

### Amended claims

**We claim,**

1. An apparatus for controlling an amount of carbon dioxide (CO<sub>2</sub>) in a subject's lung to attain a series of targeted end tidal partial pressures of CO<sub>2</sub> (PetCO<sub>2</sub><sup>T</sup>), the apparatus comprising:

(a) a gas delivery device;

(b) a control system for controlling the gas delivery device, wherein the control system is programmed to target a series of PetCO<sub>2</sub><sup>T</sup> values for a series of respective intervals, the series of PetCO<sub>2</sub><sup>T</sup> values comprising at least one of a set of PetCO<sub>2</sub><sup>T</sup> increments and a set of PetCO<sub>2</sub><sup>T</sup> decrements, the control system including means for:

a. Obtaining input of a series of logistically attainable PetCO<sub>2</sub><sup>T</sup> values for the series of respective intervals; and

b. Determining an amount of CO<sub>2</sub> required to be inspired by the subject in an inspired gas to target the PetCO<sub>2</sub><sup>T</sup> for a respective interval;

c. Controlling the amount of gas CO<sub>2</sub> in a volume of gas delivered to the subject in a respective interval to target the respective PetCO<sub>2</sub><sup>T</sup> for the interval;

wherein at least one of:

(a) the respective sizes of the at least one of the set of PetCO<sub>2</sub><sup>T</sup> increments and the set of PetCO<sub>2</sub><sup>T</sup> decrements and the size of the respective intervals; and

(b) the time over which the response is measured and the range of the vascular response;

is predetermined to reveal a dose response to at least one of the set of PetCO<sub>2</sub><sup>T</sup> increments and the set of PetCO<sub>2</sub><sup>T</sup> decrements.

2. An apparatus as claimed in claim 1, wherein each interval is a respective breath [i].

3. An apparatus as claimed in any one of claims 1 and 2, wherein the vascular response is a vasodilatory response to a set of PetCO<sub>2</sub><sup>T</sup> increments and wherein the set of logistically attainable PetCO<sub>2</sub><sup>T</sup> values produces a desired range of a vasodilatory stimulus and

wherein the series of intervals is selected to satisfy a condition, the condition defined by attainment of at least a minimum increment in the vasodilatory response to an increment in the subject's end tidal partial pressure CO<sub>2</sub> (optionally the series of PetCO<sub>2</sub><sup>T</sup> values for the series of respective intervals also revealing the time course of at least one of a partial range of a vasodilatory response and a full range of a vasodilatory response).

4. An apparatus as claimed in any of one claims 1, 2 and 3, wherein the set of increments in PetCO<sub>2</sub><sup>T</sup> for the series of respective intervals is predetermined to produce two time constants in the progress of the vascular response in a respective interval.

5. An apparatus as claimed in any of one claims 1, 2 and 3, wherein the at least one set of increments in PetCO<sub>2</sub><sup>T</sup> for the series of respective intervals is predetermined to produce three time constants in the progress of the vascular response in a respective interval.

6. A computer program product for use in conjunction with a control system for a gas delivery device for controlling an amount of carbon dioxide (CO<sub>2</sub>) in a subject's lung to attain a series of targeted end tidal partial pressures of CO<sub>2</sub> (PetCO<sub>2</sub><sup>T</sup>) for a series of respective intervals, the computer program product comprising program code for:

- a. Obtaining input of a series of logistically attainable PetCO<sub>2</sub><sup>T</sup> values for the series of respective intervals; and
- b. Determining an amount of CO<sub>2</sub> required to be inspired by the subject in an inspired gas to target the PetCO<sub>2</sub><sup>T</sup> for a respective interval; and
- c. Controlling the amount of gas CO<sub>2</sub> in a volume of gas delivered to the subject in a respective interval to target the respective PetCO<sub>2</sub><sup>T</sup> for the interval;

wherein the series of PetCO<sub>2</sub><sup>T</sup> values for the series of respective intervals is at least one of a set of PetCO<sub>2</sub><sup>T</sup> increments and a set of PetCO<sub>2</sub><sup>T</sup> decrements and wherein at least one of:

(a) the respective sizes of the at least one of the set of PetCO<sub>2</sub><sup>T</sup> increments and the set of PetCO<sub>2</sub><sup>T</sup> decrements and the size of the respective intervals; and

(b) the time over which the response is measured and the range of the vascular response;

is predetermined to reveal a dose response to at least one of the set of PetCO<sub>2</sub><sup>T</sup> increments and the set of PetCO<sub>2</sub><sup>T</sup> decrements.

7. A computer program product as claimed in claim 6, wherein each interval is a respective breath [i].
8. A computer program product as claimed in any one of claims 6 and 7, wherein the vascular response is a vasodilatory response to a set of  $\text{PetCO}_2^T$  increments and wherein the set of logistically attainable  $\text{PetCO}_2^T$  values produces a desired range of a vasodilatory stimulus and wherein the series of intervals is selected to satisfy a condition, the condition defined by attainment of at least a minimum increment in the vasodilatory response to an increment in the subject's  $\text{PetCO}_2$  (optionally the series of  $\text{PetCO}_2^T$  values for the series of respective intervals also revealing the time course of at least one of a partial range of a vasodilatory response and a full range of a vasodilatory response).
9. A computer program product as claimed in any of one claims 6, 7 and 8, wherein the set of increments in  $\text{PetCO}_2^T$  for the series of respective intervals is predetermined to produce two time constants in the progress of the vascular response in a respective interval.
10. A computer program product as claimed in any of one claims 6, 7 and 8, wherein the at least one set of increments in  $\text{PetCO}_2^T$  for the series of respective intervals is predetermined to produce three time constants in the progress of the vascular response in a respective interval.
11. A method for assessing a vascular response in a subject using a gas delivery device, the gas delivery device configured for controlling an amount of carbon dioxide ( $\text{CO}_2$ ) in a subject's lung to attain a series of targeted end tidal partial pressures of  $\text{CO}_2$  ( $\text{PetCO}_2^T$ ) for a series of respective intervals, the method comprising the steps of:
  - a. Obtaining input of a series of logistically attainable  $\text{PetCO}_2^T$  values for the series of respective intervals; and
  - b. Determining an amount of  $\text{CO}_2$  required to be inspired by the subject in an inspired gas to target the  $\text{PetCO}_2^T$  for a respective interval; and
  - c. Controlling the amount of gas  $\text{CO}_2$  in a volume of gas delivered to the subject in a respective interval to target the respective  $\text{PetCO}_2^T$  for the interval;

wherein the series of  $\text{PetCO}_2^T$  values for the series of respective intervals is at least one of a set of  $\text{PetCO}_2^T$  increments and a set of  $\text{PetCO}_2^T$  decrements

and wherein at least one of:

(a) the respective sizes of the at least one of the set of  $\text{PetCO}_2^T$  increments and the set of  $\text{PetCO}_2^T$  decrements and the size of the respective intervals; and

(b) the time over which the response is measured and the range of the vascular response;

is predetermined to reveal a dose response to at least one of the set of  $\text{PetCO}_2^T$  increments and the set of  $\text{PetCO}_2^T$  decrements.

12. A method as claimed in claim 11, wherein each interval is a respective breath [i].

13. A method in any one of claims 11 and 12, wherein the vascular response is a vasodilatory response to a set of  $\text{PetCO}_2^T$  increments and wherein the set of logistically attainable  $\text{PetCO}_2^T$  values produces a desired range of a vasodilatory stimulus and wherein the series of intervals is selected to satisfy a condition, the condition defined by attainment of at least a minimum increment in the vasodilatory response to an increment in the subject's  $\text{PetCO}_2$  (optionally the series of  $\text{PetCO}_2^T$  values for the series of respective intervals also revealing the time course of at least one of a partial range of a vasodilatory response and a full range of a vasodilatory response).

14. A method as claimed in any of one claims 11, 12 and 13, wherein the set of increments in  $\text{PetCO}_2^T$  for the series of respective intervals is predetermined to produce two time constants in the progress of the vascular response in a respective interval.

15. A computer program product as claimed in any of one claims 11, 12 and 13, wherein the at least one set of increments in  $\text{PetCO}_2^T$  for the series of respective intervals is predetermined to produce three time constants in the progress of the vascular response in a respective interval.

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