Layer-Specific Blood-Volume MRI of the Retina

G. Nair[1], Y. Tanaka[1], T. Nagaoka[1], M. T. Pardue[2], D. Olson[2], P. Thule[2], and T. Q. Duong[1]
[1]Yerkes Imaging Center, Emory University, Atlanta, GA, United States, [2]VA hospital, Atlanta, GA, United States

INTRODUCTION The retina consists of three major cell layers, namely the photoreceptor, bipolar cell, and ganglion cell layer. It is nourished by the *retinal* and choroidal *vasculatures* located on either side of the retina. While the *retinal* vasculature exists within the ganglion and bipolar cell layer, the *choroid* is located directly beneath the photoreceptor layer. The photoreceptor layer in the middle is avascular (1). Importantly, the two vascular layers are independently regulated and respond differently to physiologic stimulations. Unfortunately, the retina, including the choroid, is only ~276 µm thick (1), constituting a challenge for MRI. Nonetheless, the remarkable layout of the retina is an excellent model for testing layer-specific and high-resolution MRI technologies.

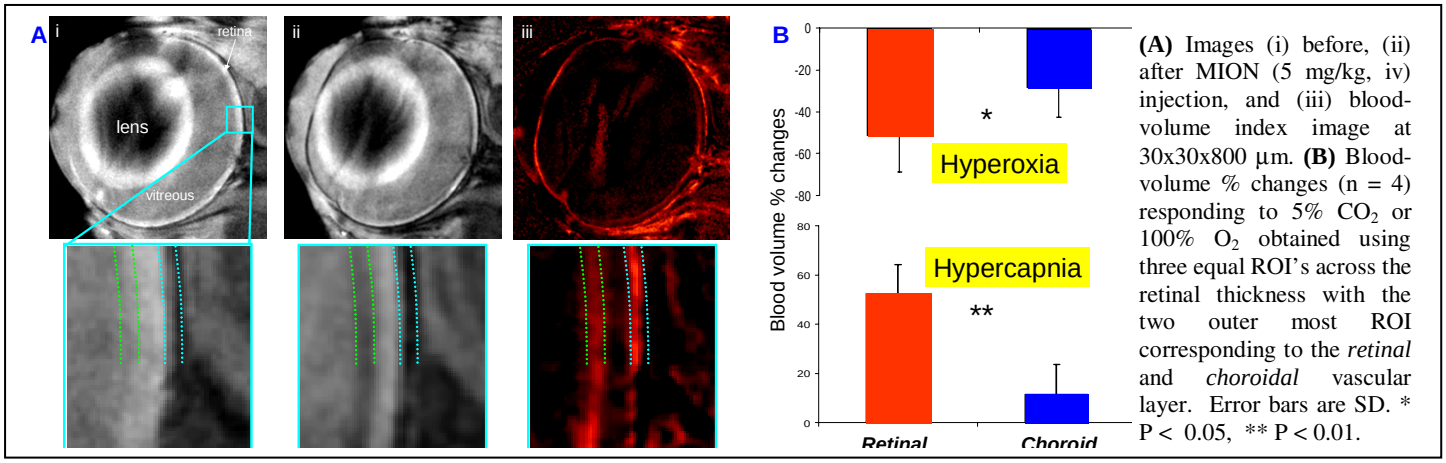
We recently reported multiple anatomical layers (1-3) and layer-specific BOLD fMRI responses in the retina (1). In this study, we extended previous findings to include MRI detection of layer-specific blood-volume (BV) and layer-specific physiologically evoked BV changes using the monocrystalline iron oxide nanocolloid (MION) (4) as a blood pool contrast agent, at high spatial resolutions.

METHODS Seven normal rats (250-350g) were studied under 1% isoflurane anesthesia, paralysis and mechanical ventilation. MION was injected intravenously (5 mg/kg). T2*-weighted images were acquired before and after MION injection, using conventional gradient-echo sequence with 200 ms TR, 6.5 ms TE, 7.5x7.5 mm FOV, 256x256 matrix, and 0.8-mm slice. Maps of T2* change due to MION was obtained to derive a blood-volume index map. Percent changes due to 5% CO_2 or 100% O_2 challenges relative to baseline (air) were tabulated using an automated technique in which signal intensity profiles across the retinal thickness were projected and averaged along the length of the retina (1).

RESULTS AND DISCUSSION Figure A shows the images before and after intravenous MION injection, and the BV index map. As expected, MION reduced signals on either side of the retina where the two vascular layers are located. The calculated BV index map shows high BV located on either side of the retina, corresponding to the *retinal* and *choroidal* vascular layers. Note that the BV signal was higher in the *choroid* than the *retinal vascular* layer and, the ratio of *choroid* to *retinal* BV index was 9.8 ± 3.2 (n = 7). In addition, we also analyzed layer-specific BV responses to 5% CO_2 and 100% O_2 inhalation by using three automated ROI's across the retinal thickness with the two outer most ROI corresponding to the *retinal* and *choroidal* vascular layers (**Figure B**). Both *retinal* and *choroidal* vessels exhibited hyperoxia-induced vasoconstriction, with the *retinal* vessels showing a larger O_2-induced BF reduction compared to the *choroid* vessels ($P < 0.05$). Similarly, both *retinal* and *choroidal* vessels exhibited hypercapnia-induced vasodilation, with the *retinal* vessels showing a significantly larger CO_2-induced BV increase compared to the *choroid* vessels ($P < 0.01$). The *choroid* is known to be less responsive to a wide range of physiologic stimuli including hyperoxia and hypercapnia when assessed by oxygen electrode and laser Doppler flow measurements (5-6). These results are also in good agreement with our layer-specific BOLD fMRI findings (1). This could be due to in part by its high basal blood flow (i.e., ceiling effects).

CONCLUSIONS We report layer-specific BV MRI and BV responses in the retina. These results further corroborate that differential layer-specific responses to physiologic stimuli are unique in the retina by providing more direct evidence of layer specific BV measurements. Further improvement in MRI sensitivity is expected. Future studies will involve layer-specific BV MRI applications to study visual stimulations, retinal diseases, and quantifying absolute BV.

REFERENCES 1. Cheng *et al.*, *PNAS* **103**, 17525 (2006). 2. Shen *et al.*, *JMRI* **23**, 465 (2006). 3. Nair *et al.*, ISMRM p2452 (2007). 4. Mandeville *et al.*, *MRM* **39**, 615 (1998). 5. Yu & Cringle, *Prog Retinal Eye Res* **20**, 175 (2001). 6. Riva et al, *IOVS* **35** 608 (1994).



(A) Images (i) before, (ii) after MION (5 mg/kg, iv) injection, and (iii) blood-volume index image at 30x30x800 µm. **(B)** Blood-volume % changes (n = 4) responding to 5% CO_2 or 100% O_2 obtained using three equal ROI's across the retinal thickness with the two outer most ROI corresponding to the *retinal* and *choroidal* vascular layer. Error bars are SD. * $P < 0.05$, ** $P < 0.01$.