Determination of T1-Dependence on Oxygenation in the Eye Using a Simple Phantom Model

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Aims: 1. To prepare a phantom (test object) that can relate T_1 to dissolved oxygen concentration (pO_2) in the vitreous humour of the eye. 2. To perform accurate and precise measurements of temperature and pO_2 without modifying the phantom during the measurement procedure.

Background: Oxygenation of the vitreous humour (the clear gel between the lens and the retina) of the eye is suspected to be reduced in various eye conditions such as retinal vascular disease and diabetic retinopathy. A therapy for these diseases is vitrectomy, where the vitreous humour is replaced with a balanced salt solution (BSS) of $CaCl_2$, $MgCl_2$, NaCl, KCl and $C_6H_5Na_3O_7$. Although the partial pressure of oxygen (pO_2) may be measured *during* vitrectomy (using an intraocular probe), there has been no direct evidence of an increase in pO_2 after the procedure. MRI provides a non-invasive method of measuring pO_2 in the eye [1] since T_1 relaxation times are decreased by the presence of paramagnetic O_2 [2-4]. However, since the changes in T_1 are subtle, a precise relationship between T_1 and pO_2 needs to be determined [5]. Here, we describe the preparation and use of a pO_2 phantom that quantifies the change in T_1 expected for a given change in pO_2 in the vitreous.

Methods: *Phantom Preparation.* The phantom (test object) was a glass bottle (500 ml volume) filled with BSS, which approximates the composition of the vitreous humour. The BSS was deoxygenated (pO_2 < 5 mmHg) by bubbling with nitrogen gas using a sinter for approximately 2 min. The bottle was sealed and vigorously shaken for up to 5 min to establish pO_2 equilibrium between the airspace above the solution and the BBS itself. An optical fluorescence fibre optic pO_2 sensor (Oxford Optronix Ltd) was used to independently measure oxygenation. To restrict the unwanted ingress of air to the bottles, the probe was delivered to the liquid via a syringe needle (1-mm diameter) that was inserted through the rubber bung on the bottle. After measurement, the probe and syringe needle were removed to reseal the bottle. The phantom was placed in a polystyrene water bath and the temperature of the BSS was measured using a thermometer sealed in the bottle. The water bath temperature was also monitored and kept constant by adding hot water when necessary. The pO_2 was measured with the fibre optic probe before and after scanning to identify any change in pO_2 during the T_1 measurement process.

The pO_2 of the BSS was intentionally increased between successive T_1 measurements by removing the rubber bung to allow air to enter the bottle. The bottle was then resealed and vigorously shaken to re-establish equilibrium of pO_2 between the air and liquid. In this way, T_1 was measured on BSS phantoms with pO_2 ranging from 5 mmHg to 80 mmHg for two temperatures: 21°C (room-) and 37°C (body- temperature).

Scanning Protocol. Phantoms were imaged with a Siemens Avanto 1.5 T scanner. T_1 mapping was performed using an inversion recovery (IR)-trueFISP sequence with 17 inversion times in the range TI=0.7s – 30s. A single slice was positioned through the centre of the phantom in the axial orientation. Other trueFISP parameters were: TR=(20+TI) s, TE = 1.52 ms, FA = 80°, matrix = 256x256, voxel dimensions = 0.9x0.9x4 mm^3. The total scan time for T_1 measurement was 15 mins [4]. T1 mapping was achieved by performing a pixel-by-pixel three-parameter fit of the signal intensity S (at each TI) to the equation $S(TI) = A + Be^{-TI/T1}$; A and B are parameters that account for inversion pulse flip angle FA, equilibrium signal intensity and TR. Since FA is included, the technique is resilient to B_1 errors.

Results: The measurement of pO_2 (with the fibre optic probe) before and after the T_1 measurement showed pO_2 changed by less than 1 mmHg. T_1 was measured with an uncertainty of ±40 ms. The plot of relaxation rate R_1 ($R_1=1/T_1$) against measured pO_2 is linear (Fig. 1, R^2>0.91) for both temperatures. The data may be expressed by the equation $R_1 = A + BpO_2$, where A = 0.307 s^{-1}, B = 2.78 x 10^{-4} s^{-1} $mmHg^{-1}$ at 21°C and A = 0.205 s^{-1}, B = 2.68 x 10^{-4} s^{-1} $mmHg^{-1}$ at 37°C. The minor deviation from linearity seen in Fig 1b is due to a slight fluctuation in temperature as the water bath cooled. The slope of the body-temperature line can be used to calculate the change in pO_2 observed *in vivo* from a simple T1 measure with MRI.

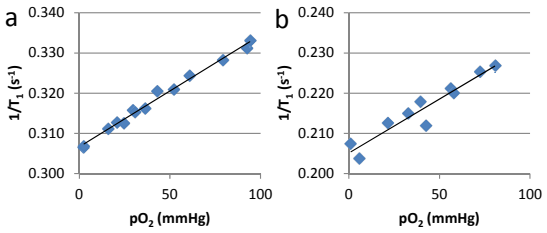

Figure 1 Plot of R_1 (=$1/T_1$) vs pO_2 for the BSS phantom at (a) room temperature, 21°C and (b) body temperature 37°C. The slope is used to determine pO_2 changes from T_1 measurements in the eye.

Conclusion: We have successfully developed a pO_2 phantom using a balanced salt solution similar to the vitreous humour of the human eye. By plotting R_1 against an independent measure of pO_2 we are able to define the relationship between T_1 and pO_2 to quantify changes in eye vitreous oxygenation using a non-invasive MRI procedure. This technique that will permit longitudinal eye oxygenation studies of, for example retinopathy or optic nerve and may help identify the therapeutic benefits of interventional procedures such as vitrectomy.

References: [1] Dowell *Proc. ISMRM* **2010**;2408, [2] Tofts *MRM* **2008**;59:190-195, [3] Berkowitz *MRM* **2001**;46:412-416, [4] Berkowitz *NMR Biomed* **2008**;21:957-967, [5] Zaharchuk *Acad. Radiol.* **2006**;13:1016-1024