

# Oxygen Enhancement of the Vitreous on FLAIR as a Marker of Retinal Oxygen Delivery

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**Introduction:** Retinal oxygenation is of clinical importance in a number of disease states, e.g. diabetic retinopathy. Therefore noninvasive monitoring of retinal oxygenation has the potential to be an important tool for defining pathophysiology as well as for evaluating therapeutic interventions. Because of the weakly paramagnetic effect of O<sub>2</sub>, inhaled O<sub>2</sub> can serve as a T1 contrast agent. Increasing the dissolved O<sub>2</sub> content of blood allows diffusion of O<sub>2</sub> into the vitreous, which can be visualized as ~1-2% changes in signal using T1 weighted techniques.<sup>1</sup> Because the inversion in FLAIR imaging utilizes the long T1 of fluid for its effect, modest shortening of the T1 of CSF result in large changes in FLAIR signal intensity.<sup>2</sup> Because FLAIR suppresses vitreous signal just as it does CSF, we explored the feasibility of using FLAIR to image O<sub>2</sub> diffusion into the vitreous as a marker of O<sub>2</sub> delivery to the retina.

## Materials and Methods:

**Subjects:** Six healthy volunteers (age range 29-46y) gave written informed consent under an IRB approved protocol.

**Breathing apparatus:** A non rebreathing airway was established with a Y-connector attached to a mouthpiece. Wall oxygen at ~10 L/min O<sub>2</sub> (100% O<sub>2</sub>) was delivered through one limb of the Y, and exhaled air exited the other limb. One way valves minimized dead space or recirculation. Nasal breathing was prevented with a nose clamp.

**MR imaging:** Volunteers were placed in a 1.5 T system with a 3 in surface coil placed close to the orbit. Five or six contiguous 5 mm axial slices were obtained in two interleaved acquisitions, obtained every 3 min for up to 60 minutes. During the scan, the volunteers were asked to fixate on a marker placed ~ 10-20 cm away. Eye movement and blinking was allowed "when the scanner was silent" which occurred during the long time interval of the 9 second TR used in this FLAIR sequence. A short dummy scan was obtained to allow the subject to get used to the rhythm of the scan, and hence, when they were allowed to blink. High spatial resolution FLAIR imaging was performed with TR 9000 TI 2200 and TE 160 ms and a 21 ETL RARE readout with a 256 x 160 matrix and 14 cm FOV. Room air was inhaled for the first six minutes and subsequently 100% O<sub>2</sub> was inhaled for the duration of the study.

**Data Analysis:** Only the center slice through the optic nerve was used for analysis. Images were coregistered using a 2D 6 parameter affine warp using a cross-correlation cost function (MIPAV, NIH). Distribution of signal intensity changes in the vitreous was assessed visually by comparing averaged data sets, difference images and time profiles from registered data sets which were temporally smoothed with a 3 point convolution (MATLAB).

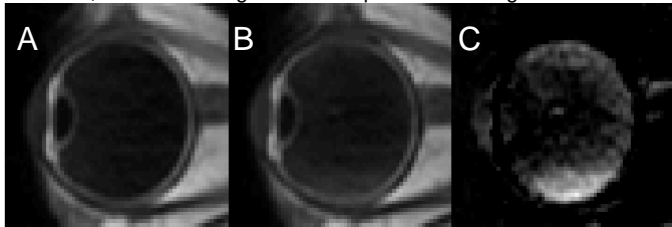


Fig. 1 FLAIR images from a single subject smoothed and registered. Baseline average of initial 3 images (A). Average of last 5 images after ~ 45 min of breathing 100% O<sub>2</sub> (B). Difference B-A shows oxygen dependent enhancement of the vitreous (C).

**Results:** Large signal changes were observed in the vitreous adjacent to the retina. These were identified in the nasal and temporal aspects of the retina to a greater degree than the macula and optic disc along the posterior aspect of the globe. Although signal changes could exceed 200%, they were difficult to visualize on the raw FLAIR images (Figure 1 B). Difference images, however, clearly demonstrate the increased signal in the vitreous (Figure 1 C). There is a clear centripetal gradient in intensity representing the gradient of O<sub>2</sub> diffusion from the retina centrally.

The temporal characteristics of the Oxygen enhancement are shown in Figure 2 for a second subject. Vitreous adjacent to the retina begins to enhance before the central portion of the vitreous, again illustrating a diffusion gradient of O<sub>2</sub> into the vitreous from the retina. It does not appear that a stable plateau of enhancement was obtained even after 45 min of O<sub>2</sub> inhalation.

**Discussion:** Because hemoglobin saturation is essentially 100% at room air, breathing 100% O<sub>2</sub> results in a marked increase in dissolved O<sub>2</sub> with little change in the ratio of oxyhemoglobin and deoxyhemoglobin. This dissolved O<sub>2</sub> may then diffuse into tissue, increasing tissue oxygen tension. Diffusion into the vitreous arises from densely vascularized retina and choroid within the globe. As has been demonstrated in the CSF, weakly paramagnetic dissolved O<sub>2</sub> shortens the T1 relaxation time of fluid altering the inversion time required to null this fluid. Vitreous humor has a T1 which is nulled with the same inversion time as CSF, and so would be expected to behave in a similar manner. We show changes in signal intensity of vitreous with oxygen inhalation.

Notably, the time course of the oxygen enhancement of the vitreous is much slower than that seen in CSF spaces. At least two factors contribute to this difference. First, the surface area to volume ratio of the pia to the CSF may be more favorable to increasing concentration locally as compared to this ratio of retinal capillary surface to vitreous volume. Second, although T1 properties are similar in vitreous and CSF, the vitreous humor is a gel in young individuals so that the diffusion properties of oxygen into the CSF differ appreciably from the diffusion into CSF.

These findings demonstrate the feasibility of using vitreous signal on FLAIR imaging as an index of oxygen delivery to the retina. Comparison of this sequence to standard T1 weighted imaging is required to determine which approach may be more suitable to pursuing the pathophysiology of retinal oxygenation abnormalities. Improvements in scan speed and use of 3D FLAIR imaging sequences may further improve the quality of the data, by allowing 3D rather than 2D registration. Our inversion slab was 50% larger than the slice thickness. Optimally an inversion slab that encompassed the entire globe would eliminate "inflow" from eye motion or bulk flow. We propose that FLAIR signal of CSF may be a valuable probe of O<sub>2</sub> delivery to the underlying brain.

## References:

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2. Deliganis AV, Fisher DJ, Lam AM, Maravilla KR. Cerebrospinal fluid signal intensity increase on FLAIR MR images in patients under general anesthesia: the role of supplemental O<sub>2</sub>. *Radiology.* 2001 Jan;218(1):152-6.

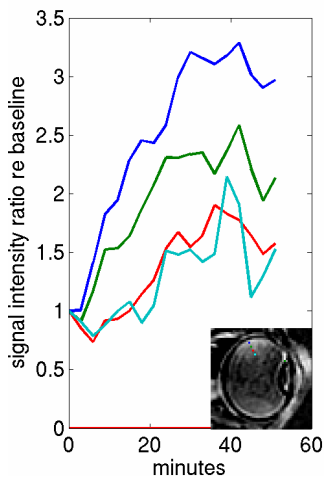


Figure 2. Time course of FLAIR SI change with 100% O<sub>2</sub> inhalation at different locations in the vitreous represented by corresponding colored voxels in inset.