Blood-flow MRI of Non-human Primate (Baboon) Retina

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INTRODUCTION Advances in MRI technologies have made it possible to achieve multilayer resolution of the thin retina of only 276 micron thick (1). In rodent and cat retinas, three to seven MRI-resolved anatomical layers have been reported depending on whether contrast agent was used (1-3). Contrast-enhanced MRI following intravenously injection of Gd-DTPA revealed two unique (retinal and choroidal) vascular layers and the avascular photoreceptor layer and segments in between (1). More recently, blood flow (BF) MRI recorded quantitative perfusion in the whole retina in rodents (4) to be about 8 times higher than cerebral BF, consistent with the microsphere technique (8). Blood flow contrast in normal human retinas has also been presented in a conference abstract in 2000 (5). Abnormal BF in the retina has been widely implicated in many retinal diseases, including diabetic retinopathy, glaucoma, and retinal ischemia, and thus the ability to reliably image BF in the retina could have many important applications.

In this study, we implemented a pseudo-continuous ASL (6) with echo-planar image (EPI) and balanced steady state free precession (bSSFP) acquisition to improve ASL contrast on clinical scanner and explored BF MRI of the retina in anesthetized/paralyzed non-human primate (baboon) as a first step toward evaluating potential human applications. Anesthetized baboons were used to exclude movement artifacts, allowing us to focus on evaluating hardware feasibility and imaging parameters for high-resolution quantitative BF imaging of the retina.

METHODS MRI studies were performed on normal female baboons (10-20kg, n = 4). Animals were anesthetized with 0.8~1.0% isoflurane, mechanically ventilated, and paralyzed with vecuronium (0.1mg/kg). End-tidal CO_2, O_2 saturation, heart rate, respiration rate, and rectal temperature were monitored continuously and maintained within normal physiological ranges throughout the entire studies. At the end of the MRI study, neostigmine (0.5-2 mg) was administered to reverse paralytic effects. BF MRI was also measured on a post-mortem animal (n = 1) to verify BF contrast.

MRI was performed on a Siemens 3T TIM TRIO. pCASL parameters were: RF pulse shape = hanning window, and spacing between two RF pulses = 0.36 ms, slice-selective gradient = 6 mT/m, tagging duration = 2.1s, post-labeling delay = 0.7s. For 2D EPI acquisition (2x2x5 mm, 8 mins), the parameters were single-shot gradient-echo EPI with TR/TE = 3500/16 ms, 10 slices, matrix = 64×64, FOV = 12.8×12.8 cm. For 3D bSSFP (1x1x2.5 mm, 20 mins), the parameters were TR/TE = 4.0/2.0 ms, bandwidth = 698 Hz/pixel, matrix = 128×64, FOV = 128×64 mm^2, linear phase-encoding order, dummy phase-encoding lines = 10, 8 second phase-encoding dimension, with 5/8 and 6/8 partial Fourier acquisitions along 1st and 2nd PE dimensions, respectively. BF was calculated as described elsewhere using partition coefficient and T1 of the brain (6).

RESULTS **Figure 1** shows the comparison of BF images obtained using 2D pCASL EPI and 3D pCASL bSSFP from one representative animal. Both techniques yielded reliable BF contrast in the retina. In pCASL EPI, BF contrast was detectable only in the posterior part of the retina whereas the anterior segment of the eye was not visible because of signal drop out in anterior segment of the eye due to magnetic susceptibility from air-tissue interface High BF expected in the ciliary bodies on either side of the lens was not observed in EPI.

In pCASL SSFP, high spatial resolution (at least eight-times higher than EPI method) can be achieved although longer scan time were required for sufficient signal. BF contrast was visible along most of the retina. The images were distortion free and without signal drop out. BF in the anterior segment of the eye around the ciliary body was visible. The group-averaged BF values in the whole-retina ROI were 81±13 mL/100g/min (mean±s.d.) and 56±13 mL/100g/min in the whole brain by pCASL EPI from the same data sets. Quantification for pCASL bSSFP is in progress.

To verify that BF contrast signals are genuine, BF was also measured post-mortem in the same setup without moving the animal. The results showed no BF contrasts in the post-mortem retina as expected (i.e., at noise levels) for both pCASL EPI and pCASL bSSFP (data not shown), demonstrating that the perfusion signals are genuine as opposed to subtraction artifacts.

CONCLUSION This study demonstrates for the first time the feasibility of quantitative blood-flow MRI of the anesthetized baboon retina using a clinical 3T scanner at reasonably high spatial and temporal resolution. The absolute BF values of the retina are consistent with those reported in rodents. Importantly, BF in the retina is significantly higher than brain BF, consistent with published findings using MRI (7) and microsphere (8) technique. pCASL 3D bSSFP has similar temporal resolution as pCASL EPI. pCASL 3D bSSFP yields effectively high spatial resolution although the same data matrix because EPI's long readout time degraded resolution. pCASL 3D bSSFP is free of distortion and signal drop out.

Lamina-specific retinal and choroid BF has been reported in rodents (7). These two circulations are affected differently in different retinal diseases. Given that there is no other available in vivo BF imaging technique to study the retina, the prospect of MRI to achieve lamina-specific retinal and choroid BF in humans and primates warrants further investigations. Irrespective of whether there will be clinical translation, this approach can be utilized to study retinal diseases and to test therapeutic interventions in non-human primates.

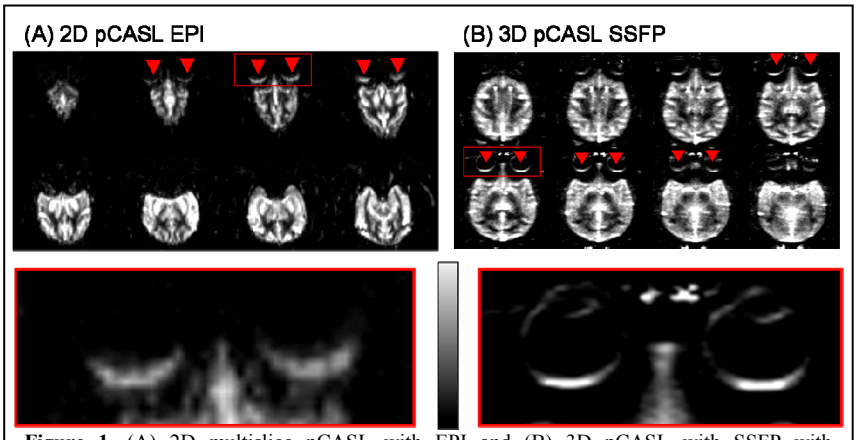

Figure 1. (A) 2D multislice pCASL with EPI and (B) 3D pCASL with SSFP with corresponding expanded views. Each data set took 4 mins. Gray scale bar = 0 – 1 ml/g/min.

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