A Compartmental Model for Oxygen-Enhanced Magnetic Resonance Imaging of the Lung

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INTRODUCTION

Dissolved oxygen can be used as a contrast agent in MRI due to the paramagnetic properties of the oxygen molecule, which causes a decrease in the T_1 of water protons which is proportional to the dissolved oxygen concentration. Oxygen enhanced MRI (OE-MRI) has been used to assess lung function by measuring the enhancement ratio between breathing air and 100% oxygen, and also by measuring the time to saturation of the increased signal effect, i.e. the oxygen wash-in rate, and also the oxygen wash-out rate. Wash-in and out time constants have been estimated using a generalised exponential fit (1). However these constants give combined information on lung ventilation, diffusion and perfusion which is difficult to interpret. Using a compartmental modelling approach similar to that used in dynamic contrast enhanced MRI allows the extraction of parameters from the enhancement information, which give more specific information on local ventilation, diffusion and perfusion. Equations to describe the rate of diffusion of gases across the alveolus membrane to pulmonary capillary blood were first formulated by Kety (2). Many workers have extended his two compartment model to other applications to model the rate of diffusion of contrast agents across capillary membranes into the intra and extra vascular spaces of tissues and tumours (3). We have applied the two compartment model to OE-MRI data by treating the administered 100% oxygen as a contrast agent, with an appropriate input function. The first compartment is the alveolus space with oxygen concentration denoted by C_A, and the second includes the alveolus membrane, interstitial space between the membrane and pulmonary capillaries and the plasma within the capillaries, with a combined oxygen concentration denoted by C_p, see Fig. 1. If we assume near saturation of oxygen in arterial haemoglobin during air breathing, the increased oxygen concentration in blood during 100% oxygen breathing will be carried mainly in the plasma. In lung the increased signal occurs in the parenchymal water and capillary blood, and therefore the measured increased concentration $C_e\left(\propto\left|\left(T_1^{O_2}\right)^{-1}-\left(T_1^{Air}\right)^{-1}\right|\right)$ can be considered equivalent to C_p. Using these approximations we can write equation 1 where V_p is the fractional volume of blood plasma and tissue water per MRI visible tissue, K^{diff} is a term describing the diffusing capacity of the alveolar membrane, E is the extraction fraction of oxygen from the tissue water and capillaries, and F_b is the rate of blood flow in the capillaries. We can solve for C_p using equation 2. Although K^{diff} in theory describes the diffusing properties of the membrane, in practice it will also reflect the variable ventilation across regions of the lung and between individuals. We present some initial values for E^*F_b and K^{diff} from regions of interest calculations and also parameter maps from the whole lung.

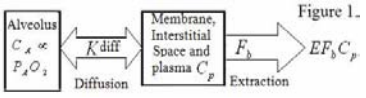

Figure 1.

$$V_p\frac{dC_p}{dt}=K^{diff}(C_A-C_p)-EF_bC_p \quad \text{Eqn. 1}$$

$$C_p=\frac{K^{diff}}{V_p}\int C_A(\tau)\exp\left(-\frac{K^{diff}+EF_b}{V_p}(t-\tau)\right)d\tau \quad \text{Eqn. 2}$$

METHODS

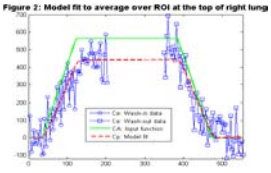
Figure 2: Model fit to average over ROI at the top of right lung

The images used in this study (1) were obtained from five normal consented volunteers, (two males, three females, ages 30-39), using a 1.5T Philips Gyroscan NT Integra MR system (Philips Medical Systems, Best, Netherlands). Subjects breathed medical air or 100% oxygen through an MR compatible Bain breathing system (Intersurgical Ltd., Wokingham, UK) and tightly fitting mask. A standard anaesthesia trolley (10 l/min capability) was used. A first set of images was acquired in order to measure T_1 during air-breathing. A half Fourier single shot turbo spin-echo (HASTE) sequence was used with 68 phase encoding steps and inter-echo spacing of 4ms, effective echo time 16ms, 128×128 matrix with field of view 450mm, coronal section with slice thickness 10mm. T_1 measurements were performed using a saturation recovery HASTE sequence with saturation times (T_{SAT}) of 100, 200, 400, 800, 1200, 1700, 2300, 3000, 3500 ms. Five images were collected for each saturation time to enable averaging over the cardiac cycle. Saturation recovery (SR) was chosen here to give a shorter total imaging time. Next, dynamic image acquisitions were performed using an IR HASTE sequence with an inversion time of 720ms (chosen to approximately null the signal from the lungs while breathing air (1)). The gas supply was switched from medical air to 100% oxygen after the tenth image in the series. A set of T_1 measurement SR images was acquired while the subject continued to breathe 100% oxygen. Finally a second series of dynamic images was acquired with the gas supply being switched back to medical air after the tenth image. For registration an active shape model (4) was used to characterize normal breathing motion and then to allow the automated identification of the outline of the lung.

$$S(T_{SAT}) = A - B\exp\left(-\frac{T_{SAT}}{T_1}\right) \quad \text{Eqn. 3}$$

The lung shapes were then transformed to an average shape using linear re-sampling. T_1 maps were calculated for air and oxygen breathing by fitting the saturation recovery images to equation 3 using a Levenberg-Marquardt fitting algorithm. To convert the dynamic signal intensity data to increase in dissolved oxygen concentration above air-breathing, the values were first converted to T_1 values using book-ending from the T_1 maps (8). They were then converted to R_1 by inversion, the baseline air-breathing R_1 was subtracted, and finally the values converted to PO_2 (mmHg) by division by the known constant r_1=4×10^{-4} s^{-1}mmHg^{-1} (5). The oxygen input function was estimated from the known ratios of alveolar gas partial pressures (6). Alveolar PO_2 (PAO_2) during air-breathing is typically 104mmHg, and during 100% oxygen breathing at an atmospheric pressure of 760mmHg it can be estimated at 665mmHg. Hence the difference in PAO_2 over air breathing can be approximated as 561mmHg. The rate of replacement of air in the lungs is typically estimated as 7.5% per breath. At rest one takes an average of one breath per 5 seconds, and therefore it takes on average approximately 1 minute for all air to be replaced. This was reflected in the sloping edges of the estimated PAO_2 input function (see Fig. 2). According to varying individual lung capacity and the position within the lung, it was found that the delay time to maximum PAO_2 required optimization. Using a Levenberg-Marquardt fitting algorithm and assuming a V_p fraction of 1, equation 2 was solved for E^*F_b and K^{diff} for averages over regions of interest at the top of each lung (see table 1). The delay time to maximum PAO_2 was a third free parameter in the fit. Parameter maps were also calculated (see Fig. 3). The values of E^*F_b were converted to standard units (ml/min/ml) presuming a lung density of 0.15g/ml near the lung periphery (7)

RESULTS

Table 1 Subject	Lung	E^*F_b (ml/min/ml)	K^{diff} (ml/min/g)	CA_{max} Delay (s)
1	Left	1.2677	4.1431	66
	Right	0.8015	3.5409	68
2	Left	1.0762	2.3612	44
	Right	1.3007	1.7382	42
3	Left	1.0106	17.5859	128
	Right	1.1345	17.0257	75
4	Left	1.3892	5.6615	53
	Right	0.7018	14.8614	61
5	Left	1.2639	0.8860	140
	Right	1.0402	19.4285	83

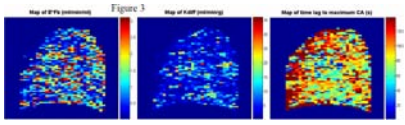
Figure 3

If we assume an extraction fraction E of 1, the F_b values given in table 1 are consistent with literature quoted values for lung perfusion (7). The diffusion-ventilation measures obtained in K^{diff} varied considerably between individuals but were mainly consistent between both lungs in each individual. The parameter E^*Fb (Fig. 3) illustrates variation over the right lung slice area with less perfusion towards the edges and top of the lung and larger values corresponding to the main pulmonary vessels in the centre. The K^{diff} parameter map shows stronger ventilation-diffusion in the centre lung but the peripheral values are more uniform to the lung edges than in the E^*F_b map. The map of time lag to maximum CA shows shorter times in the centre lung and longer times at the periphery.

DISCUSSION AND CONCLUSION

We have presented a compartmental model which allows direct assessment of pulmonary diffusion and ventilation using OE-MRI, and which may be used to detect regions of impaired ventilation or perfusion when applied to patient groups.

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