In vivo oxygen partial pressure measurement of human body fluids

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INTRODUCTION

The oxygen partial pressure (pO_2) of low-protein body fluids, such as urine, amniotic fluid, vitreous humor, and cerebrospinal fluid (CSF), is of great physiologic interest, as such measurements may yield information about surrounding tissue oxygen levels (1,2). Current pO_2 measurement methods involve either fluid removal (and are susceptible to errors caused by contamination from room air during fluid removal and analysis) or require the placement of invasive microelectrodes.

This report presents an *in vivo* method to measure pO_2 in low-protein human body fluids using a rapid, flow-insensitive, saturation recovery single-shot fast spin echo (SSFSE) sequence. Molecular oxygen is paramagnetic and has been shown to cause a linear increase in longitudinal relaxivity (R1=1/T1) with concentration (3). Prior reports have documented that the R1 effect of oxygen is the dominant source of relaxation for most low-protein (<1-2 g/L) fluids (4-7) (for reference, normal CSF protein is 0.3 g/L). Such R1 changes can account for the hyperintense CSF signal noted on FLAIR images in patients breathing supplemental oxygen (5-6).

METHODS

Phantoms were prepared by bubbling mixtures of N_2 and O_2 gas through distilled water to achieve a range of oxygenation. pO_2 was measured with a polarographic electrode (Licox, GMS, Kiel-Mielkendorf, Germany). The liquid was anaerobically sealed inside 10 ml glass vials with ground-glass stoppers. Imaging was performed in a 37 C water bath at 1.5T (GE Healthcare) using an SSFSE sequence (TR/TE = [3/10s]/200ms) with spatially-widened refocusing pulses to minimize flow artifacts (8). The MR magnetization was destroyed using crusher gradients following each image, and R1 was determined from the magnetization recovery at 3 and 10 s intervals, using an iterative method (8). Each 13 s R1 measurement was repeated 12 times to determine the mean and standard deviation. The same sequence was used in humans, except that longer TE (500-750 ms) was used to suppress non-fluid signal on CSF images, to minimize partial volume contamination. CSF, vitreous humor, and bladder urine pO_2 images were created, and preliminary quantitative measurements were compared with invasive methods. Images of CSF and vitreous pO_2 before and after 20 min of 100% oxygen inhalation via non-rebreather facemask were also acquired. pO_2 was calculated from the relationship established during the phantom study.

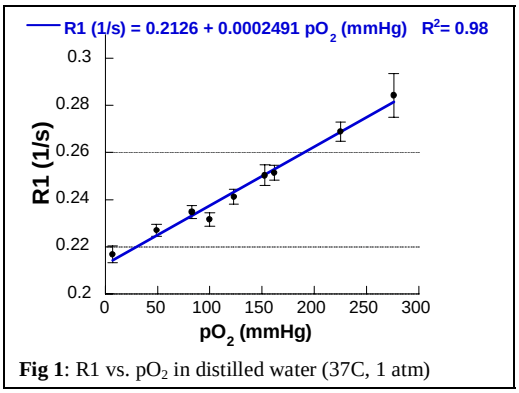

Fig 1: R1 vs. pO_2 in distilled water (37C, 1 atm)

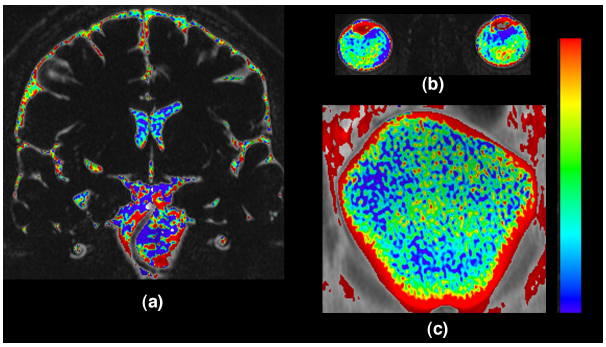

Fig 2: R1 (pO_2) maps of human body fluid. Colormap range is blue: R1=0.2126s^{-1} (T1=4.70s, pO_2=0mmHg) to red: R1=0.26 s^{-1}, (T1=3.85s, pO_2=190mmHg) (a) CSF, (b) vitreous humor, (c) bladder

Table 1: Quantitative pO_2 (mmHg) in various body fluids

Region (# of measurements)	in vivo	invasive (ref)
CSF lateral ventricles (2)	51±18	*
CSF cisterna magna (2)	67±1	31-51 (1,10)
CSF cortical sulci (2)	106±42	*
CSF lumbar SA space (2)	44±7	40-43 (1,11)
Vitreous humor (3)	64±38	*
Bladder urine (3)	59±7	35 (2)

* No prior measurements in normal adults

RESULTS

Fig 1 shows a linear relationship between pO_2 and R1 for distilled water at 37C. Body temperature, oxygen-free water R1 [R1(pO_2=0)] was measured to be 0.2126 s^{-1} (T1=4.70 s). The proportionality constant relating R1 and pO_2 ($\partial R1/\partial pO_2$) is 2.491e-4 s^{-1}/mmHg. Fig 2 presents regional pO_2 maps of human body fluid. Initial pO_2 estimates in several young subjects along with measurements from invasive studies are shown in Table 1. Fig 3 demonstrates the CSF and vitreous humor pO_2 change following 100% oxygen inhalation.

DISCUSSION

Chiarotti et al. (3) determined theoretically and confirmed experimentally that the R1 contribution from low concentrations of paramagnetic solutes (including oxygen in water) is linear with concentration. The current study verifies that this linear relationship holds in the biologic range and yields estimates of R1(pO_2=0) and $\partial R1/\partial pO_2$ of body temperature water. Hopkins et al. suggested that R1(pO_2=0) for water (or CSF) should be about 0.22 s^{-1}, and that oxygen should be much more efficient at causing R1 changes than equimolar protein changes (4). The value of $\partial R1/\partial pO_2$ they cited, based on the data of Chiarotti et al., is about twice that measured in this study. We believe this is due to the paucity of data points in the original study and the focus on the supra-biologic range. Although we consider it less likely, contamination of our water phantoms with room air could produce a similar effect.

We have demonstrated the first pO_2 measurements *in vivo* in human body fluids. SSFSE-type acquisition is ideal for imaging water-like collections, as long echo trains may be used to achieve high spatial resolution; also, a long echo time can be used to suppress signal from soft tissue to minimize partial volume effects, which is critical for accurate long T1 measurements. Regional differences in room air CSF oxygenation are evident (Figs 2,3). While regional maps of pO_2 have never previously been created *in vivo*, the initial estimates of mean pO_2 are not incompatible with the limited, more error-prone invasive methods. Significant pO_2 increases in the vitreous and CSF (cortical sulci, basilar cisterns, and quadrageminal plate cistern) following 100% oxygen inhalation (Fig 3) are consistent with hyperintensity noted on FLAIR images obtained with supplemental oxygen (5,6,9).

CONCLUSION

Noninvasive, quantitative pO_2 mapping in human body fluids *in vivo* with MRI is possible using a rapid, saturation recovery SSFSE sequence, predicated on the paramagnetic effects of molecular oxygen. We have found spatial heterogeneity of CSF pO_2 in subjects breathing room air. Significant pO_2 increases are present within CSF in a spatial distribution consistent with previously noted hyperintensity on FLAIR images following 100% oxygen inhalation. Measurement of pO_2 in health and disease or during supplemental oxygen in a wide variety of fluid collections is envisioned.

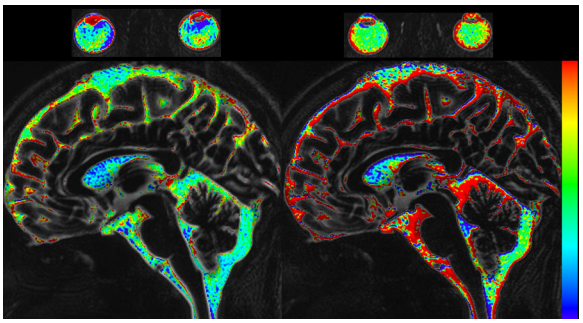

Fig 3: CSF and vitreous pO_2 map before and after 20 min of 100% oxygen by facemask (same colorscale as above). pO_2 within the cerebral cortical sulci increased from 136±61 to 230±214 mmHg. No significant change was seen in the lateral or fourth ventricles. Vitreous pO_2 increased from 81±43 to 96±24 mmHg.

REFERENCES

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