THE AUTOMATIC LUNG PARAMETER ESTIMATOR (ALPE) SYSTEM: NON-INVASIVE ESTIMATION OF PULMONARY GAS EXCHANGE PARAMETERS IN 10-15 MINUTES

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ABSTRACT. Objective. Clinical measurements of pulmonary gas exchange abnormalities might help prevent hypoxaemia and be useful in monitoring the effects of therapy. In clinical practice single parameters are often used to describe the abnormality e.g., the “effective shunt.” A single parameter description is often insufficient, lumping the effects of several abnormalities. A more detailed picture can be obtained from experiments where FiO_2 is varied and two parameters estimated. These experiments have previously taken 30–40 minutes to complete, making them inappropriate for routine clinical use. However with automation of data collection and parameter estimation, the experimental time can be reduced to 10–15 minutes. **Methods.** A system has been built for non-invasive, Automatic, Lung Parameter Estimation (ALPE). This system consists of a ventilator, a gas analyser with pulse oximeter, and a computer. Computer programs control the experimental procedure, collect data from the ventilator and gas analyser, and estimate pulmonary gas exchange parameters. Use of the ALPE system, i.e. in estimating gas exchange parameters and reducing experimental time, has been tested on five normal subjects, two patients before and during diuretic therapy, and on 50 occasions in patients before and after surgical intervention. **Results.** The ALPE system provides estimation of pulmonary gas exchange parameters from a simple, clinical, non-invasive procedure, automatically and quickly. For normal subjects and in patients receiving diuretic therapy, data collection by clinicians familiar with ALPE took (mean $\pm$ SD) 13 min 40 sec $\pm$ 1 min 23 sec. For studies on patients before and after surgery, data collection by an intensive care nurse took (mean $\pm$ SD) 10 min 47 sec $\pm$ 2 min 14 sec. Parameter estimates were: for normal subjects, shunt = 4.95% $\pm$ 2.64% and fA_2 = 0.89 $\pm$ 0.01; for patients with heart failure prior to diuretic therapy, patient 1, shunt = 11.50% fA_2 = 0.41, patient 2 shunt = 11.61% fA_2 = 0.55; and during therapy: patient 1, shunt = 11.51% fA_2 = 0.71, patient 2, shunt = 11.22% fA_2 = 0.49. **Conclusions.** The ALPE system provides quick, non-invasive estimation of pulmonary gas exchange parameters and may have several clinical applications. These include, monitoring pulmonary gas exchange abnormalities in the ICU, assessing post-operative gas exchange abnormalities, and titrating diuretic therapy in patients with heart failure.

KEY WORDS. Pulmonary gas exchange, hypoxaemia, respiratory monitoring, pulse oximetry.

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INTRODUCTION

Pulmonary gas exchange abnormalities, such as pulmonary shunt or ventilation/perfusion mismatch, are common in different patient groups, and may cause hypoxaemia. Patients with gas exchange abnormalities include

those who are mechanically ventilated and residing in the intensive care unit [1], patients with pulmonary congestion due to left sided heart failure [2,3], and patients following otherwise uncomplicated surgery [4–7]. Having measurements of pulmonary gas exchange abnormalities which can be determined routinely in a clinical setting is therefore important, both to prevent hypoxaemia, but also as a tool to monitor the severity of the abnormality and the effects of therapeutic interventions.

In practice the clinician usually relies upon simple measures describing gas exchange problems, such as arterial oxygen saturation, the alveolar-arterial oxygen pressure gradient, or as the “state of the art” [8,9] estimates of the venous admixture or “effective shunt.” However, these single parameter descriptions of oxygenation problems are often insufficient, lumping the effects of several abnormalities such as true pulmonary shunt, oxygen diffusion abnormalities and ventilation/perfusion mismatch, into a single parameter.

Mathematical models with two parameters describing shunt (shunt) and either ventilation/perfusion (V/Q) mismatch [10,11] or oxygen diffusion limitation [4,12,13] can be used to calculate curves for arterial oxygen saturation (SaO_2) and for arterial oxygen pressure (PaO_2) for different values of FiO_2 .

For each patient, the two parameters of the model can be adjusted to fit data (SaO_2 and PaO_2) for different values of FiO_2 . For a variety of patient groups [4–6, 10–17] it has been shown that the curves calculated from the model fit the measured data quite well, and that the fit is better than that which can be obtained by a single parameter “effective shunt” model [4, 10].

Obtaining a two parameter description of pulmonary gas exchange abnormalities requires an experiment where inspired oxygen fraction (FiO_2) is varied in 4–6 steps, with measurements of ventilation and arterial blood gases taken at each step. After each step change in FiO_2 , previous studies have usually waited five minutes [2,4,17] to ensure a new steady state, before recording all data manually on paper. Experiments therefore took some 30–40 minutes to complete, not including the time taken for subsequent off-line data analysis and parameter estimation. Whilst waiting 5 minutes almost ensures steady state, it is often the case that the oxygen system reaches steady state within a couple of minutes after a change in ventilation [18]. Breath by breath monitoring of oxygen steady state and automatic, on-line data analysis and parameter estimation could therefore reduce the time take to estimate pulmonary gas exchange parameters to 10–15 minutes.

This paper describes the Automatic Lung Parameter Estimator (ALPE) system, a system which combines a

ventilator, a gas analyzer with a pulse oximeter, and a computer, for conducting experiments where FiO_2 is varied and the parameters of mathematical models of pulmonary gas exchange are estimated on-line. The ALPE system includes functionality for automatic data collection, analysis of oxygen equilibrium, and on-line parameter estimation. As such the ALPE system is intended to be used to simplify the experimental procedure, ensure the collection of high quality data, and enable automatic estimation of pulmonary gas exchange parameters within 10–15 minutes, potentially making the ALPE system a suitable tool for routine clinical use.

METHODS AND MATERIALS

Equipment set-up

The ALPE system (Figure 1) includes a ventilator (A1, A2) (Servo 300, Siemens, Solna, Sweden), a gas analyser (B1) with pulse oximeter (B2) (BK104, Bruel and Kjaer, Naerum, Denmark), and a computer (C) (Pentium PC, 233 MHz). The ventilator includes two gas inlets mixing air (D) and either oxygen (E), to obtain inspired oxygen fraction (FiO_2) $>21\%$, or nitrogen (E), to obtain $FiO_2 <21\%$. The current ALPE system is used in an environment where air and oxygen are supplied from gas outlets at the wall and nitrogen via a gas cylinder.

Fig. 1. The Automatic Lung Parameter Estimator (ALPE) system.

The ALPE system can be used in patients who are breathing with or without mechanical assistance. In mechanically ventilated patients the ventilator is set according to clinical practice. In those patients breathing without mechanical assistance, gas is delivered to the patient via a face mask (F) and breathing proceeds otherwise as normal. Normal ventilation is achieved by setting the ventilator to pressure support mode with zero assistance and a normal respiratory triggering. Other ventilator modes and settings are not required.

Inspiratory and end-tidal expiratory gases are sampled by the gas analyser at the face mask on a breath by breath basis, obtaining FiO_2 , end tidal oxygen fraction (FEO_2), end tidal carbon dioxide fraction (FECO_2), and respiratory frequency (f). Continuous measurements of pulse and arterial oxygen saturation (SpO_2) are taken by the gas analyzer via a pulse oximeter placed on the patient's finger. Ventilator measurements of inspired ($V_t \text{ insp}$) and expired ($V_t \text{ exp}$) tidal volume and respiratory frequency; and gas analyzer measurements of FiO_2 , FEO_2 , FECO_2 , respiratory frequency, pulse and SpO_2 ; are sent continuously to the computer during the experimental period.

All equipment has been placed on a single trolley and is portable within the hospital.

Computer programs and mathematical models

All software has been written in JAVA (version 1.3) including that for data collection, parameter estimation, user interfaces and file management. Data collection is performed via RS232 connection between the computer and both the ventilator and gas analyzer (Figure 1, G), using the JAVA communications (comm.) class.

Included in ALPE are two mathematical models of oxygen transport under steady state conditions. Gas exchange abnormalities are described as either a pulmonary shunt (shunt) and ventilation/perfusion (V/Q) mismatch (Figure 2a) [17] or as a pulmonary shunt (shunt) and oxygen diffusion problem (R_{diff}) (Figure 2b) [4, 13]. fA_2 represents the fraction of ventilation to a lung compartment receiving 90% of blood flow, an $fA_2 = 0.9$ therefore indicates even match of ventilation to perfusion. R_{diff} represents a drop in the oxygen pressure from alveoli to lung capillary blood ($\text{kPa}/(\text{l}/\text{min})$).

The ALPE system has been tested in five normal subjects, in two patients with heart failure both before and after diuretic therapy, and in patients before or after surgical intervention, where ALPE has been used on 50 occasions. For the five normal subjects and two patients with heart failure, data collection was performed by clinicians familiar with ALPE. Studies performed on

patients before and after surgery were conducted by an intensive care nurse after a short period of training in the use of ALPE. Ethical approval for studying these patients was obtained from the Ethics Committee of North Jutland and Viborg Counties. Informed written and oral consent was obtained in all cases.

RESULTS

The results of this work are the development of the ALPE system, which provides estimation of pulmonary gas exchange parameters from a simple, clinical, non-invasive procedure taking 10–15 minutes. The ALPE system includes functionality for: a) performing/controlling the experimental procedure and minimizing the experimental time; b) ensuring the collection of high quality data; c) automatically estimating parameters describing gas exchange and hence monitoring the effects of therapeutic intervention on pulmonary gas exchange parameters.

Performing experiments using ALPE

Figure 3 illustrates the ALPE experimental screen. The screen is divided into two parts with the upper two-thirds showing the data coming from the ventilator and the gas analyser, and the lower third describing the results of the current experiment.

The upper two thirds of the screen is divided into 4 graphical displays. In the top left, breath by breath measurements of FiO_2 (red curve, left axis), FEO_2 (blue curve, left axis) and FECO_2 (green curve, right axis), obtained from the gas analyser, are plotted on a single graph for the last 120 seconds. In the top right continuous measurements of pulse (green curve, right axis) and SpO_2 (blue curve, left axis) obtained from the pulse oximeter are plotted on the same graph for the last 120 seconds. In the bottom left breath by breath plots of inspired (red bar, left axis) and expired (blue bar, left axis) tidal volume obtained from the ventilator are displayed with the measurement of respiratory frequency from the gas analyzer ($B\&K\text{Resp.Frq}$, grey line, right axis). $SV \text{ resp.Frq}$ (green line, right axis) is the respiratory frequency obtained from the ventilator from a count of the number of breaths over the past 30 seconds, displayed in breaths per minute. Occasionally, the patient may cough or the ventilator might trigger inappropriately and register a very short breath. To avoid this being counted in the respiratory frequency very short breaths (i.e., where the breath and the pause after the breath is < 2 seconds) are not counted, the

Fig. 2. Illustration of the two mathematical models of oxygen transport implemented in the ALPE system. These models include pulmonary gas exchange abnormalities represented as a pulmonary shunt (f_s) and diffusion abnormality (diffusion model Figure 2a) or as a pulmonary shunt and ventilation perfusion (V/Q) mismatch (V/Q model Figure 2b). In each of these figures equations in the 5 boxes describe the transport of oxygen from the ventilator to the tissues. Box 1 describes alveolar ventilation. Equation 1 in both models describes oxygen flow into the alveoli ($\dot{V}O_2$) in terms of alveolar ventilation ($\dot{V}_A$), and the inspired oxygen fraction (F_{iO_2}) and expired ($F_{E_{O_2}}$). $\dot{V}_A$ is calculated from tidal volume (VT), dead space (VD), and respiratory frequency (f), i.e., $\dot{V}_A = f(VT - VD)$. In the V/Q model similar equations describe the oxygen flow in each of the alveolar compartments (Equations 2 and 3), and the total oxygen flow and fraction across both alveolar compartments (Equations 4 and 5). fA_2 represents the fraction of total ventilation to an alveolar compartment with a fraction of the total blood flow (f_2). f_2 is fixed at 0.9, i.e., 90% of the non-shunted blood flow. Box 2 describes alveolar gas exchange. For the diffusion model equation 2 calculates the partial pressure of oxygen in the lung capillaries (P_{cO_2}) as the partial pressure of oxygen in the alveoli ($PaO_2 = F_{E_{O_2}}(P_B - P_{H_2O})$), minus the drop in oxygen pressure from alveoli to lung capillaries ($\Delta P_{O_2}^{A-c}$) due to the diffusion resistance (R_{diff}), i.e., $\Delta P_{O_2}^{A-c} = R_{diff} \dot{V}O_2$. For the V/Q model equations 6 and 7 calculate the partial pressure of oxygen in the two lung capillary compartments ($P_{cO_2(1)}$, $P_{cO_2(2)}$) as the partial pressure of oxygen in the alveoli compartments ($PaO_2 = F_{E_{O_2}}(P_B - P_{H_2O})$), i.e., assuming no diffusion abnormality. Also in the V/Q model equations 14 and 15 describe the concentration of oxygen in the lung capillary compartments ($CcO_{2(1)}$, $CcO_{2(2)}$) as the concentration in the veins (CvO_2) plus the increase in oxygen concentration due to equilibration with the alveoli, where Q represents the cardiac output. Box 3 describes the concentration of oxygen in arterial blood (CaO_2) when blood from the lung capillaries with a high oxygen concentration is mixed with the fraction (f_s) of venous blood with a lower oxygen concentration (CvO_2). Box 4 describes the calculation of variables describing blood and includes calculation of: oxygen saturation (SO_2) from an implementation of the oxygen dissociation curve (ODC); haemoglobin oxygen carrying capacity (O_{2cap}) adjusted for methaemoglobin ($HbMet$) and carboxyhaemoglobin ($HbCO$); and the oxygen concentration of either arterial (CaO_2) or lung capillary (CcO_2) blood, calculated as the sum of that freely dissolved and that bound to haemoglobin. Box 5 calculates the venous oxygen concentration (CvO_2) as the arterial oxygen concentration (CaO_2) minus the drop in oxygen concentration due to consumption by the tissues.

volume of the short breath being included in the following breath. This restricts the use of ALPE to an upper respiratory frequency of 30 breath/minute. In addition, the mean inspiratory (Vt_{insp}) and expiratory

(Vt_{exp}) tidal volumes are displayed at the top left of these graphs. These values are calculated as the average inspiratory and expiratory volume per breath over the last 30 seconds. In the fourth graphical display, i.e., the

Fig. 3. The ALPE experimental screen.

bottom right, four continuous plots are displayed. The green and black plots describe the minute ventilation (V_{min}) i.e., the total volume inspired ($V_{min,i}$, green line, right axis) and expired ($V_{min,e}$, black line, right axis) calculated over the last 30 seconds, and displayed in l/min. The red and blue plots display the oxygen consumption (VO_2) calculated over the past 30 seconds and displayed in liters of oxygen per minute. VO_2 is calculated using the equation $VO_2 = (FiO_2 - FeO_2) SV \text{ resp.Frq} (V_t - V_d)$, where deadspace (V_d) is assumed to be 0.20 l (i.e., 0.15 l anatomical dead space and 0.05 l measured for the face mask), and where V_t is either $V_t \text{ insp}$, giving $VO_2 \text{ insp}$ (red line, left axis), or V_t is $V_t \text{ exp}$ giving $VO_2 \text{ exp}$ (blue line, left axis). Figure 3 illustrates data collected from a patient with heart failure who is spontaneously breathing. As illustrated in this figure, the variable breathing pattern of the patient causes some variation in VO_2 calculations. In mechanically ventilated patients this variation almost completely disappears. More care is therefore required in selecting measurement points when investigating the lung function of

spontaneously breathing patients so as to ensure stability of VO_2 .

The bottom third of the screen displays the results of the current experiment in tabular and graphical format. An experiment proceeds as follows: An initial inspired oxygen fraction is selected (FiO_2) and delivered to the patient. In non-ventilated patients the initial FiO_2 is usually that of air (21%) but other values of FiO_2 may be used as the starting point so as to achieve an arterial oxygen saturation which is not considered dangerous (e.g., $SpO_2 \geq 85\%$). Very high values of FiO_2 are usually avoided as these may cause some change in lung function due to absorption atelectasis [19].

After setting FiO_2 to a new level the patients oxygen system will take time to reach steady state. This usually occurs within 2–5 minutes after the perturbation [18]. Achievement of the steady state can be monitored easily by the clinician by viewing the four graphs in the top two-thirds of the screen (Figure 3). A steady state is reached when SpO_2 , VO_2 and the $FiO_2 - FeO_2$ difference remain relatively constant over a period of time. In

Fig. 4. The patient summary screen. $\text{FeO}_2/\text{SpO}_2$ plots illustrate data and model fitted curves from a single patient with heart failure prior to (red crosses and curve) and after (blue crosses and curve) diuretic therapy.

addition the novice user can assess the steady state of the patient's oxygen system using the "equilibrium bar," displayed in the bottom right of the screen (Figure 3). The equilibrium bar displays the "percentage steady state (%SS)," and is calculated as follows. When the $\text{FiO}_2\text{-FeO}_2$ difference is outside the range 0.03 to 0.08, %SS is set to zero. Within the range $0.03 < \text{FiO}_2\text{-FeO}_2 < 0.08$ %SS is calculated by assessing the variance in FeO_2 over the last 30 seconds, calculated for n samples as:

$$\text{variance} = \frac{\sum_{t=0}^{t=n} (\text{FeO}_2(t) - \overline{\text{FeO}_2})^2}{n-1}$$

where $\overline{\text{FeO}_2}$ is the mean FeO_2 over the past 30 seconds.

%SS is then calculated as 1 minus the difference between the variance and the lower limit in variance due to measurement error (variance_0) expressed as a percentage, i.e.,

$$\%SS = [1 - (\text{variance} - \text{variance}_0)] 100$$

Where variance_0 is set to 0.01. Using this equation, %SS reaches 100% when the variance in FeO_2 over the past 30 seconds is 0.01.

When a steady state is reached a measurement is taken by clicking the "measure" button in the bottom right of the screen. The ALPE system then records the current values of FiO_2 , FeO_2 , FeCO_2 , SpO_2 , Pulse, Sv_{Resp} , Vt_{exp} , and VO_2_{exp} , plus the time since the last measurement and adds these values to the experimental results table in the bottom left hand corner of the screen (Figure 3). In addition, measured values of SpO_2 and FeO_2 are plotted on a graph (bottom, centre of screen).

This process is then repeated, varying FiO_2 and measuring values at steady state. For all experiments reported here, a complete experiment includes 4 or more measurements at different FiO_2 levels, with SpO_2 distributed within the range 85–100%.

For the 5 normal subjects, studied on one occasion, and the 2 patients with heart failure, each studied on 2

occasions, the experimental procedure took (mean $\pm$ SD) 13 minutes 40 seconds $\pm$ 1 minute 23 seconds. For the patients studied prior to or after surgical intervention the experimental procedure took (mean $\pm$ SD) 10 minutes 47 seconds $\pm$ 2 minutes 14 seconds ($n = 50$).

Quality control in ALPE

ALPE's graphical display (Figure 3) allows the user to assess both the consistency and variability of the data. The user can check that the respiratory frequency read from the gas analyser (B&KResp.Frq) is consistent with that obtained by counting the number of breaths (Sv resp.Frq). They can also check that minute ventilation and oxygen consumption calculated using inspiratory volumes (V_{min-i} , VO_2 insp) are the same as those calculated using expiratory values (V_{min-e} , VO_2 exp) to see if a leak is present in the mask or tubing. In addition, graphical display of the data on a breath by breath basis means that unexpected events, such as a sudden drop in SpO_2 can be identified immediately.

ALPE includes some automatic variability and consistency checks. All variables displayed in the ALPE experimental screen (Figure 3) have upper and lower alarm limits set prior to use of the system. In addition ALPE compares inspired and expired volumes. If inspired volumes are consistently higher than expired volumes ALPE automatically notifies the investigator of the possibility of a leak in the system.

Automatic estimation of parameters describing gas exchange

At the end of an experiment the user is presented with the "patient summary screen" illustrated in Figure 4. This screen includes data from all experiments performed on the patient. It is automatically entered after an experiment is performed but may also be accessed to review the results of previous experiments. The right half of the screen displays the patient data sheet. One is recorded for each experiment, the user selecting the one which is currently displayed. A data sheet includes, from top to bottom: data describing the details of the experiment; the patient characteristics at the time of the experiment, i.e., age, weight, the acid-base status of the arterial blood (pH, methaemoglobin (HbMet), carboxyhaemoglobin (HbCO) and haemoglobin concentration (Hb)), cardiac output, and anatomical dead space; a model selection and parameter estimation section; a section controlling the graphical display of data; and the table of results obtained from the experimental proce-

dure. Parameters describing the acid-base status of arterial blood are assumed to be pH = 7.4, HbMet = 0 mmol/l, HbCO = 0 mmol/l, and Hb = 9.3 mmol/l, or are measured from a single arterial blood sample. Cardiac output is assumed to be 5 l/min but a different value can be typed in if a measurement is available.

The left half of the screen includes the patient demographics (name, number, sex and comments), plus the plot of $FeO_2 \backslash SpO_2$ obtained from the experimental procedure. Data is plotted as crosses and is color coded so that the results of several experiments performed on a single patient can be illustrated on the same graph. Figure 4 illustrates the $FeO_2 \backslash SpO_2$ data for two experiments. The two experiments describe a patient with left sided heart failure before (crosses to the right, red) and after (crosses to the left, blue) diuretic therapy.

Curves constructed using mathematical models of oxygen transport can also be displayed on the $FeO_2 \backslash SpO_2$ plot, by ticking the "show calculated curve on graph" box. To do so the user must first select between two mathematical models of oxygen transport containing parameters describing either pulmonary shunt (shuntf) and ventilation perfusion (V/Q) mismatch (fA2) (Figure 2b) [17], or pulmonary shunt (shuntr) and oxygen diffusion resistance (Rdiff) (Figure 2a) [4,13]. A curve is constructed using the selected mathematical model and the parameter values displayed on the data sheet. Parameter values may be typed in by the user or estimated by ALPE by clicking on the "Calculate Parameters" button of the patient summary screen. The mathematical model currently selected is then fitted to the experimental data using a least squares method.

For the five normal subjects the values of model parameters estimated by ALPE were (mean $\pm$ SD) shuntf = $4.95\% \pm 2.64\%$, fA2 = 0.89 ± 0.007 , shuntr = $6.75\% \pm 1.29\%$, Rdiff = $-1.14 \text{ kPa/(l/min)} \pm 1.57 \text{ kPa/(l/min)}$. A pulmonary shunt of about 5% is consistent with that found previously for normal healthy subjects [4]. fA2 ≈ 0.90 , or Rdiff $\approx 0 \text{ kPa/(l/min)}$ illustrates the absence of any ventilation perfusion mismatch or resistance to oxygen diffusion abnormality in normal healthy subjects. For one of the two patient with left sided heart failure, (i.e., the patient illustrated in Figure 4) parameter values were estimated to be shuntf = 11.50%, fA2 = 0.41, shuntr = 11.0%, Rdiff = 12.0 kPa/(l/min) prior to diuretic therapy and shuntf = 11.51%, fA2 = 0.71, shuntr = 11.55%, Rdiff = 6.3 kPa/(l/min) following therapy. This improvement in lung parameters was consistent with the patient's clinical improvement and 2 kg reduction in weight. For the second patient parameter values were estimated to be shuntf = 11.61%, fA2 = 0.55, shuntr = 11.00%, Rdiff = 8.50 kPa/(l/min)

prior to diuretic therapy and $\text{shuntf} = 11.22\%$, $\text{fA2} = 0.49$, $\text{shuntr} = 11.5\%$, $\text{Rdiff} = 10.5 \text{ kPa/(l/min)}$ after therapy. The lack of improvement in lung parameters was consistent with a lack of clinical improvement and a 0.9 kg increase in weight in this patient.

DISCUSSION

This paper describes the Automatic Lung Parameter Estimator (ALPE) system. The ALPE system enables estimation of pulmonary gas exchange parameters from a simple procedure where FiO_2 is varied in 4–6 steps giving SpO_2 in the range 90–100%. The ALPE system uses only routinely available non-invasive clinical measurements of ventilation and blood oxygenation requiring the patient to breath normally through a mask and wear a pulse-oximeter.

The ALPE system contains features for: indicating when the patients' oxygen system is in steady state and hence when a measurement should be taken; providing quality control checks; automatically recording data; and enabling on-line estimation of pulmonary gas exchange parameters. In addition by performing several FiO_2 titrations on the same patient the results of therapeutic intervention can be monitored, both qualitatively, from the shape and position of the $\text{FeO}_2/\text{SpO}_2$ curve, and quantitatively from the values of pulmonary gas exchange parameters before and after the intervention. This is illustrated in Figure 4 which shows the effects of diuretic therapy on pulmonary gas exchange in a patient with heart failure.

The ALPE system includes two models of pulmonary gas exchange including parameters describing either the fraction of blood involved in gas exchange i.e., shunt plus a ventilation/perfusion mismatch abnormality, or shunt plus a resistance to oxygen diffusion from the lungs to the lung capillary blood. These models have been shown to provide a good fit to data similar to that generated by the ALPE system in patients following surgery [4–6, 14, 15, 17] and in patients with heart failure [2]. The two different models have been shown to give an almost identical fit to the data [17, 21], with both being included in the system so that the user can select the preferred model by which ALPE analyses the data. It has been shown using the Multiple Inert Gas Elimination Technique (MIGET) [22] that in the majority of cases the V/Q model is probably a better representation of the true physiological picture, such that an oxygen diffusion abnormality is seldom required to explain pulmonary gas exchange problems [23–25] except in cases of pulmonary fibrosis [25], exercise [26], or mild exercise during hypoxia [26, 27].

The ALPE system gives a substantial improvement in speed when compared to the studies of Andreassen [4], Rees [16], and Kjærgaard [17] estimating parameters of pulmonary gas exchange. In those studies it took some 30–40 minutes to study a single patient, estimating parameters off-line. This was largely due to the time after each change in FiO_2 to ensure that the patients' oxygen system was in steady state. By using the ALPE system all data are collected automatically and oxygen equilibrium is monitored. In most cases only 2–3 minutes are required to reach steady state after FiO_2 perturbation, meaning that the ALPE system can obtain estimates of pulmonary gas exchange parameters in 10–15 minutes.

The ALPE system could have application in numerous clinical environments and patient groups. In the intensive care unit, the ALPE system could be incorporated into the ventilator, giving routine access to parameters describing pulmonary gas exchange along with the more commonly reported parameters describing lung mechanics. In the post-surgical recovery room the ALPE system could be used to assess gas exchange abnormalities in patients following surgery. Hypoxaemia is common following major surgery both immediately [5, 28] and several days following surgery [29–31]. Use of the system in a simple 10–15 minutes procedure in the recovery room might then help to assess the risk of hypoxaemia in patients returning to the ward. Patients with poor lung parameters could then be supplemented with oxygen at the ward. In the cardiology department Malcynski et al. [2] have shown that the V/Q mismatch model included in the ALPE system can characterise the pulmonary gas exchange problems seen in patients with pulmonary congestion caused by left-sided heart failure both prior to and during therapy. As illustrated in Figure 4 the ALPE system could be used to monitor the effects of diuretic therapy, helping the clinician to give the minimum required dosage so as to normalise lung function without dehydrating the patient.

The current version of ALPE does not provide information as to the precision of the estimates of shunt and fA2 . In future ALPE should be developed to estimate these parameters as distributions rather than single values, using Bayesian statistics. In this way estimation of shunt or fA2 with narrow distributions would illustrate a high level of precision. In addition, the current version of ALPE is restricted to a maximum respiratory frequency of 30 breaths/minute. In future ALPE should be developed to allow use of the system at higher breathing rates.

The ALPE system is intended to be a clinical tool, estimating pulmonary gas exchange parameters quickly

from non-invasive measurements. As such this system should not be used to investigate detailed physiology. Where this is required experimental techniques such as the Multiple Inert Gas Elimination Technique (MIGET) [22], which has a somewhat limited use in a clinical environment [32], should be used. Despite this, the ALPE system can be seen as a substantial improvement over the current clinical standard i.e., that of estimating effective shunt [8,9] and appears to have a wide range of clinical applications.

In future, several improvements could be made to the ALPE system to simplify its construction and application. For application in surgical recovery rooms and cardiology departments the system should include only part of the functionality of the ventilator and gas analyser, i.e., excluding the multiple ventilator modes and varying pressure settings available on modern ventilators, and eliminating the measurement of gases other than O_2 and CO_2 . In addition, the ALPE system could be developed to perform the experiment automatically, by automatically varying FiO_2 , monitoring oxygen equilibrium, recording measurements and estimating parameters.

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