# Imaging Vitreous Oxygen Tension with Rapid Look-Locker T1 Measurement and Calibration with Ex Vivo Eyes

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**INTRODUCTION:** Abnormal vitreal oxygen tension has been implicated in a number of ocular and retinal diseases, such as diabetic retinopathy and nuclear cataract of the lens (1,2). Oxygen content of the vitreous can be measured in animals using invasive techniques that require inserting probes into the eye, and which cannot be used in humans. MRI could potentially be used to non-invasively map oxygen tension of the vitreous, which is 99% water, using the T1 of water which is inversely proportion to oxygen concentration (3), providing unique information on ocular physiology that would otherwise be impossible to obtain in humans.

The aim of this study was to develop and calibrate MRI methods to non-invasively measure the partial pressure of oxygen (pO2) in the human vitreous using the Look-Locker sequence which can measure T1 much more rapidly than standard T1 measurements. Rapid T1 measurement is important for imaging the eye which is prone to movement over long periods of time vitreous. Calibration of T1 to pO2 was made using ex vivo vitreous in addition to water phantoms with the aim of providing more accurate pO2 calculation from T1.

**METHODS:** Phantoms were made using distilled water bubbled with nitrogen to various pO2 and sealed in glass vials (n=10). pO2 (mmHg) of the phantoms was measured using an oxygen-sensitive fiber optic probe (Oxylab, Oxford Optronics) before and after MRI. Ex vivo eyes from a rabbit and a baboon (n=2) were obtained at the time of euthanasia and kept in saline with MRI performed within 12 hours. After MRI, the fiber optic probe was inserted into the vitreous to measure pO2. The phantoms and eyes were imaged together in a chamber with circulating heated water to 37° C. MRI studies were performed on a 3T Philips Achieva. An 8 channel head coil was used to receive. T1 measurements were made using a Look-Locker sequence (4) with a spoiled gradient echo readout, in which all inversion times are readout after a single inversion pulse. Images at all inversion times were acquired in 2 shots with FOV=100x100mm, matrix=100x100, a single 6mm slice, TR/TE=6.6/3.2ms, FA=4°, 26 inversion times with a minimum TI=108ms and time between TI=264ms, 6-9 repetitions, and 20s between repetitions of the inversion pulse. A non-linear least squares fit using the equation in (4) was used to fit T1, M0, and the flip angle. Linear regression was used to determine the slope and intercept of R1 as a function of pO2 at 37°C, and to the find the slope of T1 as a function of temperature for each phantom (5).

Five experiments were performed on 3 normal human volunteers (2 male, 1 female, age 26-28). A custom-made receive-only surface coil (7cm diameter) was used. T1 measurements were made similar to the phantom with the following differences, matrix=168x167, a single 5mm axial slice, TR/TE~6.5/3.2ms, 21 inversion times with a minimum TI~64ms and time between TI~325ms, and 5 repetitions. During the data readout train (7s), the subjects were asked to fixate on a target without blinking and between readouts they could blink or close eyes as desired.

**RESULTS:** **Fig 1** shows T1 and M0 maps of phantoms and an ex vivo eye, showing the effect of oxygen on T1. **Fig 2** shows that R1 of distilled water was linearly dependent on pO2. The R1 of deoxygenated water was 0.205s$^{-1}$ and the relaxivity of pO2 was 2.05E-4 s$^{-1}$/mmHg at 37°C. Vitreous of the ex vivo eye was found to have slightly larger R1 than distilled water. Using the relaxivity of pO2 in water, R1 of deoxygenated vitreous was calculated to be 0.209s$^{-1}$. pO2 of in vivo vitreous was then calculated using pO2=(R1-0.209)/2.05E-4. **Fig 3** shows R1 and pO2 maps from 1 subject. Group average whole vitreous pO2 was 26.8±7.5mmHg. The group-average standard deviation of whole vitreous T1 across the 5 repetitions was 18.2ms, corresponding to 4.0mmHg.

**DISCUSSION:** Previous reports of vitreous pO2 measured by inserting electrodes or fiber optics into eyes of animals or humans undergoing eye surgery were 10-23mmHg (1,6), similar to the value we measured with MRI. The gel structure of the vitreous causes additional relaxation, which could explain the higher R1 in the ex vivo eye compared to phantom at the same pO2. Thus, a linear correction was made. Without correction with the ex vivo vitreous R1, our group average pO2 would be 49.2mmHg. A previous MRI study at 1.5T using only distilled water for calibration also calculated a higher vitreous pO2 of 63±34mmHg (3).

In conclusion, the use of a fast Look-Locker T1 measurement and ex vivo eyes for calibration provided accurate human vitreous pO2 that is comparable to reports using invasive oxygen electrodes. MRI can be used to non-invasively map oxygenation of the vitreous, providing unique information on ocular physiology that would otherwise be impossible to obtain in humans. Future studies will improve spatial resolution to map pO2 around the anterior chamber and lens.

**Reference:** 1) Holekamp et al, Am J Ophthalmol 2005, 139:302. 2) Berkowitz et al, Invest Ophthalmol Vis Sci 1999, 40:2100. 3) Zaharchuk et al, Acad Radiol 2006, 13:1016. 4) Brix et al, Magn Reson Imaging 1990, 8:351. 5) Nelson and Tung, Magn Reson Imaging 1987, 5:189. 6) Quiram et al, Retina 2007, 27:1090.

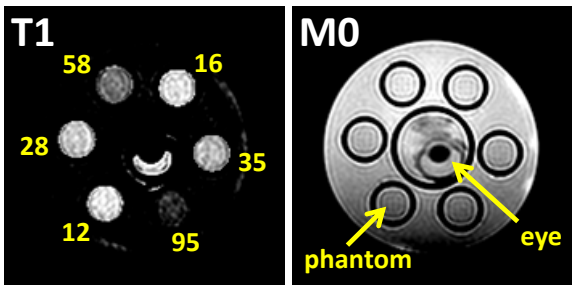


**Figure 1.** Fitted T1 and M0 maps used for calibration. A rabbit eye (in the center) and 6 phantoms (surrounding the eye) were placed in a chamber with warmed water. T1 is scaled from 4.4-4.87s. The numbers on the T1 map are the measured pO2 (mmHg) for each phantom from the fiber optic probe.

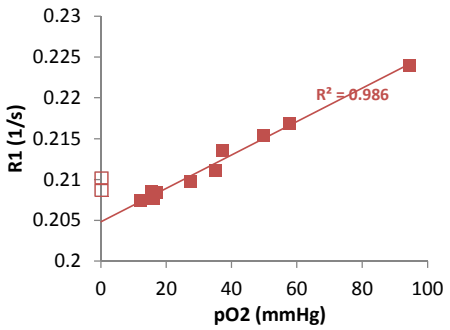


**Figure 2.** R1 vs. pO2 of distilled water phantoms (solid points) and vitreous (open points).

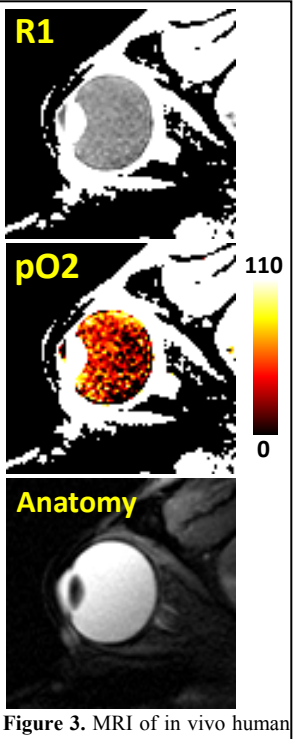


**Figure 3.** MRI of in vivo human eye showing R1 (s$^{-1}$, scaled 0.17-0.25s$^{-1}$), pO2 (mmHg), and anatomy.