Comparison of hypercapnia- and hyperoxia-induced blood flow changes in the retina detected by MRI and laser Speckle Imaging

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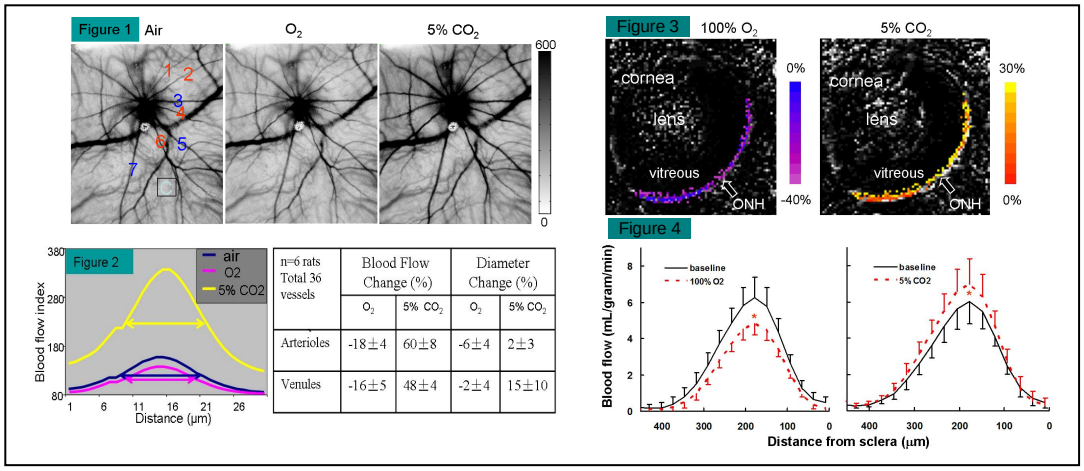
INTRODUCTION We recently reported blood-flow (BF) MRI of the rat retina using the continuous arterial-spin-labeling technique (ASL-MRI) with a separate neck coil at 90x90x1500-μm resolution (1). We found that hyperoxia (100% O_2) decreased blood flow 25±6% relative to baseline (air) and hypercapnia (5% CO_2 + 21% O2) increased blood flow 16±6% (1) (fig3,4). BF measurements of physiologic stimuli in the retina are sparse due to a lack of reliable blood-flow imaging techniques to study the retina. Available data indicated that hypercapnic responses in the retina are controversial with some reporting no changes and others reported significant changes in humans using Laser Doppler Flowmetry at a single point (usually at the optic nerve head (2)). To corroborate our novel MRI findings, we developed and applied a novel laser speckle imaging (LSI) to measure BF in the rat retina. This approach offers two dimensional BF images of the retina at very high spatial and temporal resolution without scanning.

Methods Six male Sprague-Dawley (SD) rats (300-400g) were anesthetized with 1% isoflurane, paralyzed and mechanically ventilated. End-tidal CO_2, heart rate and O_2 saturation and rectal temperature were maintained within normal physiological ranges unless purposefully altered. 100% O_2 and 5% CO_2 challenges were used with air as baseline. LSI apparatus was built by modifying a commercial video imaging system (Imager 3001) as described elsewhere (2). Images of LSI were obtained using an infrared laser diode (785 nm) to avoid the visual stimuli effect at 25 Hz and 4 μm resolution with an image area of 2-3 mm and optimized exposure time of 10 ms. BF index maps obtained by the LSI were computed as described in (3). In addition, BF and diameter changes in individual arteriole and venules vessels were also quantified using an automated profile analysis (4). Arterioles and venules vessels were identified based on qualitative oximetry (green light).

RESULTS To compare with our MRI findings, here we showed both LSI (fig 1, 2) and ASL-MRI BF results (fig 3, 4). LSI results show that oxygen breathing decreased BF (amplitude of the profiles) and vascular diameter (width of the profiles) whereas CO_2 breathing increased BF and vascular diameter relative to air. These are consistent with our MRI findings (fig 3, 4). LSI results are tabulated for physiologically induced BF and diameter changes in 36 individual arteriole and venule vessels (**Table 1**). These vessels had a diameter range of 17-20 μm. Arterioles changes are generally larger in the arterioles than venules in term of BF. Diameter changes were surprisingly larger in venules under 5% CO_2, which remains to be investigated.



n=6 rats Total 36 vessels	Blood Flow Change (%)		Diameter Change (%)	
	O_2	5% CO_2	O_2	5% CO_2
Arterioles	-18±4	60±8	-6±4	2±3
Venules	-16±5	48±4	-2±4	15±10

Fig 1. Retinal BF index maps of a rat breathing air, oxygen and 5% CO_2. BF changes were analyzed for representative retinal vessels (diameter range 17-20 μm) where arterioles are labeled red and veins labeled blue. The ROI (C) represents capillaries void of large vessels. **Fig 2.** BF profiles across a single retinal vessel (#3) under air, oxygen and 5% CO_2. **Table 1** on the right summarizes the group-average data. **Fig 3.** ASL-BF percent-change maps responding to 100% O_2 or 5% CO_2. Percent-changes are overlaid on blood flow maps. Color bars indicate blood-flow percent changes. ONH: optic nerve head. **Fig 4.** Blood-flow profiles across the thickness under basal, 5% CO_2 or 100% O_2 conditions.

DISCUSSION & CONCLUSION The major findings of this study is that robust changes in blood flow and diameters were detected using LSI associated with hyperoxic and hypercapnic challenges. These findings corroborate our BF MRI findings, although the magnitudes of changes are different. The discrepancies in percentage of BF changes between the two methods are likely due to the differences in techniques and signal sources (i.e., LSI is more sensitive to surface vessels compared to deep vessels). In conclusion, LSI provides unparallel spatial and temporal resolution to investigate blood flow and diameter changes in the retina with a large field of view. LSI BF data corroborated our MRI detection of robust hyperoxic and hypercapnic BF responses in the retina. LSI can be readily applied to retinal diseases and humans. We anticipate that these two methods will provide complementary and mutually supporting data toward characterizing normal retinal physiology and pathophysiology in retinal diseases.

References. 1) Li et al. NeuroImage 2007, in press. 2) Riva et al, IOVS 1994, 35, 608. 3) Cheng et al., Opt.Lett. 2007, 32:2188. 4) Cheng et al., PNAS, 2006, 103:17525. 5) Sternn et al., Br J Ophthal, 1997, 81:360. 6) Alm & Bill Acta Physiologica Scand 1972, 84:306.