INTRODUCTION

• Qualitative assessment of lung function has been shown to be feasible using oxygen-enhanced MRI (OE-MRI) in which hyperoxia is used to induce signal change in the lung parenchyma as a result of the paramagnetic effect of dissolved oxygen [1]. However, there has been little attempt to date to relate the observed OE-MRI signal directly to physiological parameters indicative of lung function [2]. Here, by consideration of gas exchange processes in the lung we present a two-compartment mathematical model to relate the observed signal change during a dynamic OE-MRI experiment with the ventilation-perfusion ratio V/Q.

TWO COMPARTMENT MODEL

• For the purpose of describing oxygen exchange within a unit volume lung parenchyma, we consider two compartments. The first is the gaseous space within the alveolus and the second is the parenchymal water within tissues and blood within alveolar capillaries. In the first compartment oxygen exists in a gaseous state, in the second we must consider both the oxygen dissolved in water and blood plasma and that bound to haemoglobin.

Two-COMPARTMENT Model

Figure 1 presents a schematic diagram of the model. \( V_i, V_A \) are the inspired and expired alveolar ventilations (ml gas/min/ml lung); \( F_{\text{O}_2}, F_{\text{A}_2} \) are the fractional inspired and alveolar oxygen concentrations; \( P_{\text{A}_2}, P_{\text{WO}_2} \) are the alveolar partial pressures of oxygen in the alveolar and in the capillary blood and parenchymal tissue water space (mm Hg); \( \Delta P_{\text{WO}_2} \) is the diffusing capacity of the alveolar membrane to oxygen (ml O₂/min/mm Hg/ml lung); \( V_{\text{O}_2} \) is the oxygen transfer across the membrane (ml O₂/min/ml lung), \( Q \) is the capillary blood flow (ml blood/min/ml lung), \( C_{\text{cO}_2} \) is the systemic venous oxygen concentration (ml gas/ml blood), \( C_{\text{vO}_2} \) is the end-capillary oxygen concentration (ml gas/ml blood). We assume the two compartments are instantaneously well-mixed with respect to oxygen. In the second compartment this assumption neglects diffusion gradients within the tissue water space and across the tissue-capillary membranes. Mixed-venous blood in the capillary is assumed to equilibrate rapidly with the compartment on entering. In the first compartment, in equilibrium, the net input of oxygen into the space due to ventilation is balanced by the net transfer of oxygen across the alveolar membrane into the second compartment.

\[
\frac{dF_{\text{A}_2}}{dt} = VA(F_{\text{O}_2} - F_{\text{A}_2}) - DM_{O_2}(P_{\text{A}_2} - P_{\text{WO}_2}) \tag{1}
\]

which may be rewritten,

\[
\frac{dP_{\text{A}_2}}{dt} = VA \left( F_{\text{O}_2} - \frac{P_{\text{A}_2}}{P_{\text{B}_2}} \right) - DM_{O_2}(P_{\text{A}_2} - P_{\text{WO}_2}) \tag{2}
\]

by substituting the alveolar fractional oxygen concentration by the alveolar partial pressure of oxygen \( P_{\text{A}_2} \) is the barometric pressure minus water vapour pressure, \( V_A \) is the fractional alveolar volume). The diffusing capacity of the membrane is determined by the diffusion coefficient and solubility of oxygen in the solvent of the membrane (i.e. water), and the surface area per unit volume and thickness of the membrane. In the second compartment, in equilibrium, the transfer of oxygen across the alveolar membrane is balanced by the net removal of oxygen in the blood, determined by the difference in end-capillary and systemic venous oxygen contents and the capillary blood flow. (We neglect metabolism by the lung parenchyma, estimated at 5% of the whole-body metabolism [3], but note that if included, as long as it remained constant, it would not affect the final result.) If the system is not in equilibrium, the rate of change of the oxygen concentration \( C_{\text{vO}_2} \) in compartment 2 (with fractional volume \( v_w \)) is given:

\[
\frac{dC_{\text{vO}_2}}{dt} = DM_{O_2}(P_{\text{A}_2} - P_{\text{WO}_2}) - Q(C_{\text{cO}_2} - C_{\text{vO}_2}) \tag{3}
\]

where we rewrite in terms of partial pressure,

\[
\alpha' C_{\text{vO}_2} \frac{dP_{\text{WO}_2}}{dt} = DM_{O_2}(P_{\text{A}_2} - P_{\text{WO}_2}) - Q(C_{\text{cO}_2} + \beta_0 P_{\text{WO}_2} - C_{\text{vO}_2}) \tag{4}
\]

by: 1. representing the oxygen content of blood at a partial pressure \( P_{\text{A}_2} \) as \( C_{\text{PO}_2} = C_0 + \alpha P_{\text{O}_2} \) where the oxygen solubility in blood \( \beta_0 \) is the gradient of the oxygen content curve (according to the haemoglobin dissociation curve) evaluated at the partial pressure \( P_{\text{O}_2} \) and \( C_0 \) is the extrapolation to zero pressure as illustrated in fig. 2. (Note that both \( \beta_0 \) and \( C_0 \) depend on the partial pressure); 2. similarly representing the oxygen exchange in the capillary plus tissue water compartment, \( C_{\text{cO}_2} = \alpha C_{\text{cO}_2} + \beta_0 P_{\text{WO}_2} \) with \( f_{\text{w},c} \) and \( f_{\text{w},h} \) the fractions of water and whole blood respectively in this compartment and \( \alpha_{\text{cO}_2} \) the solubility of oxygen in water; 3. making the approximation that for the change in partial pressure that we are modelling (i.e over the course of the OE-MRI study) the time-varying solubility \( \beta_0 \) may be approximated by its average value (such that \( \beta_0 \) and \( C_0 \) are constant over time); 4. defining \( \alpha_{\text{cO}_2} = f_{\text{w},c} \beta_0 f_{\text{w},h} \); Equations (2) and (4) form coupled equations for the rate of change of partial pressure in the two compartments under the assumptions outlined.

Diffusion across the alveolar membrane is rapid such that equilibration between alveolar and capillary partial pressures occurs in a time that is short compared to the capillary mean transit time (of around 0.75 s). This remains true in disease for diffusion impairments down to around ¼ of normal values [4] and for a wide range of VA/Q ratios. This means that while the end capillary oxygen partial pressure may be low compared to normal values due to pathology (and end-capillary haemoglobin may be significantly below normal values) it remains true in disease for diffusion impairments down to around ¼ of normal values [4] and for a wide range of VA/Q ratios. This means that while the end capillary oxygen partial pressure may be low compared to normal values due to pathology (and end-capillary haemoglobin may be significantly below normal values) it remains true in disease for diffusion impairments down to around ¼ of normal values [4] and for a wide range of VA/Q ratios.