Human Retinal Blood Flow MRI using Pseudo-continuous Arterial Spin Labeling and Balanced Steady State Free Precession

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Introduction The retina is only 276 micron thick including the choroid (*1*) but it has one of the highest blood flow (BF) per unit weight based on destructive microsphere studies (*2*). Abnormal BF in the retina has been implicated in many retinal diseases, including diabetic retinopathy, glaucoma, and retinal ischemia. With the exception of anatomical optical coherence tomography, optical imaging techniques are limited to probing the retinal surface. Moreover, there are currently no available in vivo techniques to measure quantitative BF in the retina. MRI is an established technique for measuring BF. Imaging BF of the retina is however challenging because the retina is very thin, is located in a region of high magnetic susceptibility, and is susceptible to eye motion. BF MRI has been reported in the rat retina without (*3*) and with (*4*) laminar resolution. BF MRI of the human retinas has also been reported in a conference abstract (*5*). Blood flow MRI is often obtained using ASL with EPI acquisition. EPI of the retina is challenging because eye is located in a region of large magnetic inhomogeniety and is thus highly susceptible to signal drop off and distortion

In this study, we implemented the pseudo-continuous arterial spin-labeling technique (pcASL) (*6*) with 2D balanced steady-state free precession (bSSFP) acquisition (*7*), and explored BF MRI of the human retina. pcASL is used to improve BF sensitivity and bSSFP is used to achieve high SNR, high temporal and spatial resolution without susceptibility-induced signal drop off and distortion. Experiments were designed to confirm blood flow signals in retina to be genuine and not as results of motion or bSSFP banding artifacts.

Material and Methods MRI was performed on 2 subjects using a 3T TIM TRIO whole-body scanner with 12-channel head matrix coil and body coil for reception and transmission, respectively. pCASL (*6*) parameters were: RF pulse shape = hanning window, RF duration = 0.5 ms, flip angle = 25°, and spacing between RF pulses = 0.92 ms, slice-selective gradient = 6 mT/m, tagging duration = 1500 ms, postlabeling delay = 1200 ms, residual gradient moment = 18°, with balanced tagging scheme. bSSFP parameters were: TR = 4.6 ms, TE = balanced at half of TR, acquisition bandwidth = 500 Hz/pixel, matrix size = 128×86, corresponding FOV = 240×180 mm^2, number of slices = 1, and slice thickness = 5 mm. A tagged and a nontagged image were acquired alternately with a temporal resolution of 8 s per pair images. Blood flow image was derived from 32 averages (2.3 mins).

To examine whether the retina blood flow signal from the abovementioned labeling condition (Label On) is real rather than from motion artifact, we obtained blood flow image without tagging power (Label Off). To examine the effects of banding artifacts, another perfusion map was acquired with combination of the four different phase cycling angles (0, 90, 180, 270°) (*8*) each with 8 repetitions (Label On (mPC)).

Results Figure 1 shows SSFP image without (A) and with (B) multiple phase cycling angles. Without phase cycling, banding artifacts were observed. These banding artifacts were essentially eliminated by multiple phase cycling angles. No noticeable distortion effects were observed in any images. **Figure 2** shows the subtraction images with (A) and without (B) labeling power. When pCASL labeling power was on, there were clear perfusion contrast along the retina (arrowheads in A), whereas no discernible perfusion signal in the retina was detected when the labeling power was off (arrowheads in B). Note that the region of banding artifacts produced artifacts on BF images (bright perfusion signals). Banding artifacts were essentially eliminated by multiple phase cycling angles in the perfusion image (**Figure 3)**. The perfusion signal ΔS/S from the entire retina with labeling power was 2.1±0.4% of signal before subtraction, consistent with brain perfusion signal.

Discussion and Conclusion This study demonstrates a combined pCASL and bSSFP readout to obtain reliable human retinal blood flow images without distortion and signal drop off that are commonly observed with EPI acquisition. The retinal blood signals were confirmed to be genuine. The retina is located in a region of large spatial inhomogeneity and multiple phase cycling approach successfully reduces banding artifacts in perfusion images. Although multiple phase cycling yields poorer time resolution, it can be used to derive a single optimal phase cycling angle that "move" the banding artifact location away from the region of interest (retina). Future studies will improve sensitivity, temporal and spatial resolution to visualize retinal layers. Given that there is no available blood flow technique to image the in vivo retina, this approach warrants further investigations. This approach could open up new avenues for retinal research and should complement existing retinal imaging techniques.

References 1. Cheng *et al.*, *PNAS* 103, 17525 (2006). 2. A. Bill, in *Handbook of physiology Part 2 in Microcirculation,* E. M. Renkin, C. C. Michel, Eds. (American Physiological Society, Bethesda, MD, 1984), pp. 1001-1035. 3. Li *et al.*, *Invest Ophthalmol Vis Sci* 50, 1824 (2009). 4. Muir and Duong, ISMRM 2009. 5. Alsop et al, ISMRM 2000. 6. W. C. Wu et al., Magn Reson Med 58:1020-1027 (2007). 7. Oppelt et al, Electromedica 54:15-18 (1986). 8. Elliot et al, Magn Reson Imag 25:359-364 (2007). This work is funded in part by R01 EY014211, R01 EY018855, VA MERIT

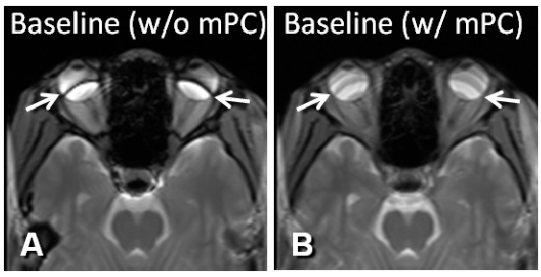

FIG. 1. Baseline bSSFP images without (A) and with (B) multiple phase cycling angles. The banding artifacts (arrows in A) are significantly reduced with multiple phase cycling angles (arrows in B).

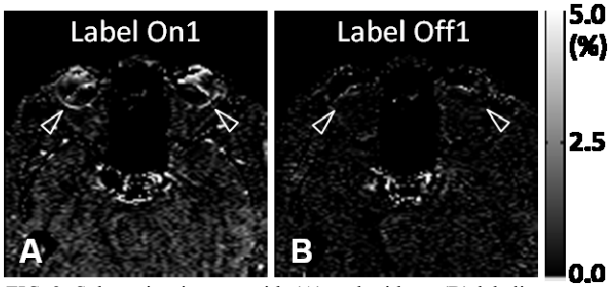

FIG. 2. Subtraction images with (A) and without (B) labeling RF power. Retinal perfusion signals (arrowheads in A) disappeared when labeling RF power was off (arrowheads in B).

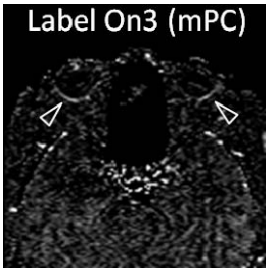

FIG. 3. Subtraction image with multiple phase cycling angles. The artifactual perfusion signal around the banding artifacts disappeared.