Blood Flow MRI of the Human Retina/Choroid during Rest and Isometric Exercise

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Purpose. To investigate blood flow (BF) in the human retina/choroid during rest and handgrip isometric exercise using magnetic resonance imaging (MRI).

Methods. Four healthy volunteers (25–36 years old) in multiple sessions (1–3) on different days. MRI studies were performed on a 3-Tesla scanner using a custom-made surface coil (7 × 5cm in diameter) at the spatial resolution of 0.5 × 0.8 × 6.0 mm. BF was measured using the pseudo-continuous arterial-spin-labeling technique with background suppression and turbo-spin-echo acquisition. During MRI, subjects rested for 1 minute followed by 1 minute of handgrip, repeating three times, while maintaining stable eye fixation on a target with cued eye blinks at the end of each data acquisition (every 4.6 seconds).

Results. Robust BF of the unanesthetized human retina/choroid was detected. Basal BF in the posterior retina/choroid was 149 ± 48 mL/100 mL/min with a mean heart rate of 60 ± 5 beats per minute, mean arterial pressure of 78 ± 5 mm Hg, ocular perfusion pressure of 67 ± 4 mm Hg at rest (mean ± SD, $n = 4$ subjects). Handgrip significantly increased retina/choroid BF by 25% ± 7%, heart rate by 19% ± 8%, mean arterial pressure by 22% ± 5% (measured at the middle of the handgrip task), and ocular perfusion pressure by 25% ± 6% (averaged across the entire handgrip task) ($P < 0.01$), but did not change intraocular pressure, arterial oxygen saturation, end-tidal CO_2, and respiration rate ($P > 0.05$).

Conclusions. This study demonstrates a novel MRI application to image quantitative BF of the human retina/choroid during rest and isometric exercise. Retina/choroid BF increases during brief handgrip exercise, paralleling increases in mean arterial pressure. Handgrip exercise changes ocular perfusion pressure free of potential drug side effect and can be done in the MRI scanner. MRI offers quantitative BF with large field of view without depth limitation, potentially providing insights into retinal pathophysiology. (*Invest Ophthalmol Vis Sci.* 2012; 53:4299–4305) DOI:10.1167/iovs.11-9384

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Blood flow (BF) in the retina is intricately coupled to basal metabolic function under normal physiological conditions, and it is often perturbed in disease states.[1] Although the relationship between perfusion pressure and BF has been well studied in the brain,[2] similar studies in the retina are sparse by comparison. Isometric exercise, such as handgrip where working performance involves muscle contraction but maintains constant muscle length, can increase heart rate, arterial pressure, and sympathetic activity. This approach offers an opportunity to study the relationship between perfusion pressure and BF without pharmacologic manipulation.

Ocular BF measurements during and immediately after isometric exercise have been reported using optical-based imaging techniques, such as laser Doppler velocimetry (LDV), laser Doppler flowmetry (LDF), and laser interferometry. Ocular BF measurement in the retina during isometric exercise is challenging due to potential motion. Some have reported that retinal BF and optic nerve head (ONH) BF did not change during isometric exercise until mean arterial pressure (MAP) increased by 40%[3] or ocular perfusion pressure (OPP) increased more than 30%.[4] Similar autoregulated trend has been observed in choroidal BF in the macular area that choroidal BF maintained within 10% to 12% of baseline until OPP increased by 67%.[5,6]

Magnetic resonance imaging (MRI) can measure BF quantitatively using the arterial spin labeling (ASL) technique[7–9] without the need for a contrast agent. The ASL technique, by magnetically tagging endogenous water in blood, allows repeated measurements that can be used to study real-time BF changes associated with a task (i.e., functional MRI), to augment signal-to-noise ratio (SNR) and/or spatial resolution. The unique advantages of BF MRI over optical imaging findings are that it yields tissue perfusion in the quantitative and classical unit of mL/min/mL tissue without the need to measure velocity in individual vessels, and it provides large field of view (FOV) and without depth limitation. The disadvantages are its low spatiotemporal resolution and high cost compared with optical-based techniques. BF MRI has been widely used to image BF in rodent retinas. The feasibility of MRI to image quantitative retina/choroid BF in the human retina was recently demonstrated under basal[10,11] and gas-challenge conditions.[11]

The goal of the present study was to explore a novel application of BF MRI to investigate BF changes in the retina/choroid complex associated with isometric exercise in the unanesthetized human retina. A custom-made receive-only eye coil was used to improve SNR on a 3-Tesla clinical MRI scanner. Pseudo-continuous ASL technique (pCASL)[12] with static tissue suppression and single-shot turbo-spin-echo (TSE) acquisition were implemented. pCASL was used to improve BF sensitivity, static tissue suppression was used to enhance BF sensitivity and minimize eye movement artifacts, and TSE acquisition was used to achieve high spatiotemporal resolution free of susceptibility-induced signal drop off and image distortion.

Stable eye fixation on a target with synchronized eye blink was successfully used to minimize eye motion effects on time-series MRI data. Quantitative basal BF and BF changes associated with handgrip were analyzed.

Materials and Methods

Isometric Exercise

Four healthy subjects (3 males, 1 female, 25–36 years old) were studied with institutional review board approval. Each subject was imaged in multiple sessions (1–3) on different days. Multiple trials (2–4) were acquired within each session. A break of 10 minutes was given between trials to allow complete rest before the next trial. BF measurements were continuously measured over the entire functional MRI (fMRI) trial during which subjects rested for 1 minute, performed handgrip by squeezing stress balls for 1 minute, and the cycle repeated 3 times, followed by another 1 minute of rest. The total scan duration for each trial was 7 minutes.

Subjects were instructed to squeeze a stress ball as hard as possible while maintaining similar strength over 1 minute. To minimize eye motion, subjects were also instructed to maintain stable fixation on a target inside the magnet bore and blink only at the end of each data acquisition block (every 4.6 seconds), which generated a distinct sound as a cue. Moreover, to avoid hypo- or hyperventilation, subjects were instructed to inhale only (or exhale only) at the end of each data acquisition block during the entire fMRI trial. With an interimage repetition time of 4.6 seconds, such synchronized breathing and eye blinking were achieved comfortably. Subjects practiced the entire paradigm before the MRI study.

Blood pressure and heart rate (HR) were measured using a MRI-compatible physiological monitor (Precess; InVivo, Orlando, FL) in the middle of each rest and handgrip period during the entire MRI studies, at the rate of once per minute. Blood pressure was measured on the contralateral arm for unilateral handgrip or one leg for bilateral handgrip. Both unilateral and bilateral handgrips were used to achieve a wide dynamic range of MAP changes. Respiration rate (RR), end-tidal CO_2 ($EtCO_2$), and arterial oxygen saturation (SaO_2) were continuously recorded during the entire MRI study (Precess, InVivo, Orlando, FL). Confirmatory measurements of RR, $EtCO_2$, and SaO_2 were repeated on some subjects outside the scanner under identical experimental conditions.

To evaluate repeatability and reproducibility, three repeated MRI BF scans were performed on each of three different days over the course of a month. Scans on different days were repeated at the same time of the day. All other physiological parameters were measured repeatedly within a day in a similar time interval as the MRI BF measurements.

In separate measurements outside the scanner under identical rest-exercise paradigm in the supine position, the percentage of maximum strength achieved by handgrip was determined using a custom-built dynometer that was not MRI-compatible. This dynamometer consisted of a squeeze ball (of similar size and shape as the ones used in the MRI scanner) connected to a pressure sensor (Model 2.2; Iowa Oral Performance Instrument Medical LLC, Carnation, WA). Three trials with a 10-minute rest period between trials were measured.

Intraocular Pressure

IOP measurements were made by a certified clinical technologist or an ophthalmologist using a Tono-Pen XL (Reichert Inc., Depew, NY) on a separate day from the MRI study under the identical rest-exercise paradigm in the supine position. Measurements were made during rest and in the middle of the handgrip task, in similar manner as the blood-pressure measurement paradigm during MRI. Ocular perfusion pressure (OPP) was calculated as MAP-IOP.[5]

Magnetic Resonance Imaging

MRI was performed on a 3T Philips whole-body clinical scanner (Achieva; Philips Healthcare, Best, The Netherlands) using the commercial body coil for transmission and a custom-built single-loop surface coil for reception (oval shape, 7 × 5 cm in diameter). To minimize partial-volume effect (PVE), only a single central axial slice roughly bisecting the ONH of the right eye was imaged.

BF was imaged using the pCASL technique as previously described.[11,13] Briefly, pCASL used maximum labeling gradient = 6 mT/m, labeling duration = 2000 ms, and postlabeling delay = 1500 ms with balanced gradient scheme. The control images were acquired with a 180° phase shift to the labeling radiofrequency (RF) pulse. The ASL labeling plane was 7 cm inferior to the imaging plane. ASL background suppression used two inversion pulses at 2061 and 3405 ms after the initial saturation pulse, which was placed before the labeling RF pulse train.[14]

Image acquisition used the single-shot TSE sequence with: repetition time (TR) = 4.6 s, echo time (TE) = 30 ms, slice thickness = 6 mm, bandwidth = 12.8 kHz, FOV = 50 × 43 mm, and matrix = 100 × 53 (resolution of 0.5 × 0.8 mm). The higher spatial resolution was placed along the readout direction, perpendicular to the posterior retina. Label and control images were acquired alternately with a temporal resolution of 9.2 s per paired image. Equilibrium signal intensity M_0 for quantitative BF calculation was acquired on a separate TSE scan with long TR = 15 s without labeling module and background suppression module. Based on the safety monitor of the scanner, the specific absorption rate (SAR) was 2.9 W/Kg for TR = 4.6 s, which was below the limit recommended by the Food and Drug Administration. We previously verified that this protocol showed no residual magnetization-transfer effect when the labeling plane was shifted to 7 cm superior to the imaging plane.[11,15]

Data Analysis

All images from each scan were first aligned using custom algorithms written in Matlab (MathWorks Inc, Natick, MA). Image intensity profiles across the retinal thickness were obtained on the raw ASL images via automatic radial projection perpendicular to the retina[16] with four times the spatial interpolation. Some interpolations were necessary for the profile analysis to be completely automated and such spatial interpolation was previously confirmed not to significantly alter peak width and height.[16] Profiles at different time points were then coregistered to the averaged profile by minimizing the root-mean-square distances. Aligned images were played in bounced movie to ensure no residual motion or drift before further processing.

BF Calculation. Voxel-by-voxel BF was quantified in units of mL/100 mL/min to generate the BF map based on[17]:

$$BF = \frac{6000}{2 \cdot \lambda \cdot \alpha \cdot \alpha_{inv} \cdot T_{1,blood}} \cdot \frac{\Delta M_{ASL}}{M_o} \cdot e^{TI/T_{1,blood}} \cdot e^{TE/T_{2,blood}},$$

where ΔM_{ASL} is the difference of the control and label images. λ is the water content of blood in unit of milliliter water per milliliter arterial blood (0.85).[18] The blood $T_{1,blood}$ and $T_{2,blood}$ are 1.7 s at 37°C[19] and 275 ms at 3T.[20] α, the ASL efficiency, was assumed to be 0.85.[21] α_{inv} was 0.83, which corrected for the loss of perfusion signal due to the two background suppression pulses.[22] TI is the post-labeling delay and M_0 is the equilibrium signal intensity of vitreous calculated from the reference scan corrected for scaling factors and amplifier differences with the ASL sequences. The equilibrium signal intensity of the vitreous was used as an intensity reference for pure water, avoiding the use of unknown retina-blood partition coefficient in the quantitative BF calculation.

Correlation Analysis. Cross-correlation *Z*-score "activation" maps for display purpose were calculated via FSL software (FMRIB Library, The University of Oxford, UK)[23] by matching the BF signal time courses to the expected stimulus paradigm. Color statistical maps were overlaid on anatomy. To objectively quantify BF data and minimize PVE,

automated profile analysis was performed to generate the BF profiles across the thickness of the retina and along the length of the retina.[16] BF values were taken at the peaks of the projection profiles. A region of interest (ROI) outlining the posterior retina with the size of 6 to 10 mm along the retina and 0.7 to 0.8 mm across the retinal/choroidal thickness was used to obtain the BF signal time courses and averaged BF values.

Statistical Analysis. BF values were plotted against MAP and HR. Percentage changes of BF, MAP, HR, RR, IOP, OPP, $EtCO_2$, and SaO2 were analyzed. All reported values and error bars on graphs were in mean ± SD. All statistical tests used one-way ANOVA with correction for correlated samples with P less than 0.05 indicating statistical significance unless otherwise stated.

Results

A cross-sectional quantitative BF image (axial image slice, 0.5 × 0.8 × 6.0 mm) under basal condition from a single trial showed excellent BF contrast (Fig. 1). High BF was highly localized to the posterior retina/choroid complex. BF dropped significantly at the distal edges of the retina. The intrasubject, interday, and intersubject variations of BF MRI in the retina are 10, 30, and 56 mL/100mL/min, respectively.

Under rest conditions, MAP was 78 ± 5 mm Hg, IOP was 11 ± 3 mm Hg, OPP was 67 ± 4 mm Hg, arterial oxygen saturation was 99% ± 1 %, heart rate was 60 ± 5 beat per minute (bpm), respiration rate was 12 ± 6 bpm, $EtCO_2$ was 20 ± 3 mm Hg, and retina/choroid BF was 149 ± 48 mL/100mL/min or 1.98 ± 0.64 μL/mm²/min. There were no significant differences in these parameters between inside and outside scanner.

Isometric exercise increased BF in the retina as indicated by the activation map and BF time course (Fig. 2). Quantitative BF profile from one representative study is plotted across the retinal/choroidal thickness from sclera to vitreous (Fig. 3). Handgrip increased retina/choroid BF (peak value).

Figure 4 shows the BF versus OPP from multiple trials for all four subjects. BF was positively correlated with OPP for most subjects, although the correlation was not significant except in subject 1. The group-averaged quantitative BF and MAP data during rest and handgrip are shown in Figure 5. Isometric exercise robustly and significantly increased in MAP (22% ± 5%) and BF (25% ± 7%).

The group-averaged percent changes of IOP, MAP, OPP, SaO2, HR, and BF are listed in Table 1. Relative to rest, isometric exercise did not change IOP, SaO_2, $EtCO_2$, or RR ($P > 0.05$) but significantly increased MAP by 22% ± 5%, OPP by 25% ± 6%, HR by 19% ± 8%, and BF by 25% ± 7% ($P < 0.05$). Such handgrip induced 57% ± 6% of maximum strength (determined outside the magnet under identical experimental conditions).

Table 1. Group-Averaged Measurements during Rest, Handgrip Exercise, and the Percentage Changes of MAP, IOP, OPP, HR, SaO_2, $EtCO_2$, RR, and BF as a Result of Isometric Exercise

	Rest	Handgrip Exercise	Percentage Changes (%)
MAP (mm Hg)	78 ± 5	95 ± 2	22 ± 5*
IOP (mm Hg)	11 ± 3	11 ± 3	4 ± 14
OPP (mm Hg)	67 ± 4	84 ± 1	25 ± 6*
HR (bpm)	60 ± 5	72 ± 9	19 ± 8†
SaO_2 (%)	99 ± 1	96 ± 2	−3 ± 3
$EtCO_2$ (mm Hg)	20 ± 3	21 ± 3	4 ± 4
RR (bpm)	12 ± 6	13 ± 8	7 ± 27
BF (mL/100 mL/min)	149 ± 48	184 ± 53	25 ± 7*

Mean ± SD, $n = 4$ subjects.
* $P < 0.01$.
† $P < 0.05$.

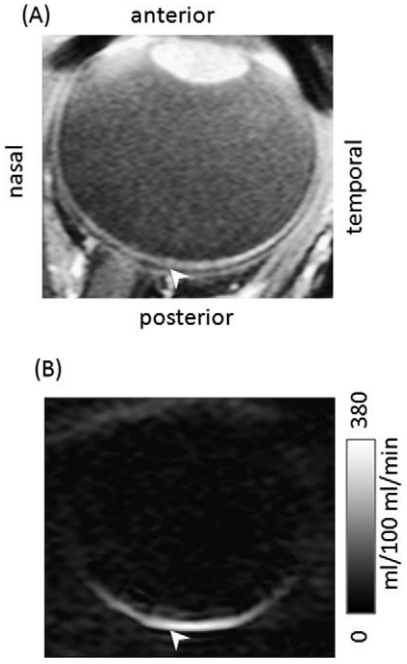

Figure 1. (**A**) Scout image and slice position, and (**B**) quantitative BF under resting condition in gray scale with unit of mL/100 mL/min. *White arrowhead* roughly indicates the foveal region.

Discussion

This study demonstrates a novel MRI application to image *quantitative* basal BF and its responses to handgrip in the unanesthetized human retina/choroid. MRI provides quantitative tissue perfusion with a large FOV and is not depth ambiguous. Relative to rest, isometric exercise did not change IOP, SaO_2, Et CO_2, or RR but significantly increased MAP, OPP, HR, and BF. BF MRI has the potential to become a valuable tool to study how BF is regulated in the normal retina (i.e., neurovascular coupling and autoregulation), and how retinal diseases may affect basal BF and BF regulation in the in vivo retina. Although future improvement in spatial resolution is expected, this study sets the stage for further exploration of BF MRI in the human retina.

Potential Issues

The eye is located close to air-tissue and bone-tissue interfaces and thus has severe magnetic field inhomogeneity, which could cause MR image distortion and signal drop off. TSE acquisition was used to overcome magnetic field inhomogeneity. A custom-designed eye surface coil was used to improve SNR and a pCASL technique was used to improve BF sensitivity. To minimize eye movement during MRI, a robust eye fixation protocol with synchronized eye blink and respiration (every 4.6 seconds) was used. All subjects studied felt comfortable with a blink period of every 4 to 8 seconds. Residual eye movement was successfully corrected by image coregistration.

The intrasubject, interday, and intersubject variations of BF MRI in the retina are 10, 30, and 56 mL/100 mL/min, respectively. These results demonstrated reasonable reproducibility consistent with brain BF measurements[24] which were demonstrated to have high intra- and interday reproducibility

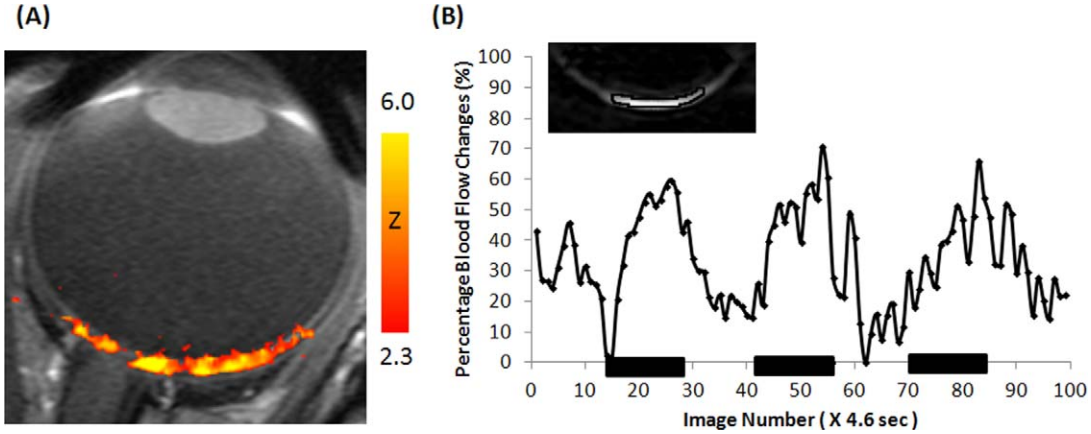

Figure 2. BF (**A**) activation map and (**B**) time course time during rest and handgrip from one trial from one subject. Time course was averaged from a posterior ROI showed on the inset image. Color maps are overlaid on the anatomical images. *Color bar* indicates *Z* scores.

within subjects.[25] Accuracy of absolute BF quantification in the brain has been cross-validated with positron emission tomography and autoradiographic techniques.[26] Ultimately, ASL MRI of the retina needs to be cross-validated with the microsphere technique in animal models. Finally, it is important to note that BF MRI measures volume flow without the need to visualize individual vessels. BF MRI is sensitive to smaller vessels, such as capillaries, venules, and arterioles (i.e., tissue perfusion), with relatively less weighting to large vessels.[25,27]

Given the spatial resolution, BF signals in this study came from both retinal and choroid vasculatures. Because choroid BF is significantly higher than retinal BF (see below), the reported BF value was likely dominated by choroid BF in this study. Future studies will improve spatial resolution to separate retinal and choroid BF quantification.

MAP was measured at one time point in the middle of the handgrip task, whereas BF was averaged over 1 minute. Continuous MAP measurements every 10 seconds outside the MRI scanner showed that handgrip MAP increased in proportion to the exercise duration and reached plateau at 2 to 3 minutes (data not shown). Although MAP measured at one time point may not accurately reflect the averaged MAP over the rest or handgrip period, this drawback would not invalidate the overall conclusions of this study.

Basal Blood Flow

Basal BF contrast was the highest in the posterior retina in the macular region and around the ONH, and dropped significantly at the distal edges of the retina, consistent with the expected vascular density. Basal BF of the retina/choroid complex was 149 ± 48 mL/100 mL/min (posterior retina ROI) in awake humans. The large SD was due to intersubject variation. This basal BF value was similar to, but slightly higher than, the previously reported value from our laboratory using the same eye coil (93 ± 31 mL/100 mL/min, mean ± SD, $n =$

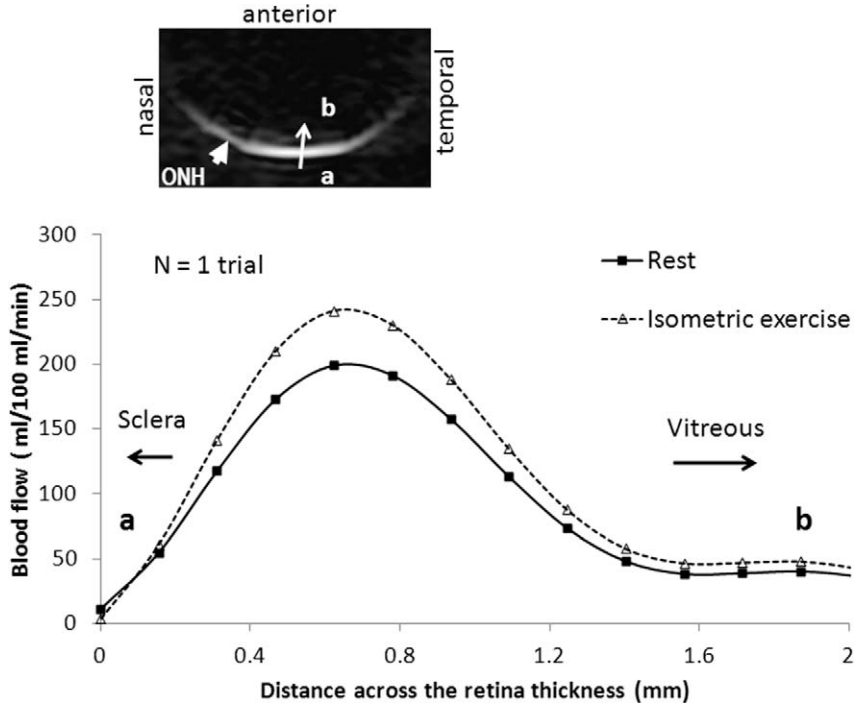

Figure 3. BF profile during rest and handgrip across the retinal/choroidal thickness from the sclera to the vitreous as shown in the inset.

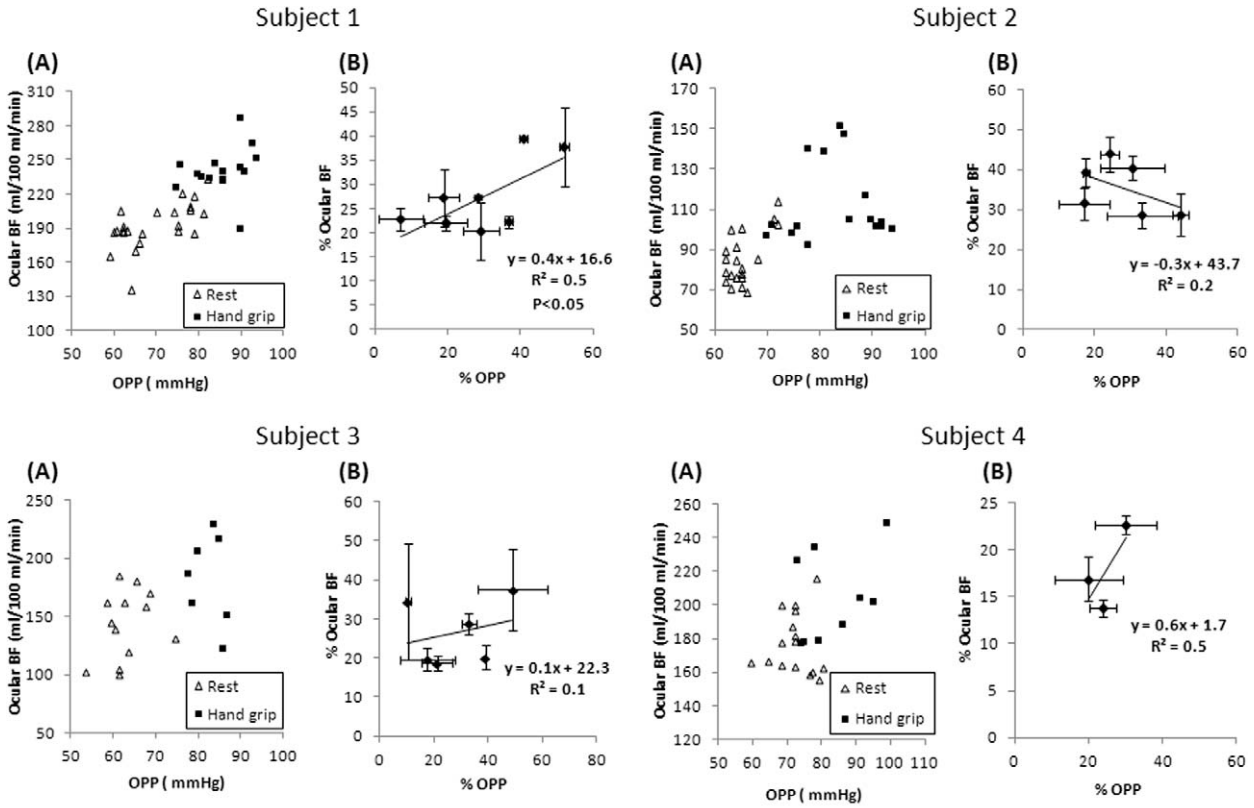

Figure 4. Scatter plot of BF versus OPP in (**A**) quantitative unit and (**B**) percent changes for all trials for each individual subject. Error bar: SD from three repeated rest-exercise cycles within a trial.

5),[11] due to a larger posterior retina ROI used in a previous report. In another retinal MRI study using a brain coil, Maleki et al.[10] reported retina/choroid BF to be 80 mL/100 g/min. This minor discrepancy could be explained by differences in subjects, PVE caused by different spatial resolutions, regions analyzed, and analysis methods (e.g., this study and Peng et al.[11] used a full-width-half-maximum of the BF profile whereas Malaki et al.[10] used an ROI). Age of the subjects could also be a factor.

In rats, retina/choroid BF has been reported to be 630 ± 100 mL/g/min using continuous ASL MRI[28] in rats anesthetized with 1% isoflurane.[29,30] The difference between human and rat retina BF values could be due to differences in species, PVE, and/or anesthetic versus awake conditions. Smaller animals generally have higher metabolic rates and thus higher BF. Isoflurane used in the animal study is a vasodilator and yields higher BF compared with human awake conditions. PVE with the neighboring vitreous and sclera,

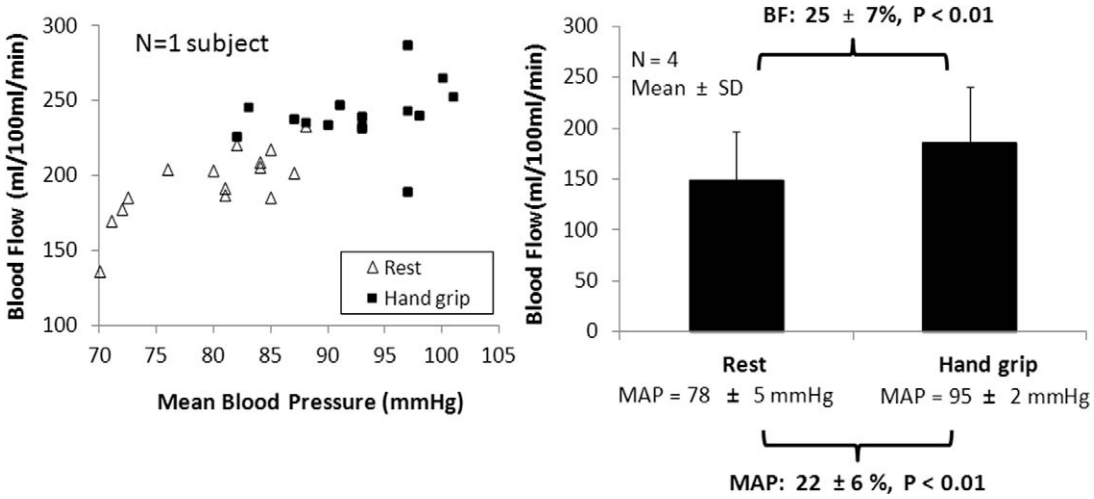

Figure 5. Quantitative BF during rest and handgrip with the corresponding MAP.

which have no BF, would lead to underestimation of retina/choroid BF. Because the spatial resolution of current human study is lower than those of previous rat studies, higher PVE in human data would lead to a larger underestimation of BF in the human retina.

Isometric Exercise

Isometric exercise increased BF in the retina/choroid by 25% ± 7%. Because choroid has considerably higher BF, these changes likely reflected mostly choroidal BF changes. Our isometric exercise paradigm is considered mild compared with leg extension (moderate) and squatting (strong). Our paradigm is also considered shorter in duration than many previous studies. We were surprised by the marked MAP and BF increases. The reasons for the marked BF increase during exercise include increased $EtCO_2$ and increased OPP.

BF increase in the retina could be caused by an increase in arterial carbon dioxide tension (pCO_2), or $EtCO_2$ as a result of involuntarily breath-hold during handgrip.[31] Arterial pCO_2 has been shown to increase choroidal BF by various BF measurement methods.[32,33] Using the same BF MRI approach, we previously reported that inhalation of 5% CO_2 (balance air) increased BF in the retina/choroid by 13% ± 6% compared with air.[28] In the current study, subjects were instructed to maintain the same breath pattern during the entire MRI scan. $EtCO_2$ and RR were not statistically different between rest and isometric exercise. Thus, it is unlikely that $EtCO_2$ changes in our isometric exercise paradigm contributed significantly to BF increase in the retina.

Handgrip increased MAP by 22% ± 5% and OPP by 25% ± 6% in our study. By contrast, Kiss et al.[6] reported no significant changes of ocular BF in the macular area during isometric squatting exercise until OPP exceeded the rest value by 69%. In another study using LDV, it was reported that retinal BF as measured from retinal veins did not change during isometric exercise until MAP reached approximately 115 mm Hg.[3] Choroid BF did not change during isometric exercise over a wide range of MAP studied.[34] Kiel et al.[35,36] also used LDF to investigate the relation among IOP, MAP, and choroid BF in rabbits. They found that choroid BF did not vary with MAP over the range of 40 to 80 mm Hg when IOP was not controlled. The ability to maintain constant choroid BF has been attributed to the increased vascular resistance in proportion to increase in OPP,[4,5] which is supported by the observation of a significant vasoconstriction in retinal arterioles and venules during handgrip exercise.[37]

The discrepancy between our study and other studies could be due to methodological differences. For example, Kiss et al.[6] used a theoretical model of an eye ball in their deviation of choroidal BF from the fundus pulsation amplitude as measured by laser interferometry. The model assumed that the pulsatility property of the ophthalmic artery is essentially the same as that of choroidal vasculature, which may not be the case because uncoupling between BF in the choroid and ophthalmic artery could be present, for example, during an artificial increase in IOP.[38] LDV and LDF have been used to study BF in the optic nerve head or the macula, whereas we measured BF on a larger area of the posterior retina, including the temporal disk of ONH and the macula. ONH contains large arteries and draining veins that generally vasoreact to smaller extents than smaller vessels in tissue.[3,37]

Another explanation of the discrepancy is that our handgrip paradigm is short in duration (1 minute) during which MAP continues to increase and autoregulation has not fully acted to return BF to normal basal physiological value. A previous study reported that BF took a few minutes to return to baseline following aorta occlusion to increase MAP in monkeys.[39] Our preliminary rat studies with occlusion of descending aorta to acutely increase MAP demonstrated that it took several minutes for cerebral and retina/choroid BF to return close to baseline (data not shown). Future studies will investigate handgrip exercise of longer durations in the retina and brain with real-time MAP measurements.

Conclusions

This study demonstrates a novel application of BF MRI to measure quantitative BF during rest and isometric exercise in the unanesthetized human retina. Retina/choroid BF increases during brief handgrip exercise paralleling increases in MAP. These data provide a means to evaluate BF regulation in the retina noninvasively, which may be used to probe retinal pathophysiology. The advantages are that BF MRI measures tissue perfusion with a large FOV and that it is not depth limited. The disadvantages include its significantly longer acquisition duration and its relative low cost effectiveness compared with optical techniques. BF MRI may have the unique potential to image layer-specific, quantitative BF in human retina if higher spatial resolution can be achieved. In addition to BF, MRI could also provide anatomical, oxygen tension, and functional data in the same setting as well demonstrated in animal models. Translating these approaches to image the human retina could have important clinical applications. Future studies will need to improve sensitivity and spatiotemporal resolution, incorporate three-dimensional BF and other (e.g., BOLD and anatomical) MRI methods, and apply MRI to study retinal diseases. This approach could open up new avenues for retinal research and complement existing retinal imaging techniques.

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