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Assessment of lung function using a non-invasive oscillating gas-forcing technique☆

Lei Clifton[a,b,*], David A. Clifton[b], Clive E.W. Hahn[a], Andrew D. Farmery[a]

[a] Nuffield Division of Anaesthetics, Nuffield Department of Clinical Neurosciences, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU, UK
[b] Institute of Biomedical Engineering, Department of Engineering Science, University of Oxford, Old Road Campus, Roosevelt Drive, Oxford OX3 7DQ, UK

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ABSTRACT

Conventional methods for monitoring lung function can require complex, or special, gas analysers, and may therefore not be practical in clinical areas such as the intensive care unit (ICU) or operating theatre. The system proposed in this article is a compact and non-invasive system for the measurement and monitoring of lung variables, such as alveolar volume, airway dead space, and pulmonary blood flow. In contrast with conventional methods, the compact apparatus and non-invasive nature of the proposed method could eventually allow it to be used in the ICU, as well as in general clinical settings. We also propose a novel tidal ventilation model using a non-invasive oscillating gas-forcing technique, where both nitrous oxide and oxygen are used as indicator gases. Experimental results are obtained from healthy volunteers, and are compared with those obtained using a conventional continuous ventilation model. Our findings show that the proposed technique can be used to assess lung function, and has several advantages over conventional methods such as compact and portable apparatus, easy usage, and quick estimation of cardiopulmonary variables.

1. Introduction

Patients in the intensive care unit (ICU) often require mechanical ventilatory support using positive pressure ventilation (Rouby et al., 2004). Estimation of lung variables benefits these patients because they help the clinician to determine the most suitable values in therapeutic measures such as positive end-expired pressure (PEEP). They could also help to avoid the common problem of ventilator induced lung injury (VILI). Three key lung variables are:

1. alveolar volume at the end of an expiration, V_A
2. airway dead space volume, V_D
3. pulmonary blood flow, $\dot{Q}_P$

Current techniques for measuring these variables can require the cooperation of the patient, or a modification of the patient's ventilator system. ICU patients depend on complex life support and monitoring equipment, and thus are usually unable to cooperate with the physician. These patients are therefore some of the most difficult to assess using conventional lung function tests.

Zwart et al. pioneered the non-invasive oscillating gas-forcing technique (Zwart et al., 1976, 1978), and used halothane as the forcing gas at a very low concentration (around 0.02, v/v) to measure the average ventilation-perfusion ratio ($\dot{V}/\dot{Q}$) in the lung. Hahn et al. further developed this method by using biologically inert gases such as nitrous oxide (N_2O) and argon (instead of halothane) to measure V_A, V_D, and $\dot{Q}_P$ non-invasively (Hahn et al., 1993; Williams et al., 1994). They later proposed that oxygen (O_2) can be used to measure V_A and V_D (Hahn, 1996; Hamilton, 1998). When O_2 was used together with N_2O, their model can also be used to measure $\dot{Q}_P$. However, their initial technique required a respiratory mass spectrometer that presented considerable difficulty when used in the ICU due to its size, noise, complexity, high maintenance requirements, and lack of portability (Farmery, 2008). Moreover, their prototype gas mixer is not compatible with modern ICU ventilators. There was therefore a clinical need to design a new system to deliver indicator gases according to the patient's breathing flow rates in real time.

A conventional existing model based on continuous ventilation is described in Section 2; we propose a novel non-invasive method for estimating the cardiopulmonary variables, V_A, V_D, and $\dot{Q}_P$ in Section 3. Indicator gases O_2 and N_2O are injected into the patient's

* Corresponding author at: Institute of Biomedical Engineering, Department of Engineering Science, University of Oxford, Old Road Campus, Roosevelt Drive, Oxford OX3 7DQ, UK. Tel.: +44 01865 617670.
E-mail addresses: lei.clifton@eng.ox.ac.uk (L. Clifton), david.clifton@eng.ox.ac.uk (D.A. Clifton), clive.hahn@ndcn.ox.ac.uk (C.E.W. Hahn), andrew.farmery@ndcn.ox.ac.uk (A.D. Farmery).

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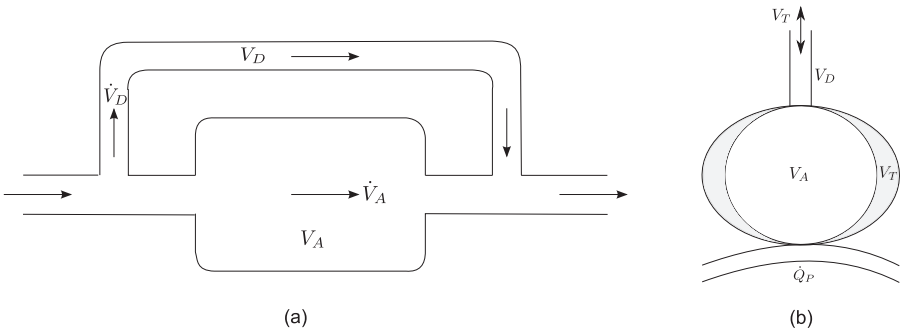

Fig. 1. Schematic diagrams for a continuous ventilation model and the breath-by-breath "balloon-on-a-straw" tidal ventilation model, shown in (a) and (b), respectively. Whereas the traditional continuous ventilation model regards the lung as a box of a rigid volume with a continuous flow passing through it, and a parallel dead space also with a continuous flow, the tidal ventilation model, has a volume V_A at the end of an expiration and which expands to volume $V_A + V_T$ at the end of an inspiration. The inspired gas enters the dead space of volume V_D before entering the lung, and the expired gas travels through the dead space before entering the mouth. Gas enters and leaves the lung at flow rate $\dot{V}(t)$ at time t.

airway breath-by-breath "on the fly" to make the concentration of these gases vary sinusoidally in the inspired gas. The apparatus is compact in size and is portable, consisting of a flow rate sensor, a gas concentration sensor, and two mass flow controllers (MFCs). We improve the original Bohr equation for dead space calculation in Section 4. Results obtained using the proposed single alveolar compartment tidal ventilation model are compared with those obtained using the continuous ventilation model in Section 5. A discussion is presented in Section 6, and conclusions are drawn in Section 7. A list of abbreviations can be found in the appendix.

2. The continuous ventilation model

The continuous ventilation model (Zwart et al., 1976; Hahn et al., 1993; Hahn, 1996; Williams et al., 1994), as shown in Fig. 1(a), treats the lung as a rigid volume with a constant and continuous flow passing through it. Dead space is regarded as a tube of negligible volume parallel to the lung, with another constant flow passing though it. The inspired concentration of an indicator gas $F_I(t)$ is controlled by a gas mixing apparatus, and is forced to vary sinusoidally at a chosen frequency.

$$F_I(t) = M_I + \Delta F_I \sin(2\pi f t + \phi), \tag{1}$$

where M_I and ΔF_I are the mean and amplitude of the forcing indicator gas sinusoid, respectively, f is the forcing frequency in min^{-1}, and ϕ is the phase of the sine wave.

In the absence of venous recirculation, and assuming that the inspired indicator gas concentration is in equilibrium in all tissues throughout the respiratory and cardiovascular systems, the mixed-expired and end-expired (i.e., alveolar) indicator gas concentrations are also forced to be sinusoidal (Zwart et al., 1976; Hahn et al., 1993; Williams et al., 1994).

Let F_A be the indicator gas concentration in the alveolar compartments of the lung, and ΔF_A be the amplitude of F_A measured from its mean; we therefore have (Hahn et al., 1993)

$$\frac{\Delta F_A}{\Delta F_I} = \frac{1}{\sqrt{\left(1 + \lambda_b(\dot{Q}_P/\dot{V}_A)\right)^2 + \omega^2\tau^2}} \tag{2}$$

in which λ_b is the blood-gas solubility coefficient; note that $\lambda_b = 0.03$ for O_2, and $\lambda_b = 0.47$ for N_2O. ω is the forcing frequency in radians; i.e., $\omega = 2\pi f$. τ is the lung ventilatory time constant,

$$\tau = \frac{V'_A}{\dot{V}_A}, \tag{3}$$

where V'_A is the *effective* lung volume given by (4) below, and $\dot{V}_A$ is the ventilation rate in L/min (Gavaghan and Hahn, 1995). The relationship is given by

$$V'_A = V_A + \lambda_b V_{bl} + \lambda_{tl} V_{tl}, \tag{4}$$

where V_{bl} is the volume of blood in the lung, V_{tl} is the volume of lung tissue, and λ_{tl} is the lung tissue-gas partition coefficient. Indicator gas O_2 can be approximately regarded as a non-soluble gas with $\lambda_b \approx 0$ and $\lambda_{tl} \approx 0$, hence $V'_A = V_A$. Therefore, τ for O_2 is

$$\tau_{O_2} \approx \frac{V_A}{\dot{V}_A}, \tag{5}$$

For the soluble gas N_2O, using the values of the above variables given in Gavaghan and Hahn (1995), (4) can be re-written as $V'_A = V_A + 0.43$. Therefore τ for N_2O is

$$\tau_{N_2O} = \frac{V_A + 0.43}{\dot{V}_A}. \tag{6}$$

We can express the ventilation rate $\dot{V}_A$ by (Williams et al., 1994)

$$\dot{V}_A = R(V_T - V_D), \tag{7}$$

where R is the respiration rate in breaths/min, V_T is the tidal volume, and V_D is the airway dead space volume.

At high frequencies ω, the term $\omega^2\tau^2$ dominates the denominator in (2), therefore allowing τ to be estimated using

$$\frac{\Delta F_A}{\Delta F_I} \to \frac{1}{\omega\tau}, \tag{8}$$

where ΔF_A, ΔF_I, and ω are known values. The estimated τ is then subsequently used to determine lung volume V_A using (3) and (4).

Conversely, at low values of ω, the term $\lambda_b \frac{\dot{Q}_P}{\dot{V}_A}$ dominates the denominator in (2), and therefore reveals information concerning $\dot{Q}_P$. This indicates that careful selection of ω allows the variable determination of both lung volume V_A and lung perfusion $\dot{Q}_P$.

Hahn et al. (1993) found that the forcing sinusoidal frequency should be $f > 1\ \text{min}^{-1}$, when N_2O is used as the forcing gas.

Lung volume V_A derived from a continuous ventilation model is greater than the actual V_A, due to the assumption that V_A is constant. In reality, the lung volume including dead space volume V_D varies tidally between $(V_A + V_D)$ at the beginning of inspiration and $(V_A + V_D + V_T)$ at the end of inspiration. Sainsbury et al. (1997) showed that subtracting a correction term V_c from the lung volume determined by the continuous ventilation model produces a more realistic estimate of the lung volume,

$$V_c = \frac{1}{2}(V_T + V_D) \tag{9}$$