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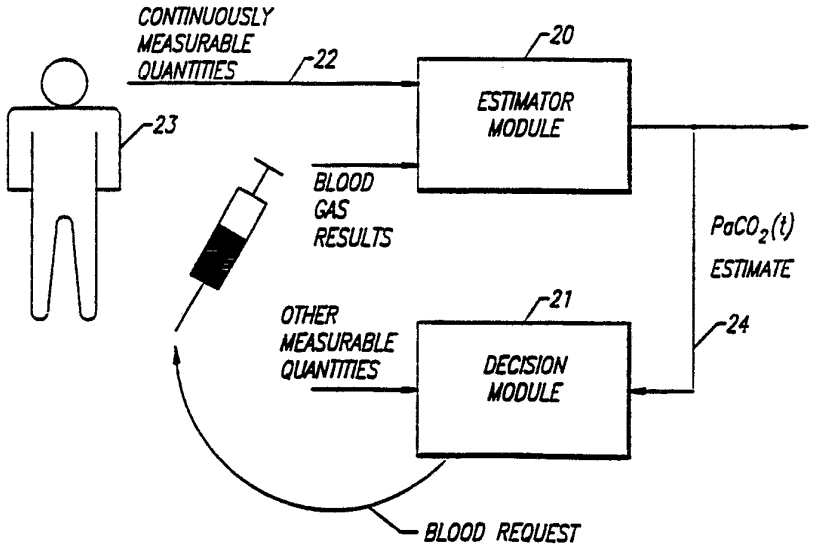

(57) Abstract

The arterial CO_2 monitor and closed loop controller for use with a ventilator monitors a patient's breath and determines $PaCO_2$ based upon a determination of a deadspace ratio, which is the ratio of the alveolar deadspace to alveolar tidal volume. The method generally comprises the steps of continuously monitoring measurable parameters of a patient's breath; obtaining an input value of $PaCO_2$ from a blood sample of the patient and using the patient's breath parameters and the input value to calculate the deadspace ratio; and continuously determining $PaCO_2$ based on the assumption that the deadspace ratio subsequently remains constant. Decision rules obtained from other measurable data are preferably also used to identify the onset of changes in the deadspace ratio, and a new deadspace ratio is then determined from the patient's breath parameters and further input value of $PaCO_2$ from the patient's blood sample.

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ARTERIAL CO_2 MONITOR AND CLOSED LOOP CONTROLLER

BACKGROUND OF THE INVENTION

Field of the Invention:

This invention related to a method and apparatus for continuously and non-invasively monitoring arterial blood CO_2 partial pressure ($PaCO_2$) of artificially ventilated patients.

Description of Related Art:

Mechanical ventilation is required by patients in an intensive care unit who are unable to control their own respiration. The rate of ventilation must be adjusted so that arterial CO_2 is within a desirable range. Conventionally clinicians adjust the ventilator settings based on periodically drawn blood samples. In order to monitor rapidly changing $PaCO_2$ (for monitoring or closed loop control purposes), a continuous and non-invasive monitor is desirable. Known transcutaneous transducers are non-invasive but require heating of the patient's skin to 44°C and a long stabilization time of 30 minutes which renders them unsatisfactory for continuous monitoring. The known method of assuming a constant arterial to end-tidal CO_2 difference is not reliable during ventilation/perfusion changes, and attempts to implement closed loop ventilation control have failed largely due to the inability to continuously and non-invasively observe the variable to be controlled, that is, the $PaCO_2$.

Thus, the direct methods of monitoring $PaCO_2$ are invasive, and indirect methods are not reliable, particularly because end-tidal CO_2 is influenced by deadspace, which is an unmeasurable quality.

It would thus be desirable to provide a method and apparatus for providing a continuous and substantially non-invasive $PaCO_2$ estimation.

SUMMARY OF THE INVENTION

Briefly, and in general terms the invention provides a method and apparatus for continuously and non-invasively monitoring arterial blood CO_2 partial pressure ($PaCO_2$) of artificially ventilated patients, by monitoring a patient's breath and determining $PaCO_2$ based upon a determination of a deadspace ratio, which is the ratio of the alveolar deadspace to alveolar tidal volume. The method generally comprises the steps of continuously monitoring measurable parameters of a patient's breath; obtaining an input value of $PaCO_2$ from a blood sample of the patient and using the patients breath parameters and the input value to calculate the deadspace ratio; and continuously determining $PaCO_2$ based on the assumption that the deadspace ratio subsequently remains constant.

Decision rules obtained from other measurable data are preferably also used to identify the onset of changes in the deadspace ratio, and a new deadspace ratio is then determined from the patient's breath parameters and a further input value of $PaCO_2$ from the patient's blood sample.

The determination of $PaCO_2$ is preferably based upon the equation

$$\frac{V_D^{alv}}{V_T^{alv}} = \frac{PaCO_2 - P\bar{E}^{\bullet}CO_2}{PaCO_2 - PiCO_2}$$

where V_D^{alv} is the alveolar deadspace,

V_T^{alv} is the alveolar tidal volume,

$P\bar{E}^{\bullet}CO_2$ is the mixed-expired CO_2 from the alveolar tidal volume, and

$PiCO_2$ is inspired CO_2.

The mixed-expired CO_2, inspired CO_2, alveolar tidal volume and the alveolar deadspace are the measurable parameters of the patient's breath.

The other measurable data used to determine decision rules for identifying changes in the deadspace ratio are preferably related to lung mechanics and trends in CO_2 production.

The method preferably further involves adjusting patient ventilation based on the determined value of $PaCO_2$.

In another aspect of the invention, an apparatus is provided for continuously and non-invasively monitoring arterial blood CO_2 partial pressure ($PaCO_2$) of artificially ventilated patients. The apparatus preferably includes a capnograph for monitoring continuously measurable parameters relevant to a patient's breath and providing data relating thereto, and means for determining a deadspace ratio connected to the capnograph to receive the breath parameter data and adapted to receive information relating to the $PaCO_2$ of a blood sample of the patient based upon the $PaCO_2$ information and the breath parameter data. Means are also preferably provided for continuously determining $PaCO_2$ based on the deadspace ratio, and the assumption that the deadspace ratio remains subsequently constant. However, means are also preferably provided for further receiving decision rules enabling identification of the onset of changes in the deadspace ratio to thereby signal the need for a further blood sample to re-calculate the deadspace ratio.

The apparatus is preferably connected to a mechanical ventilator to control operation of the ventilator based on the values of $PaCO_2$ determined by the apparatus.

These and other aspects and advantages of the invention will become apparent from the following

detailed description, and the accompanying drawings, which illustrate by way of example the features of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGURE 1 is a basic functional block diagram of the apparatus of the invention;

FIGURE 2 is a block diagram in the form of a software flow chart for the apparatus of Figure 1;

FIGURE 3 is a graph of airwave CO_2 partial pressure versus expired volume for each breath of the patient;

FIGURE 4 is a schematic diagram showing the main method steps according to the invention;

FIGURE 5 is a graph of test results showing $PaCO_2$ estimation; and

FIGURES 6(A) and 6(B) show a detailed functional block diagram of the apparatus of the invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

In Figure 1 the outlet port of capnograph 10 is connected, via connection 11, to analogue to digital (A/D) converter 12. The capnograph 10 may, for example, be a HP-78356 and the A/D converter 12 may comprise analogue devices such as an RT1-815.

The A/D converter 12 is connected via connections 13 and 14 to computer 15 which may, for example, be an IBM compatible PC-AT286. The connection 13 is to the interrupt port of the computer 15 and the connection 14 is to the data port.

A mechanical ventilator 16 such as a Puritan-Bennett 7200 is typically connected both to the A/D converter 12 and the computer 15 as shown. The connections 17 and 18 are to the analogue ports of the ventilator and carry signals related to the pressure and flow respectively. The connection 19 is to the digital port of the ventilator 16 and provides an RS-232 link to the computer 15.

Referring now to Figure 4, the method in fact involves two major modules, the first of which is the $PaCO_2$ estimator 20 and the second of which is the decision module 21. The estimation module 20 receives information on input 22 related to measurements taken from each breath of patient 23, that is, by a breath-by-breath analysis. The decision module 21 receives information on input 24 obtained from other measurable quantities relevant to the patient such as lung mechanics and trends in CO_2 production for example, and contains decision rules obtained by previous experimentation. The rules are implemented as the rule-base of an Expert system.

The $PaCO_2$ estimator 20 is described by equation (1).

$$\frac{V_D^{alv}}{V_T^{alv}} = \frac{PaCO_2 - P\bar{E}^{\bullet}CO_2}{PaCO_2 - PiCO_2} \qquad (1)$$

where V_D^{alv} is the alveolar deadspace,

V_T^{alv} is the alveolar tidal volume,

$P\bar{E}^{\bullet}CO_2$ is the mixed-expired CO_2 from the alveolar tidal volume, and

$PiCO_2$ is inspired CO_2.

The deadspace ratio is the ratio of alveolar deadspace to alveolar tidal volume.

The various parameters may be obtained from the plot of airwave CO_2 partial pressure versus expired volume for each breath a shown in the single breath test graph

of Figure 3. On the graph $PE^{1}CO_2$ is end tidal CO_2, and V_T^{alv} is tidal volume involved in gas exchange. The alveolar deadspace (represented by area Y) is that part of inspired gas which reaches the alveoli but does not take part in gas exchange. VD^{aw}, the airway deadspace, is the point of maximum inflection of the plot. From Figure 1, $PE^{*}CO_2$ and $PiCO_2$ may be found using Equation (2) - (5).

$$P\bar{E}^{*}CO2 = areaX/V_T^{alv} \quad (2)$$

$$PiCO_2 = P\bar{E}^{*}CO_2 - P\bar{E}^{*bag}CO_2 \quad (3)$$

$$PE^{bag}CO_2 = P\bar{E}^{bag}CO_2 * V_T/V_t^{alv} \quad (4)$$

$$P\bar{E}^{bag}CO_2 = \frac{\dot{V}CO_2 * 863}{V_T * f}$$

where f is the respiratory rate. $\dot{V}CO_2$ is carbon dioxide production which can be calculated each minute by integrating the CO_2 fraction (FCO_2) and the flow signal, as shown in Equation (6) - (7).

$$\dot{V}CO_2 = \sum_{k=1}^{1\ min} \dot{V} * FCO_2 \quad (6)$$

$$FCO_2 = \frac{PCO_2}{P_{airway} + P_B + P_{H20}} \quad (7)$$

where $\dot{V}$ is flow, FCO_2 is fraction of CO_2, PCO_2 is the capnograph signal, P_{airway} is airway pressure, P_B is barometric pressure and P_{H20} is vapor pressure.

Breath-by-breath processing yields the mixed-expired CO_2, inspired CO_2, alveolar tidal volume and the airway deadspace. The only unknowns being $PaCO_2$ obtained after a blood sample analysis, the deadspace ratio can be calculated. Assuming that the deadspace ratio remains subsequently constant, further $PaCO_2$ can be calculated using Equation (1). A $PaCO_2$ estimate is calculated once

every minute based on the average of the breaths in the minute.

Certain corrections are needed when implementing the system as set forth below:

(a) Flow signals have to be corrected form BTPS (Body Temperature Pressure Saturated) to STPD (Standard Temperature Pressure Dry).

(b) Correction must be made for delay-time between the flow signals and capnograph signals. Delay time is found by simple breath-holding and rapid expiration through the airway tubing, and lining up the start of flow and capnograph signals.

(c) Correction for compliance of the airway tubing. Flow due to compliance volume is subtracted form the analog flow signal, using $\frac{dP}{dt} C = V$,

where P = airway pressure,
C = tubing compliance,
V = flow due to compliance.

(d) Correction for rebreathing is done by continuously integrating flow and CO_2 fraction, using Equation (6).

(e) Correction of capnograph signal for vapor pressure and airway pressure is done by Equation (7).

As mentioned above the decision rules are obtained by experimentations to determine rules which indicate a change in the deadspace ratio whereby the system may signal that a new blood test is required.

The following are the decision rules derived:

(i) If Alveolar minute volume increases and CO_2 production decreases, deadspace ratio may have changed.

(ii) If Alveolar minute decreases and CO_2 production increases, deadspace ratio may have changed.

(iii) If Alveolar minute volume increases and arterial or end-tidal CO_2 increases, deadspace may have changed.

(iv) If Alveolar minute volume decreases and arterial or end-tidal CO_2 decreases, deadspace may have changed.

It is possible to derive further rules to indicate a change in deadspace ratio. For example, changes to airway resistance, peak airway pressure (PAP), peak flow, SaO_2 , inspiratory to expiratory ratio, and positive end-expiratory pressure (PEEP) should indicate a change in the deadspace ratio. By automatically recording these parameters during a clinical trial, including blood test results, correlation between the change in parameters and change in deadspace ratio can be performed.

If desired, a closed-loop control of ventilation may be implemented based on the predicated $PaCO_2$. The controller in this case is a set of rules which decides on the tidal volume and respiratory rate settings for the mechanical ventilator, to achieve and maintain $PaCO_2$ at a set-point. The controller rules are based on existing clinical protocol for ventilator settings.

The control algorithm is presented below:

First, a $PaCO_2$ setpoint has to be determined as follows:

Given the pH value from the most recent blood gas result, if pH is between 7.36 and 7.44, the $PaCO_2$ setpoint is 40 mm Hg, the default value. If pH exceeded the limits, the following equation is used to calculate a new $PaCO_2$ setpoint.

$$pH = 6.1 + \log (HCO_3^-/(0.03 * PaCO_2))$$

where pH = 7.4, and HCO_3^- is from the most recent blood gas analysis results. The $PaCO_2$ setpoint can also be set by the clinician, overriding the above calculations.

Next, ventilation settings for the next 5 minutes can be set by the following equation.

$$PCO_2 * (V_T^{alv} * f) = PaCO_2' * (V_T^{alv'} * f')$$

where $PaCO_2$ is the setpoint, $(V_T^{alv} * f)$ is the alveolar minute ventilation needed to achieve the setpoint, $PaCO_2'$ is the latest estimation, and $(V_T^{alv'} * f')$ is the latest minute ventilation.

To decide on the actual V_T and f, from the minute volume, the following procedures are followed:

Increase V_T and keep f constant, so that

(1) V_T is not smaller then 500 ml.

(2) V_T is not bigger than 1000 ml.

(3) Peak airway pressure (PAP) is not greater than 40.

If (2) or (3) cannot be satisfied, keep V_T constant and increase f such that -

(a) f is not smaller than 10 bpm.

(b) f is not bigger than 20 bpm. (and not less than 10 bpm.)

(c) Inspiratory to expiratory ratio (I:E) is smaller than 1:2.

If (b) or (c) is exceeded, Peak air flow (PAF) should be increased.

If the required minute volume cannot be achieved without exceeding the limits in any one of V_T/f/PAP/mean pressure/PAF/I:E, a warning message will be displayed to alert the clinician.

As is evident above, the system of the invention is implemented, according to one embodiment, on a PC-AT computer. Analogue flow and pressure signals from the Puritan-Bennett 7200 ventilator and airwave CO_2 signals from the HP-78356 capnograph are analogue-to-digital converted and processed in real time using the computer. Each breath is checked to reject unphysiological waveforms, such as incomplete spontaneous breaths, before further processing. A $PaCO_2$ estimate is calculated every minute and the decision rules are invoked.

Tests have been performed to verify all calculations made in formulating the decision rules. CO_2

production and mixed-expired CO_2 were tested against the Douglas bag method. Airway deadspace was checked by introducing a known deadspace into the ventilator circuit. Corrections had to be made to account for airway tubing compliance, time delay between the flow and capnograph signal, and rebreathing. To test the accuracy of $PaCO_2$ estimation, clinical trials were carried out on ICU patients. For each patient, tidal volume and ventilation rate were changed in different combinations to a maximum of 30% of the initial settings. After each change and a stabilization period of about 10 minutes, a blood sample was drawn to check the estimation. Each clinical experiment involved 6-8 manipulations, over 90 minutes.

To identify the factors and the degree that they affect the alveolar deadspace ratio, specific procedures are incorporated into the clinical experiments to change the deadspace. Posture of the patient is changed by tuning the patient or inclining of the bed. Another procedure has been to administer bronchodilators. Various measurable parameters are recorded during the experiments for correlation with deadspace changes. These include airway compliance and resistance, peak airway pressure, peak air flow, inspiratory time, positive end-expiratory pressure (PEEP), inspiratory to expiratory ratio (I:E), slope of the CO_2 versus expired-volume waveform, end-tidal CO_2 and SaO_2.

The test results show reliable estimation ($\pm$ 5 mmHg) of $PaCO_2$, even when deadspace ratio changed by up to 30% of the initial value. This indicates that the estimator is robust to some changes in the deadspace ratio.

Test results also showed that deadspace ratio change can be expected when alveolar tidal volume and frequency changes are not followed by expected changes in end-tidal CO_2, estimated $PaCO_2$ or CO_2 production. Results from a trial are presented in Fig. 5. At point A, the

increase in alveolar tidal volume and ventilation rate product (alveolar minute-volume) is not followed by a drop in both end-tidal CO_2 and estimated $PaCO_2$, indicating a blood test is needed. At point B, alveolar minute-volume decrease is not followed by an increase in end-tidal CO_2. In each case, the new estimation system correctly identifies the deadspace ratio change and estimates $PaCO_2$ reliably, compared to using the traditional method based on a constant arterial - end tidal difference.

Changes to compliance and resistance, peak airway pressure, peak flow, SaO_2 and I:E should indicate a change in the deadspace ratio but more results are needed before these relationships can be quantified.

The results show that the $PaCO_2$ estimator is sufficiently rebuts to permit continuous estimation for a wide range of ventilator settings. For large deadspace changes, the experimentally derived rules can be relied upon to signal for a blood gas test. Nevertheless, further clinical runs are necessary to cover all possible cases of deadspace ratio changes. By incorporating an Expert System, the knowledge base may be easily extended as more clinical data becomes available.

For the purpose of an even fuller understanding of the invention, the following description provides the pseudo code for programming the apparatus according to the invention. The program should be read in conjunction with Figure 6 which is a self-explanatory functional block diagram of the apparatus.

MAIN PROGRAM

System setup: Hardware setup and parameters initialization.

Repeat

Timer: Keeping track of real-time, using each interrupt service form fixed-frequency AtoD conversion as

time counter. Sets flags after each minute ("onemin" flag) and five minutes ("fivemin" flag).

If "one min" flag is true,

Ventrequest: Request data from ventilator by sending request codes to serial port. The first request is "SPD", send patient data.

FndCO_2prod: Request calculate carbon dioxide production and mixed expired carbon dioxide for the minute.

Checkcomq: checking comm. queue. If queue is not empty,

Readvent: Read characters received from ventilator.

If calculation above are satisfactory,

Sbt_CO_2calc: Request calculation of physiological parameters and $PaCO_2$ prediction.

If "fivemin" flag is true and calc. above are satisfactory,

InvokeExpert: Test if deadspace ratio changes.

InvokeControl: Control rules.

Checkkey: Check keyboard for keyhit. If Keyhit,

Processkeyhit: "M" for marking of blood taken. Entering of $PaCO_2$, pH, HCO_3.

"Q" to exit from program.

If hardware test failed,

Safe-exit.: Disables all interrupts, turn off A/D conversion, and close all files before exiting.

If 0.5-4.0 seconds have elapsed, process data from queue:

Toscrn: Display on screen.

Tostore: Store in file.

FndCO_2prod: ongoing CO_2 production calc.

Sbt_CO_2calc: Ongoing SBT calc.

Until exit from system

SYSTEM SETUP

Initialize variables.

Initialize graphics (axes for plotting, etc.)

Hardware setup: Setting up interrupts for digital and analog interfacing.

HARDWARE SETUP

Setup a circular buffer (AtoDqueue) for storing real-time data.

Set up a circular buffer (Commqueue) for storing character strings received from serial port.

Program Analog to Digital Conversion card to convert at set frequency (100Hz), and to generate an interrupt on completion of each conversion, for the first channel of three. (The three channels are the airway flow, pressure and capnograph signals.)

Set and enable interrupt vector (Interrupt Service Routine: SetAtoD) for A/D card, to read analog flow and pressure from the ventilator, and capnograph waveform from the capnograph.

Set and enable interrupt vector (Interrupt Service Routine: SetComm) for serial port, to read digital data from ventilator.

INTERRUPT SERVICE ROUTINE: SetAtoD

Increment timing counter, for "Timer" routine.

Read converted data from port.

Request and read the other two channels. (The three channels are flow, pressure and capnograph waveform).

Put delay time between flow, pressure waveforms and the capnograph waveform to synchronize the signals.

Put data into the circular buffer (AtoDqueue).

INTERRUPT SERVICE ROUTINE: SetComm

Put characters received in circular buffer (Commqueue).

TIMER

If "onemin" or "fivemin" flag has been set, clear it (Token removal to ensure that the token is passed around the real-time loop only once).

Checks timing counts. (Generated by ISR, SetAtoD).

If one minute ha elapsed, set "onemin" flag.

If five minutes have elapsed, set "fivemin" flag.

FndCO$_2$ prod

During ongoing calculations (by the data count),

Repeat from queue head to tail,

Read CO$_2$ (mmHg), airway flow (Lpm) and pressure signals (mmHg).

Calculate CO$_2$ fraction:

CO$_2$ fraction = CO$_2$ / (PB -P_{H20} + pressure),

where PB=760, P_{H20}=47.

Correction for flow:

Flow(Lpm) = flow:

Compliance * (pressure-previous pressure) * 60/PTTOMS, where

Compliance=5.17ml/mmHg, PTTOMS = 10.

If airway flow > +1.2 lpm (expiration phase),

CO$_2$flow = CO$_2$flow + flow*CO$_2$fraction.

(Integration of airway flow and CO$_2$ fraction)

Expvol = expvol + flow. (Calculation of expired volume in the breath)

If request for a minute's CO$_2$ production,

CO$_2$production = CO$_2$flow * BTPStoSTPD * PTTOMS/60.

where BTPStoSTPD=0.8262.

Expvol (ml) = expvol * BTPStoSTPD * PTTOMS/60.

Mixed-expired

CO$_2$(mmHg)=CO$_2$ production*863*0.8262/Expvol.

Return

READVENT

Read characters from circular buffer (Commqueue).

If carriage return is encountered (ie. end of message received),

Check whether the heading of message is SPD (send patient data), SLM (send lung mechanics) or SVS (send ventilator status).

For each message received, error checking by size of message, and whether various parameters read are within physiological range.

If SPD is received, SLM will be requested.

If SLM is received, SVS will be requested.

If SVS is received, and if all data are acceptable, a flag will be set to indicate completion of ventilator requests.

(Parameters read from ventilator include : RR (rate), MV (minute volume), MAP (mean air pressure), IE (inspiratory to expiratory ratio), VT (tidal vol), SMV (spontaneous MV), PAP (peak airway pressure), SRR (set rate), SVT (set VT), PIF (peak inspiratory pressure), PEEP (positive end expiratory pressure), DMC (Dynamic Compliance), DMR (Dynamic Resistance)).

Sbt CO_2calc

If ongoing calculation,

For each breath, if flow <-1.2Lpm (inspiration phase),

Tinsp (inspiratory time) is counted.

For each breath, if flow >+1.2Lpm (expiration),

Correct for compliance flow.

Calculate tidal volume(Vt):

Expvol(ml) = expvol + (flow*PTTOMS/1000).

Plot Single Breath Co_2 Expiration curve (airway CO_2 (mmHg) vs expvol(ml)).

Calculate gradient of airway CO_2 vs expvol.

Record the maximum inflection point of CO_2 vs expvol;

This is the airway deadspace, VD_{airway}.

At end of expiration (flow<-1.2Lpm),

Reject data from the breath if waveform is unphysiological (Less than 50 data points, or maximum inflexion point is not found).

Determine end-tidal Co_2, the maximum airway CO_2.

Calculate the plateau slope of CO_2 vs expvol.

Calculate the area under the Single Breath CO_2 (area X), by summation.

Parameters calculated for this breath are summed with parameters from previous breaths within a

minute. The parameters are: the number of breaths, areaX, VD_{airway}, tidal volume (V_T), end-tidal CO_2 ($ETCO_2$), plateau phase slope, Tinsp and number of rejected waveforms.

If request for a CO_2 prediction,

If arterial CO_2 sample is drawn (marked) but not available yet,

The minute's parameters are kept in a buffer.

If arterial CO_2 is available,

An average for all parameters over the last minute is calculated. (The average value of each parameter is the summation/total number of breaths.)

From the average, the following calculations are done:

V_t^{alv}(alveolar tidal vol) = $V_T - VD_{airway}$.

PE^*CO_2 (bag mixed expired CO_2) = area X/V_T^{alv}.

$PE^{bag}CO_2$ (bag mixed expired CO_2) = $CO_2prod*863/(V_T*f)$

$PE^{bag}CO_2 = PE^{bag}CO_2 * V_T/V_T^{alv}$.

$PiCO_2 - PECO_2 = PE^{bag}CO_2$.

If $PaCO_2$ is new,

Calculate new deadspace ratio:

V_D^{alv}(alveolar deadspace) = $V_T^{alv}(PaCO_2)/(PaCO_2-PiCO_2)$.

Alvcon (deadspace ratio) = V_D^{alv}/V_T^{alv}.

VDphy(physiological deadspace) = $V_D^{alv} + A_D^{airway}$.

Estimated PCO_2($EPaCO_2$) = $(PECO_2-AlvconPiCO_2)/(1-Alvcon)$.

InvokeExpert: Rules to check if deadspace ratio has changed.

(Parameters needed are: MV, $ETCO_2$, $EPaCO_2$, CO_2prod, slope, DMC, DMR, Tinsp, PEEP, PAP).

Whenever the rules below are triggered three times consecutively, a warning is generated (Note that

the parameters are compared with the values obtained from the most recent blood gas results):

If MV increases by 800 ml or more and $ETCO_2$ does not drop by at least 2 mmHg.

If MV decreases by 800 ml or more and $ETCO_2$ does not increase by at least 2 mmHg.

If MV increases by 800 ml or more and $EPaCO_2$ does not drop by at least 2 mmHg.

If MV decreases by 800 ml or more and $EPaCO_2$ does not increase by at least 2 mmHg.

If MV increases by 800 ml or more and CO_2prod does not increase by at least 20 ml.

If MV decreases by 800 ml or more and CO_2prod does not decrease by at least 20 ml.

If slope changes by more than 0.5 mmHg/ml.

IF DMR changes by more than 10 cmH20/L/s.

IF DMC changes by more than 10 ml/cmH20.

If Tinsp changes by more than 0.5 s.

If PAP changes by more than 10 cmH20.

If previous PEEP is less than 10 cmH20 and changes by more than 5 cmH20.

If previous PEEP is equal or more than 10 cmH20 and changes by more than 2 cmH20.

InvokeControl: Rules for ventilator control.

(Parameters needed are:

Entered from blood gas results: pH, HCO_3, settings limits (I:E ratio minimum, rate limits, volume limits, peak pressure limit).

From ventilator requests: RR, MV, MAP, IE, VT, SMV, PAP, SRR, SVT, PIF, PEEP, DMC, DMR.

From Calculations: Vdphy, $EPaCO_2$.)

If new blood test result is available, calculate new CO_2 setpoint:

If (pH<7.36) or (pH>7.44)

CO_2 setpoint = $1.6706*HCO_3$

Calculate alveolar minute volume needed (AMVneeded);

AMV (Alveolar minute volume(ml)) = (MV*1000-RR*VDphy).

AMVneeded = $EPaCO_2$ * AMV/CO_2 setpoint.

Correct for spontaneous breathing; If (SMV>0) and (RR>SRR)

RRspont (Spontaneous rate) = SRR-RR.

AMVneeded = AMVneeded - (SMV*1000 - RRspont*VDphy).

Control.

Control

Calculate an initial tidal volume needed using current frequency, to produce the required minute volume:

newVT = (AMVneeded/RR) + VDphy.

If PAP>PAP limit,

Repeat

Check the proposed VT & RR to rest if their limits have been exceeded (CheckVT, CheckRR); Results of these checks are entered into the look-up table. Calculate VT & RR using look-up table 1; Results from look-up table decides whether calculated settings are acceptable.

Until the result from look-up table is either "Implement" or "Impossible".

else

Repeat

Check VT & RR if limits exceeded.

Calculate VT & RR using look-up table 2.

Until the result is either "Implement" or "Impossible".

Checking VT & RR

CheckVT:

If VT>maximumVT, result is "Not Increase".

If VT<minimumVT, result is "Not Decrease".

Otherwise result is "OK".

Check RR:

If RR>maximumRR, result is "Not Increase RR".
If RR<minimumRR, result is "Not Decrease RR".
Otherwise result is "OK".

Lookup tables

After doing the checks for VT & RR, the VT & RR results are used with the appropriate look-up table to determine the next calculation.

Lookup Table 1

VT result / RR result	OK	Not Increase	Not Decrease
OK	Implement	Drop V	Inc V
Not increase	DropRR	Impossible	Inc V
Not Decrease	Inc RR	Drop V	Impossible

Lookup Table 2

VT result / RR result	OK	Not increase	Not Decrease
OK	Implement	Drop V	Impossible
Not Increase	Impossible	Impossible	Impossible
Not Decrease	Drop V	Drop V	Impossible

If result is "Inc V", increase VT by 50 ml.
If result is "Drop V, decrease VT by 50ml.
If VT has changed, calculate new RR for the required minute volume (AMVneeded):
new RR = AMVneeded/(VT - VDphy).
If result is "Inc RR", increase RR by 1 BPM.
If result is "Drop RR", decrease RR by 1 BPM.
If RR has changed, calculate new VT for the required AMVneeded:
new VT = (AMVneeded/RR) + VDphy.
If result from the look-up tables is "Implement",
If (IE<minimumIE)

If (new RR is bigger or equal to the current setting)

Increase PAF by 10 LPM. (Ensure IE ratio is above the minimum by increasing peak air flow).

Implement the new VT & RR.

If result is "Impossible",

A warning alarm is generated to indicate inability to implement required settings.

It will be apparent from the foregoing that while particular forms of the invention have been illustrated and described, various modifications can be made without departing from the spirit and scope of the invention. Accordingly, it is not intended that the invention be limited, except as by the appended claims.

IN THE CLAIMS:

1. A method of continuously and non-invasively monitoring arterial blood CO2 partial pressure of artificially ventilated patients by monitoring a patient's breath, and determining PaCO2 based upon a determination of a dead space ratio, comprising the steps of:

a) continuously monitoring measurable parameters of a patient's breath;

b) obtaining an input value of PaCO2 from a blood sample of the patient and using the patient's breath parameters and the input value to calculate the deadspace ratio; and

c) continuously determining PaCO2 based on the assumption that the deadspace ratio subsequently remains constant.

2. The method of Claim 1, wherein said step of continuously monitoring measurable parameters of a patient's breath comprises monitoring mixed-expired CO2 partial pressure, inspired CO2 partial pressure, and alveolar tidal volume.

3. The method of Claim 2, wherein said step of continuously monitoring measurable parameters of a patient's breath further comprises monitoring alveolar deadspace.

4. The method of Claim 1, wherein said step of continuously determining PaCO2 is based upon the equation $V_D^{ALV}/V_T^{ALV} = (PaCO_2-PE^{\bullet}CO_2) / (PaCO_2 - PiCO_2)$

where V_D^{ALV} is the alveolar deadspace,

V_T^{ALV} is the alveolar tidal volume,

$PE^{\bullet}CO_2$ is the mixed-expired CO_2 partial pressure from the

alveolar tidal volume, and
$PiCO_2$ is inspired CO_2 partial pressure.

5. The method of Claim 1, further comprising the steps of identifying the onset of changes in the deadspace ratio by decision rules obtained from other measurable data; and determining a new deadspace ratio from the patient's breath parameters and a further input value of PaCO2 from the patient's blood sample.

6. The method of Claim 1, wherein said step of identifying the onset of changes in the deadspace ratio by decision rules obtained from other measurable data comprises monitoring parameters related to lung mechanics and changes in CO_2 production as measured by $PE'CO_2$ partial pressure from the alveolar tidal volume.

7. The method of Claim 1, further comprising the step of adjusting patient ventilation based on the determined value of $PaCO_2$.

8. An apparatus for continuously and non-invasively monitoring arterial blood CO2 partial pressure of artificially ventilated patients, comprising:

a) means for monitoring continuously measurable parameters relevant to a patient's breath and providing data relating thereto;

b) means for determining a deadspace ratio, connected to the means for monitoring said parameters to receive the breath parameter data, and adapted to receive information relating to the $PaCO_2$ of a blood sample of the patient based upon the $PaCO_2$ information and the breath parameter data;

c) means for continuously determining PaCO2 based on the deadspace ratio, and the assumption that the deadspace ratio remains subsequently constant.

9. The apparatus of Claim 8, wherein said means for monitoring continuously measurable parameters relevant to a patient's breath and providing data relating thereto comprises a capnograph.

10. The apparatus of Claim 8, wherein said means for determining a deadspace ratio comprises microprocessor means.

11. The apparatus of Claim 8, further including means for identifying the onset of changes in the deadspace ratio to thereby signal the need for a further blood sample to re-calculate the deadspace ratio, based upon decision rules.

12. The apparatus of Claim 8, further including means for controlling the operation of a mechanical ventilator based upon the values of $PaCO_2$ determined by the apparatus.

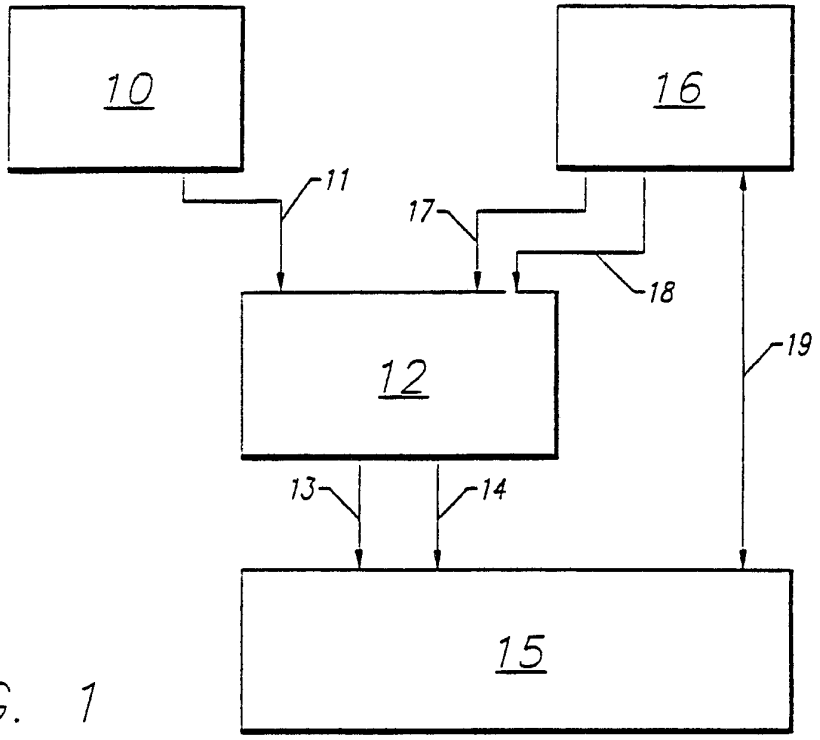

10
16
11
17
18
19
12
13
14
15

FIG. 1

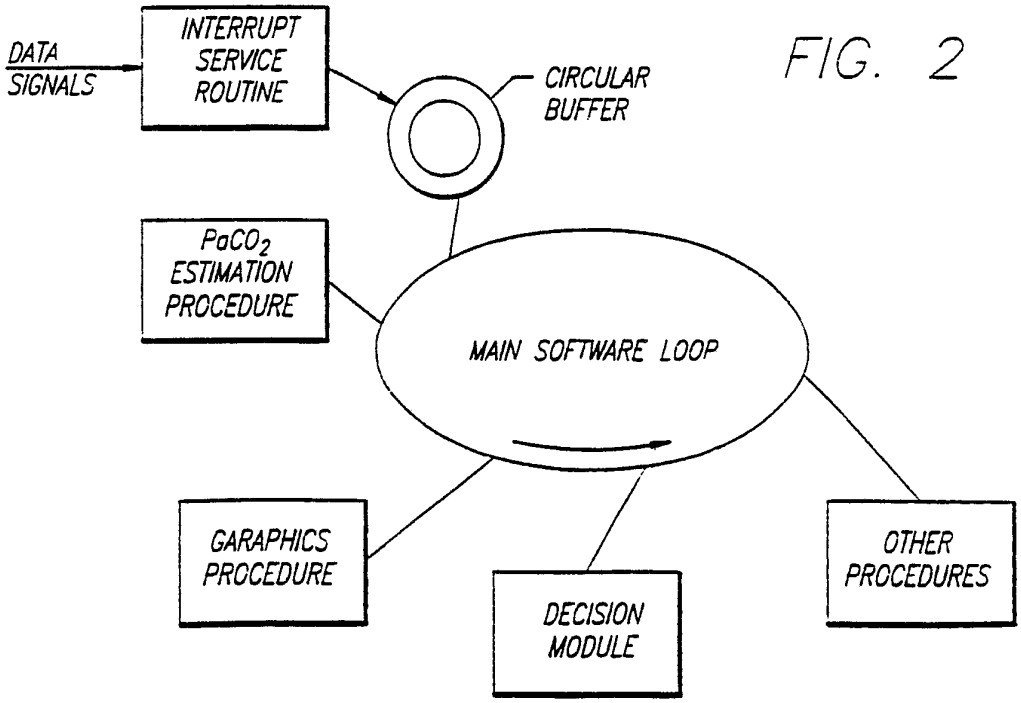

DATA SIGNALS
INTERRUPT SERVICE ROUTINE
CIRCULAR BUFFER
$PaCO_2$ ESTIMATION PROCEDURE
MAIN SOFTWARE LOOP
GARAPHICS PROCEDURE
DECISION MODULE
OTHER PROCEDURES

FIG. 2

FIG. 3

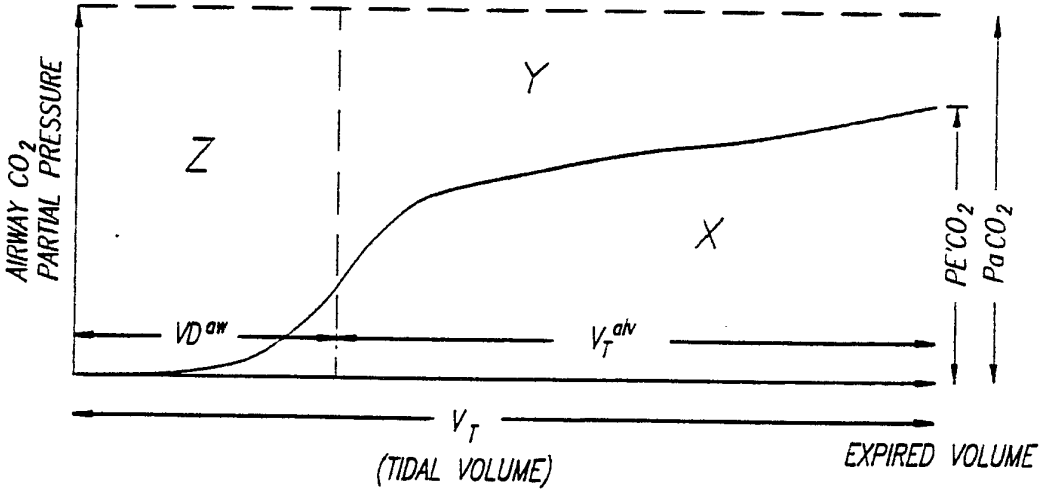
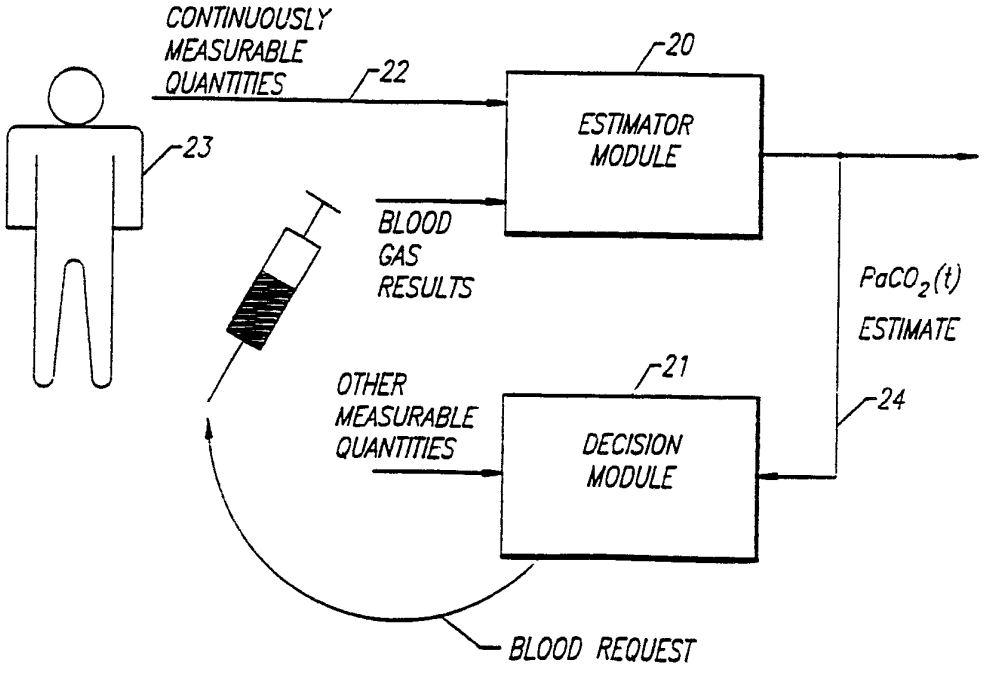

AIRWAY CO_2 PARTIAL PRESSURE
Y
Z
X
$PE'CO_2$
$PaCO_2$
VD^{aw}
V_T^{alv}
V_T
(TIDAL VOLUME)
EXPIRED VOLUME

FIG. 4


CONTINUOUSLY MEASURABLE QUANTITIES
22
20
ESTIMATOR MODULE
23
BLOOD GAS RESULTS
$PaCO_2(t)$ ESTIMATE
OTHER MEASURABLE QUANTITIES
21
DECISION MODULE
24
BLOOD REQUEST

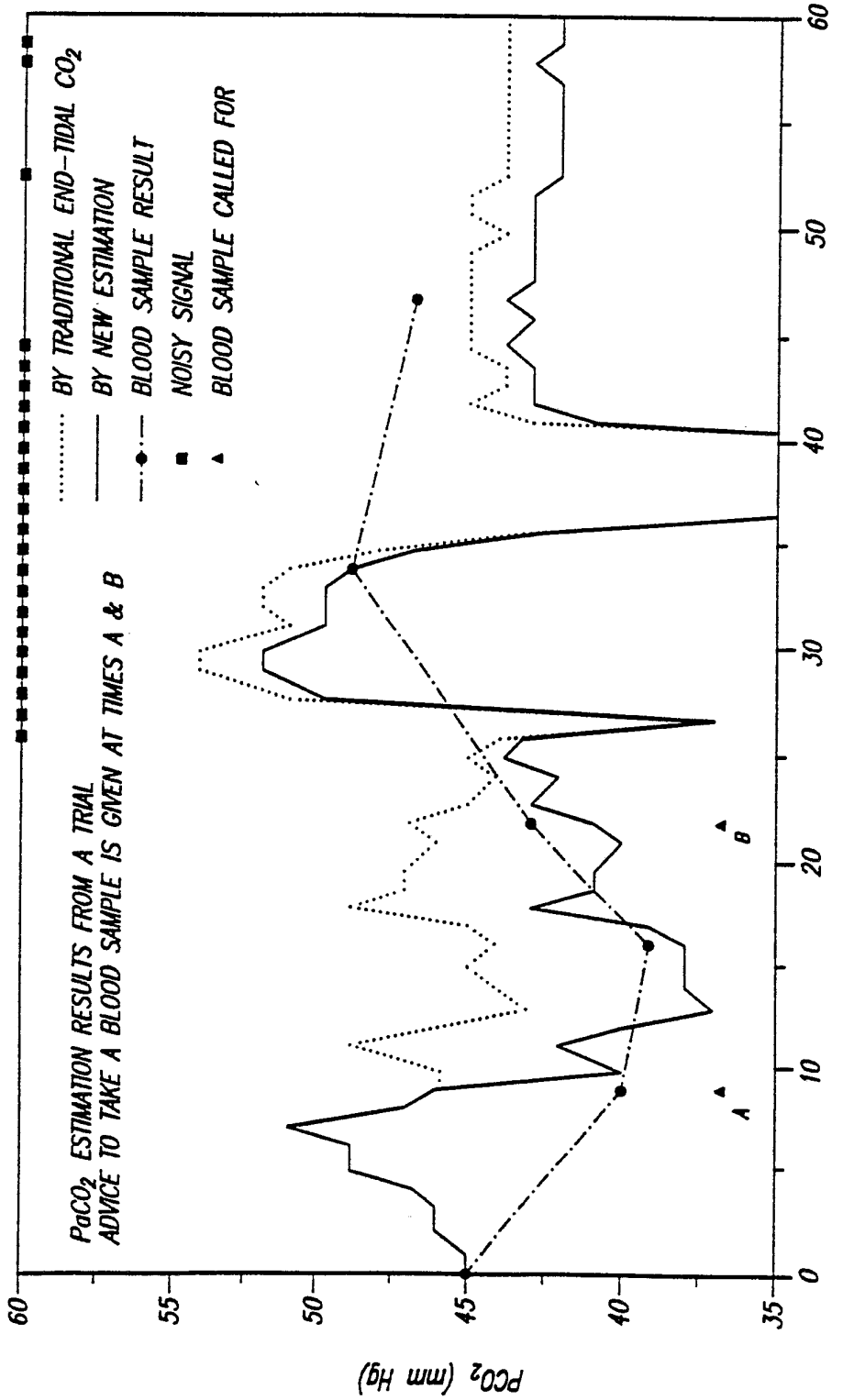

BY TRADITIONAL END-TIDAL CO_2
BY NEW ESTIMATION
BLOOD SAMPLE RESULT
NOISY SIGNAL
BLOOD SAMPLE CALLED FOR
$PaCO_2$ ESTIMATION RESULTS FROM A TRIAL
ADVICE TO TAKE A BLOOD SAMPLE IS GIVEN AT TIMES A & B
A
B
PCO_2 (mm Hg)
TIME (MIN)
60
55
50
45
40
35
0
10
20
30
40
50
60

FIG. 5

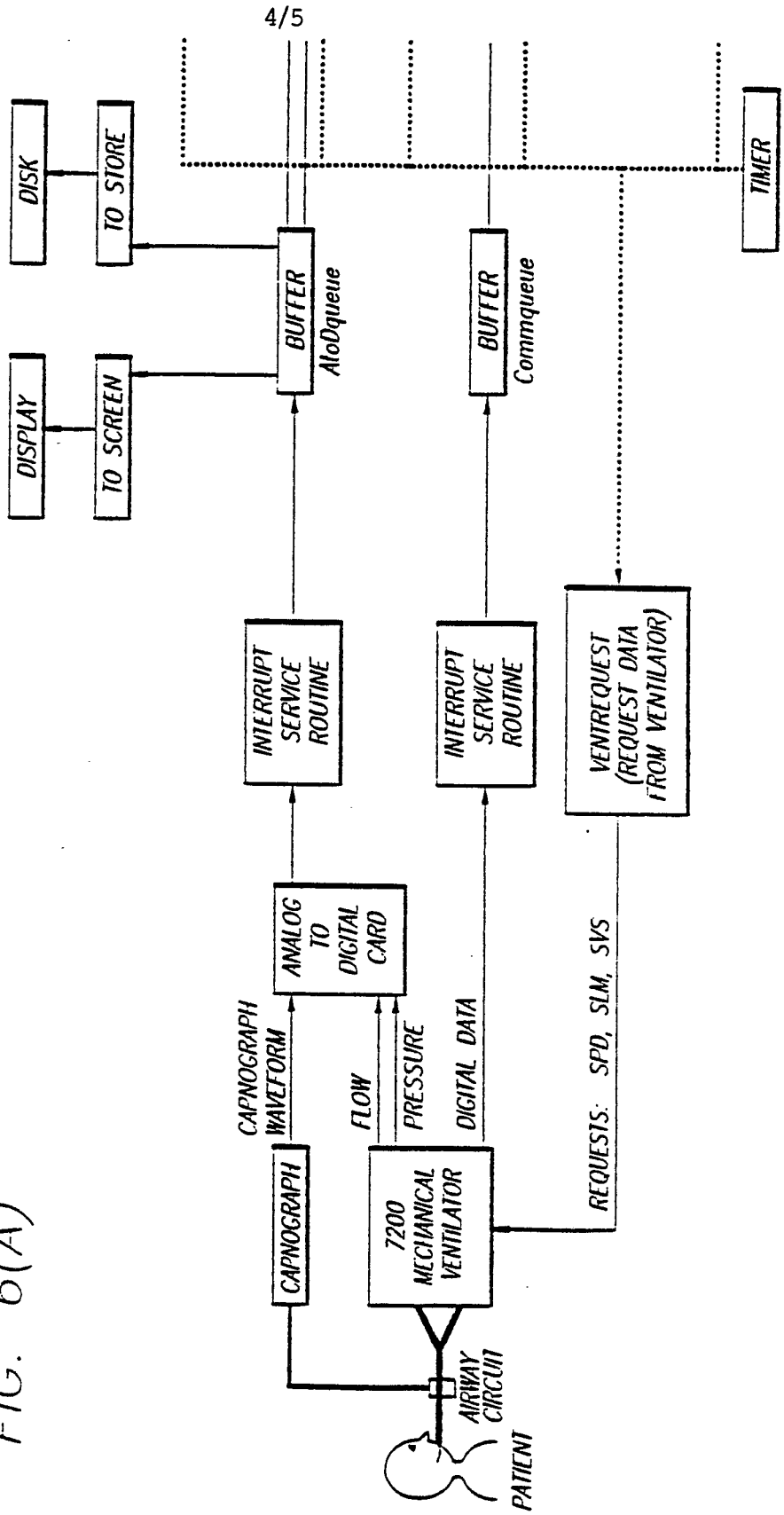

DISK
TO STORE
DISPLAY
TO SCREEN
BUFFER
AtoDqueue
BUFFER
Commqueue
TIMER
INTERRUPT SERVICE ROUTINE
INTERRUPT SERVICE ROUTINE
VENTREQUEST (REQUEST DATA FROM VENTILATOR)
ANALOG TO DIGITAL CARD
CAPNOGRAPH WAVEFORM
FLOW
PRESSURE
DIGITAL DATA
REQUESTS: SPD, SLM, SVS
CAPNOGRAPH
7200 MECHANICAL VENTILATOR
AIRWAY CIRCUIT
PATIENT

FIG. 6(A)

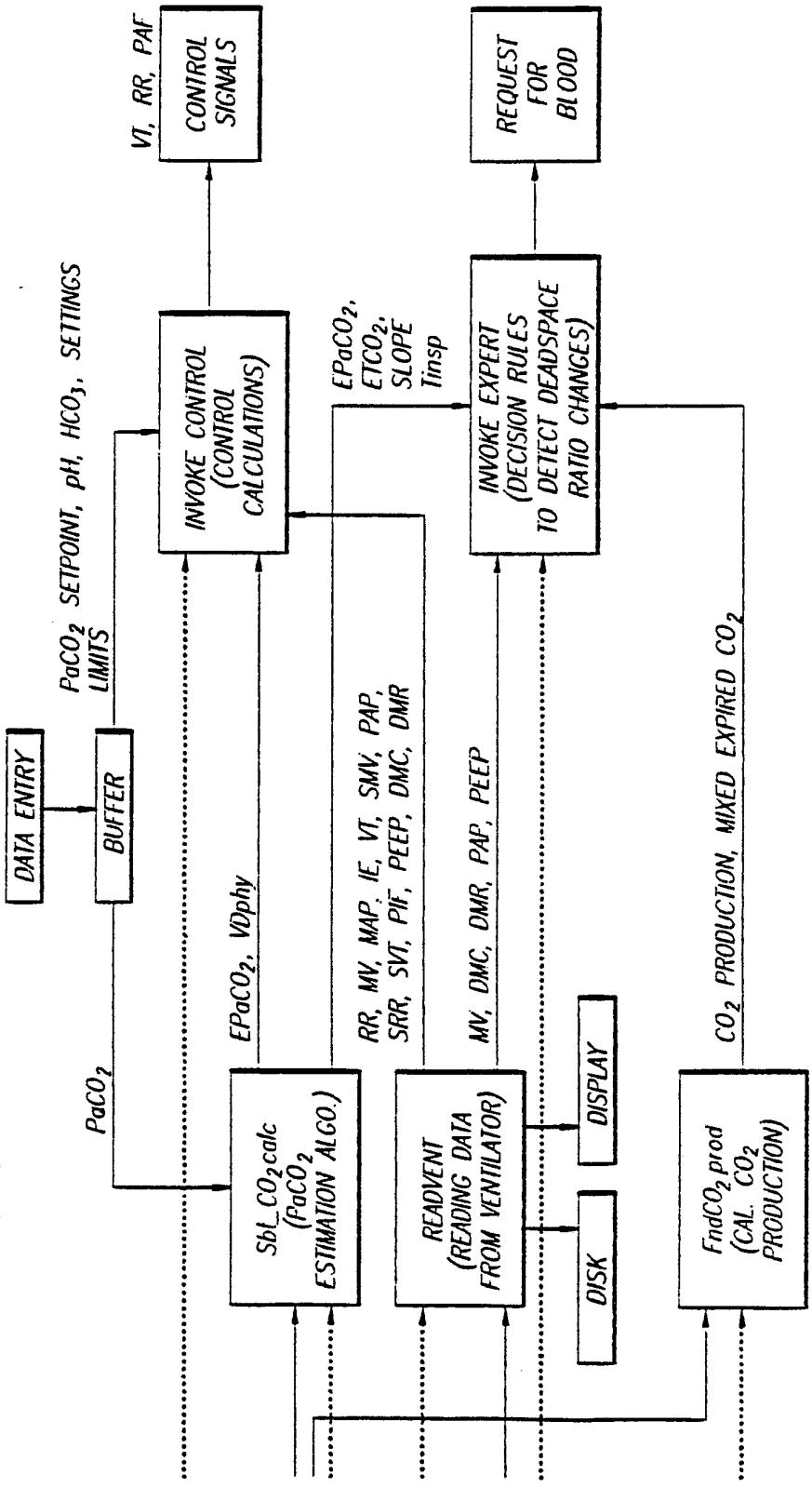

DATA ENTRY
BUFFER
$PaCO_2$ SETPOINT, pH, HCO_3, SETTINGS
LIMITS
INVOKE CONTROL (CONTROL CALCULATIONS)
VT, RR, PAF
CONTROL SIGNALS
$EPaCO_2$, $ETCO_2$, SLOPE Tinsp
INVOKE EXPERT (DECISION RULES TO DETECT DEADSPACE RATIO CHANGES)
REQUEST FOR BLOOD
$PaCO_2$
$EPaCO_2$, VDphy
RR, MV, MAP, IE, VT, SMV, PAP, SRR, SVT, PIF, PEEP, DMC, DMR
MV, DMC, DMR, PAP, PEEP
CO_2 PRODUCTION, MIXED EXPIRED CO_2
Sbl_CO_2 calc ($PaCO_2$ ESTIMATION ALGO.)
READVENT (READING DATA FROM VENTILATOR)
DISPLAY
DISK
FndCO_2 prod (CAL. CO_2 PRODUCTION)

FIG. 6(B)

INTERNATIONAL SEARCH REPORT

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent classification (IPC) or to both National Classification and IPC

Int. Cl.[5] A61B 5/08, A61M 16/00

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
IPC	A61B 5/08, A61M 16/00

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

AU : IPC as above

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category*	Citation of Document, [11] with indication, where appropriate of the relevant passages [12]	Relevant to Claim No [13]
A	IEEE Transactions on Biomedical Engineering, volume BME-29, number 11, published 1982 by IEEE Inc, New York, USA. T.D. East et al, `A Microcomputer-Based Differential Lung Ventilation System', pages 736-740.	1, 2, 7, 8, 10, 12
A	US,A, 4537190 (CAILLOT et al) 27 August 1985 (27.08.85). See column 2 line 55-column 3 line 56.	1, 2, 7-10, 12

* Special categories of cited documents : [10]

"A" Document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document 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 t 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

"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

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
12 December 1991	24 December 91
International Searching Authority	**Signature of Authorized Officer**
AUSTRALIAN PATENT OFFICE	A. HENDRICKSON

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

A	US, A, 4941476 (FISHER) 17 July 1990 (17.07.90). See column 4 line 43-column 5 line 2	1, 2, 7-10, 12
A	WO, A, 83/00613 (ANDROS ANALYZERS INCORPORATED) 3 March 1983 (03.03.83). See page 2 lines 20-28	1, 2, 8, 10

(continued)

V. ☐ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE [1]

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

1. ☐ Claim numbers ..., because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim numbers ..., 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. ☐ Claim numbers ..., because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4a

VI. ☐ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING [2]

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 of the international application.
2. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:
3. ☐ 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 claim numbers:
4. ☐ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

☐ The additional search fees were accompanied by applicant's protest.

☐ No protest accompanied the payment of additional search fees.

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category*	Citation of Document, [11] with indication, where appropriate of the relevant passages [12]	Relevant to Claim No [13]
A	EP, A, 22144 (DRAGERWERK AG) 14 January 1981 (14.01.81) See page 6 line 18-page 7 line 5	1, 8
A	US, A, 4269196 (TOMS et al) 26 May 1981 (26.05.81) See column 1 lines 28-61	2

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL APPLICATION NO. PCT/AU 91/00435

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 4537190	AR 229775	BR 8207176	EP 82041
	ES 518088	FR 2517961	IL 67428
	JP 58105762	MX 152294	
US 4941476	US 4947860	CA 1238416	
WO 8300613	AU 89259/82	CA 1178082	EP 86828
	FI 831371	IT 8249023	IT 1154319
	US 4423739	EP 77068	JP 58175583
	NZ 198614	US 4536959	
EP 22144	DE 2926747	US 4326513	
US 4269196			

END OF ANNEX