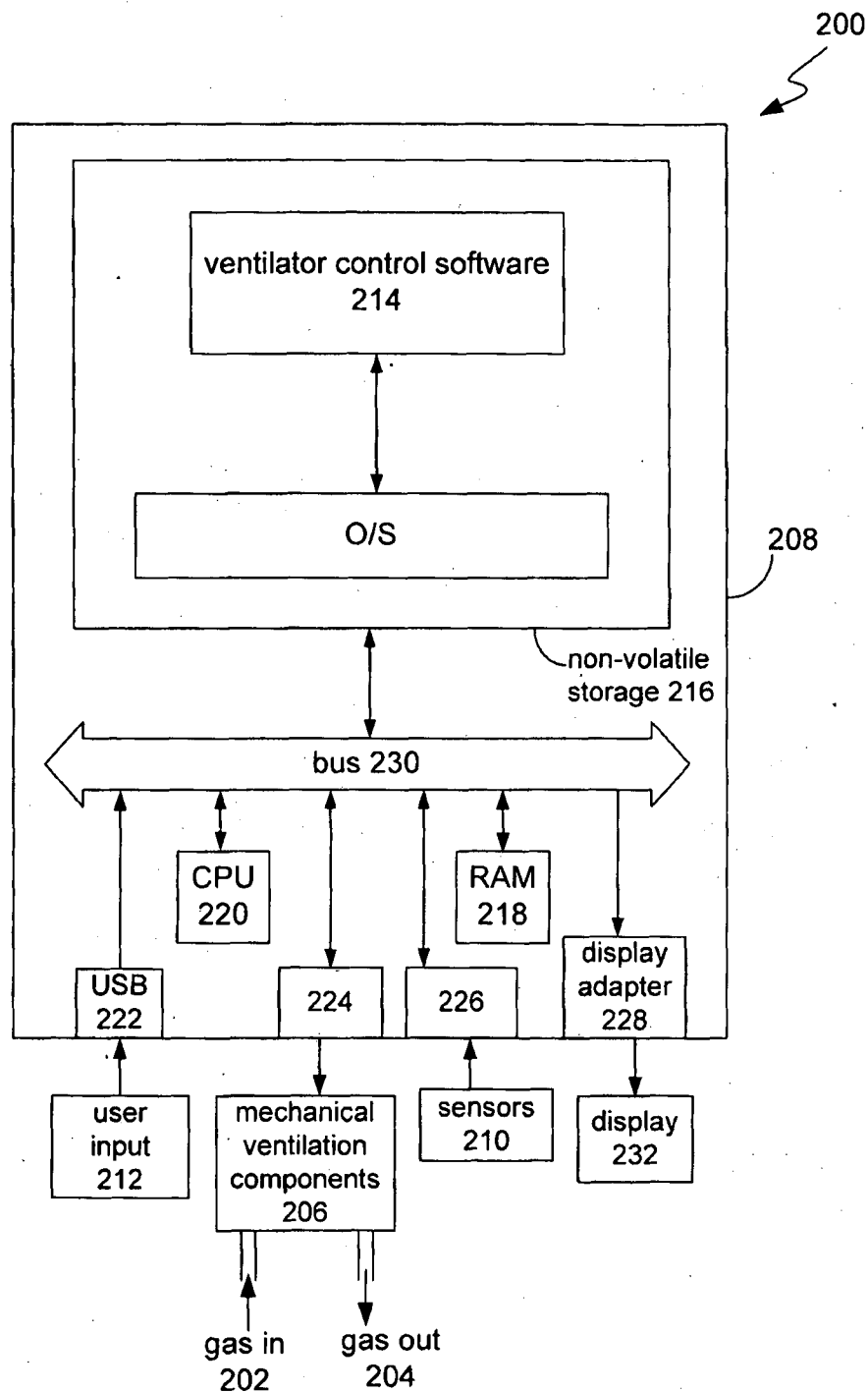


Figure 2

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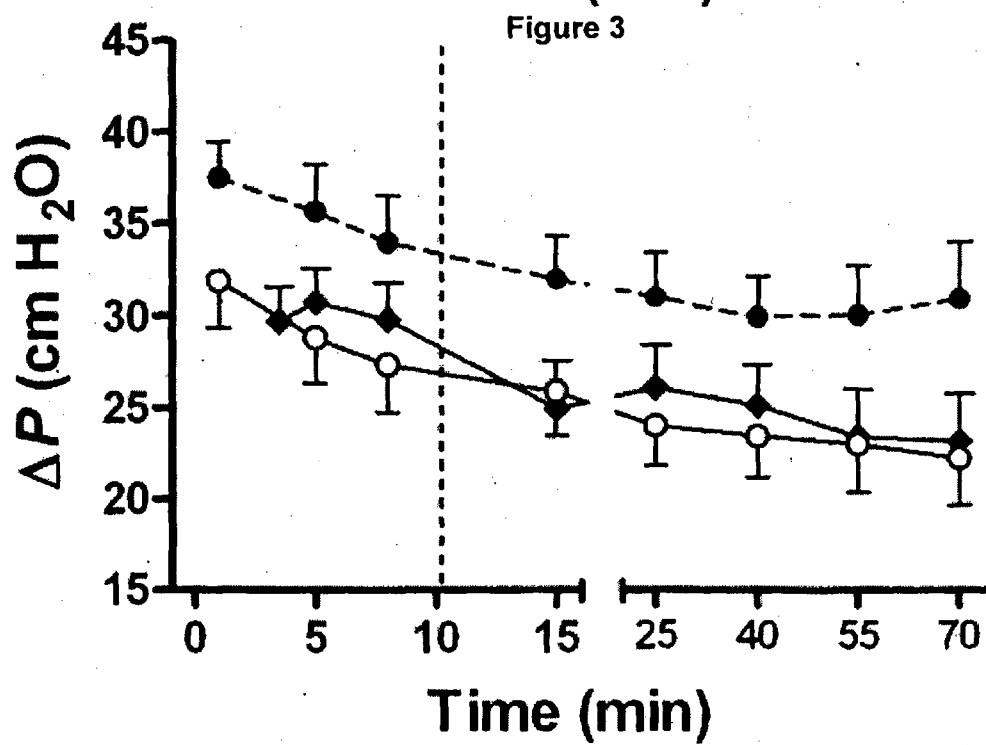
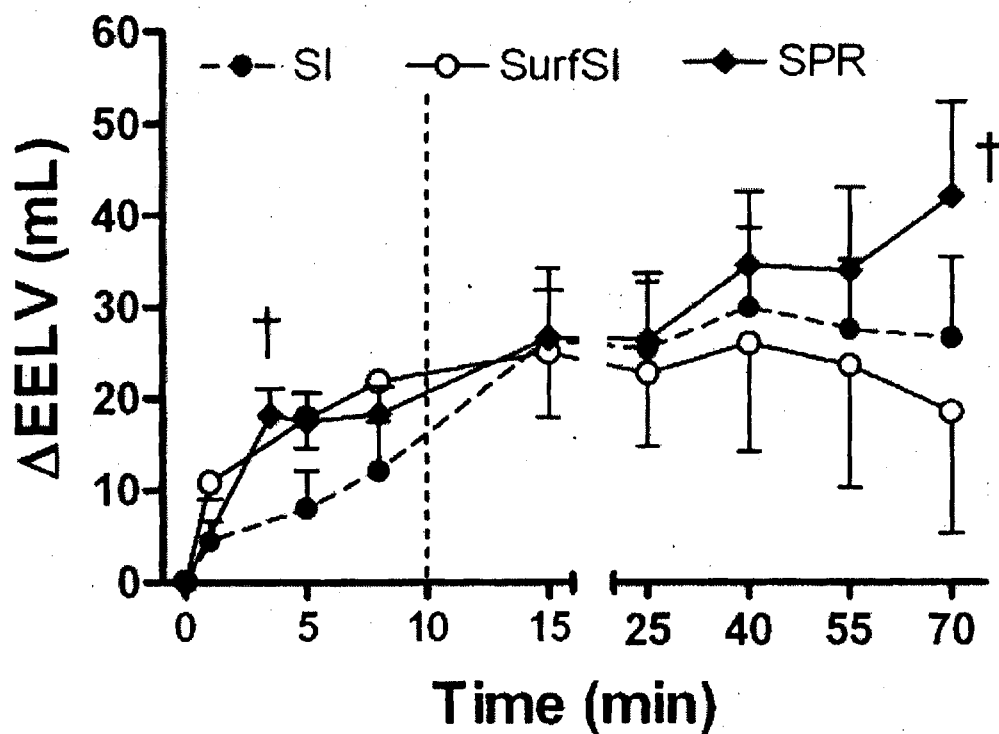


Figure 4

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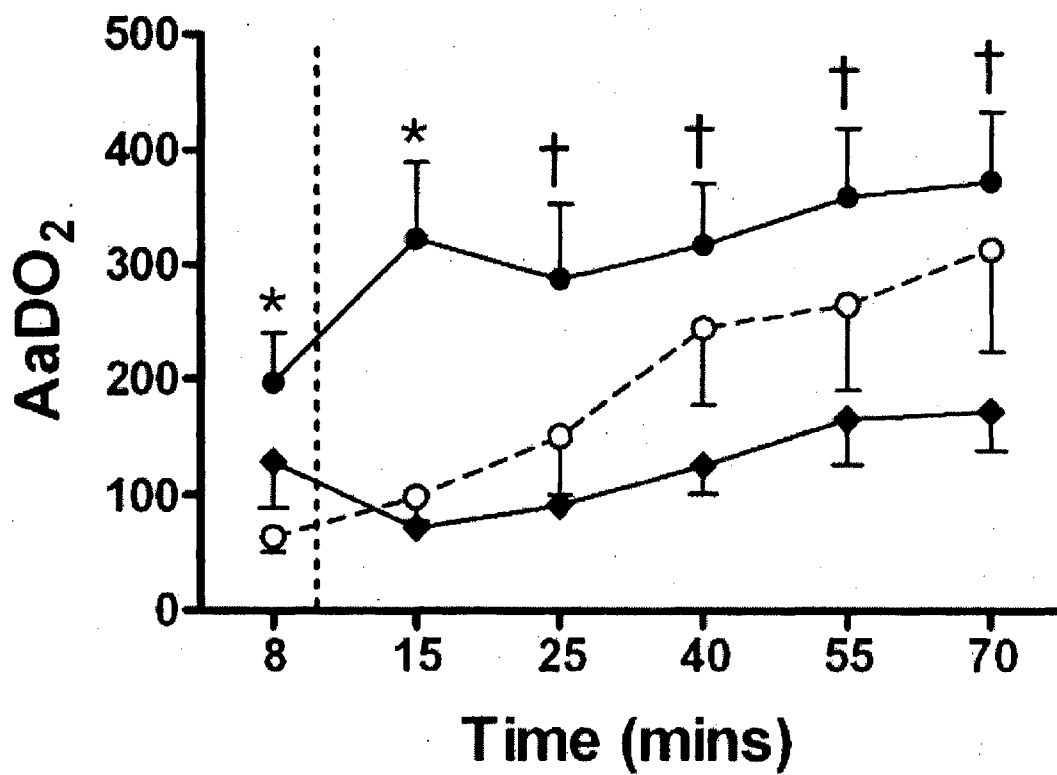


Figure 5

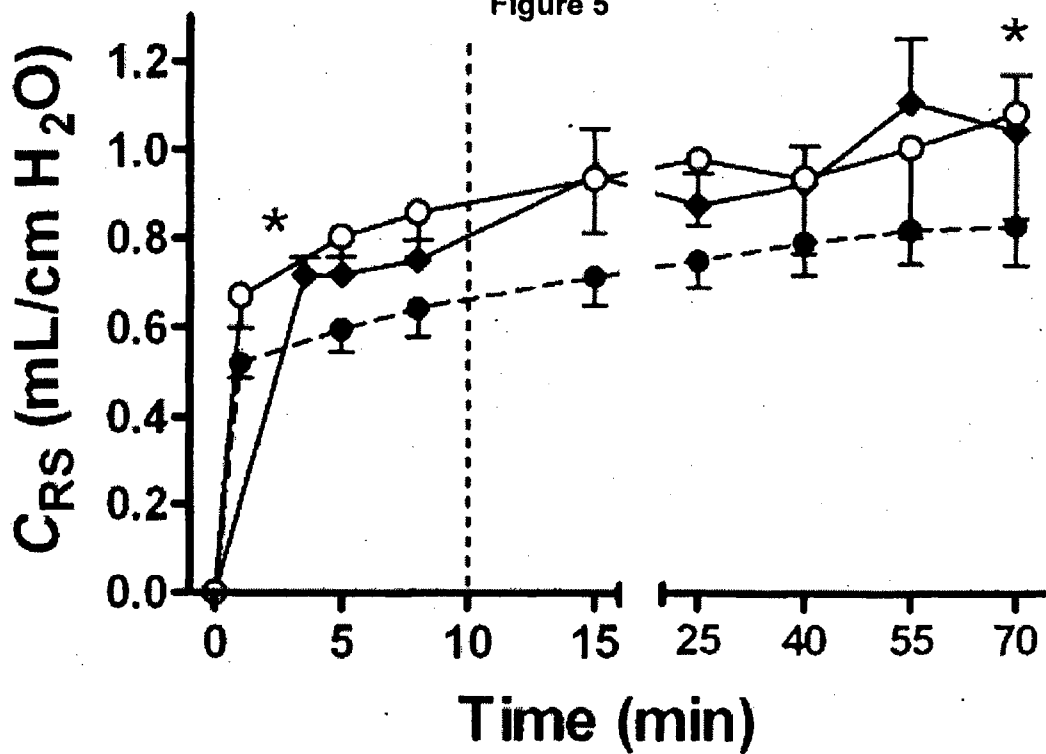


Figure 6

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2012/000370

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl.

A61M 16/00 (2006.01)

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)

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)

WPI and EPODOC and A61M 16/-, A61B 5/- and keywords: ventilate and compliance and PEEP and similar terms.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2008/0091117 A1 (CHONCHOLAS et al.) 17 April 2008 Paragraph 93 to 95, 76, 112 to 116 Figure 9B	1-29
X	US 2009/0272381 A1 (DELLACA et al.) 5 November 2009 Paragraphs 17, 27 to 35, figure 3	1-29
A	US 2004/0097821 A1 (BLOMBERG et al.) 20 May 2004 Whole document	
A	US 5915381 A (NORD) 29 June 1999 Whole document	

☒ 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	"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
"E"	earlier application or patent but published on or after the international filing date	"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
"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)	"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
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search
23 May 2012Date of mailing of the international search report
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2012/000370

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 2007/0240717 A1 (KACZKA et al.) 18 October 2007 Whole document	
A	US 2009/0293877 A1 (BLANCH et al.) 3 December 2009 Whole document	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/AU2012/000370

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report				Patent Family Member			
US	2008091117	DE	102007047105	US	2011087123		
US	2009272381	EP	2061538	IT	MI20061755	WO	2008031822
US	2004097821	EP	1421902	JP	2004167252	US	7322937
US	5915381	EP	0776672	JP	9173456	SE	9504312
US	2007240717	WO	2006044981				
US	2009293877	EP	1765442	JP	2008504068	US	2005284476
		US	7562657	WO	2006012205		
Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001. END OF ANNEX							