Changes in Choroidal Blood Flow and Morphology in Response to Increase in Intraocular Pressure

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Purpose. The purpose of this study was to determine the effects of an elevation in IOP on the choroidal blood flow and morphology.

Methods. We studied 27 healthy subjects. The mean blur rate (MBR) determined by laser speckle flowgraphy was used to measure the choroidal blood flow. The subfoveal choroidal thickness (SFCT) was measured in the optical coherence tomographic images of the macular region. The luminal and stromal areas of the choroid were determined by the binarization method before, during, and after the IOP was elevated 20 and 30 mm Hg with pressure using an ophthalmodynamometer.

Results. The ocular perfusion pressure (OPP) was significantly reduced by the elevation of the IOP by 20 (−52.0%, P < 0.001) and 30 mm Hg (−77.9%, P < 0.001). The percentage reduction in the macular choroidal MBR was −52.5% at an IOP elevation of 20 mm Hg (P < 0.001) and −46.6% at an IOP elevation of 30 mm Hg (P < 0.001). The SFCT was reduced by −5.8% (P = 0.014) and −7.7%, (P < 0.001) during an elevation of IOP of 20 and 30 mm Hg, respectively. The luminal area of the choroid was reduced during an elevation of the IOP of 20 (P = 0.001) and 30 mm Hg (P < 0.001). However, the stromal area did not change significantly. There was no significant correlation between the reduction ratio of OPP and other factors during the elevation of 20 mm Hg, but the correlation between the reduction ratio of OPP and the choroidal MBR during the elevation of 30 mm Hg was significant. The choroidal MBR had recovered significantly at 7 (P = 0.037) and 10 minutes (P = 0.022) compared with that immediately after the IOP elevation of 30 mm Hg.

Conclusions. The choroid can autoregulate its blood flow in response to experimental changes in the OPP induced by IOP elevations.

Keywords: choroidal blood flow, choroidal structure, intraocular pressure, elevation

The choroid is a highly vascularized tissue that provides nourishment to the RPE, outer retina, and optic disc. Histologic studies on eyes with primary open-angle glaucoma have demonstrated a reduction of the choroidal thickness and a decrease in the density of both the large choroidal vessels and the capillaries in the choriocapillaris layer. Two studies have shown a decrease in the blood flow in the choroid of patients with glaucoma. However, Grunwald et al. reported that the choroidal blood flow in the foveal area of glaucomatous eyes was not significantly different from that of normal eyes.

Autoregulation is defined as the ability of a vascular bed to keep the blood flow constant when the perfusion pressure is changed. For decades, the choroidal vasculature was considered to be a passive vascular bed in which a decrease of perfusion pressure led to a linear decrease in blood flow. Kiel et al. were the first to report that the choroid had some ability to autoregulate, which is particularly pronounced when the ocular perfusion pressure (OPP) is decreased by increasing the IOP while the mean ophthalmic artery pressure remains unchanged in rabbits. They concluded that the choroid has a weak but significant ability of autoregulate its blood flow in response to changes the OPP. Although the choroidal blood flow should be affected to some degree by changes in the OPP, it is still unclear whether the blood flow in the choroid is reduced in eyes with lower OPPs due to high IOPs (e.g., glaucoma).

There have been several studies of the choroidal blood flow and its regulation using different instruments to measure the choroidal blood flow in eyes with elevated IOPs. However, it is not easy to determine the choroidal blood flow accurately because the measurements must be made through the RPE. In addition, the results obtained by the various instruments could be different because of the properties each of the instruments is different.

A relatively new instrument that can be used to measure the relative choroidal blood flow is the laser speckle flowgraphy (LSFG) instrument (Softcare Co., Ltd., Fukatsu, Japan). It is a noninvasive, real-time method that has been used to measure the relative blood flow rate without the use of intravenous contrast agents. LSFG uses the speckle contrast pattern produced by the interference of the observation laser light scattered by the movement of erythrocytes in the blood vessels. The changes in the speckle pattern represent changes in the relative blood flow rate in the vessels, and it is expressed by the mean blur rate (MBR). The measurements have excellent reproducibility with a coefficient of variation (COV) of 4.7. Therefore, LSFG is considered a suitable method to measure the ocular blood flow including the choroidal blood flow.
The choroidal thickness has been reported to increase after the IOP is reduced by trabeculectomy, indicating that the choroidal morphology is closely related to the IOP. However, there is one study that reported that there was no significant relationship between the macular choroidal thickness and glaucoma. Thus, whether there is a significant association between the choroidal thickness and glaucoma remains controversial.

The choroid is composed mainly of vessels, the luminal area, extravascular tissues, and the stromal area, and the lack of a well-organized structure makes it difficult to differentiate the luminal from the stromal areas of the choroid by imaging devices. Recently, Sonoda et al. reported the use of a binarization method that can be used to differentiate the choroidal luminal from the stromal areas in the of spectral domain–optical coherence tomography (SD-OCT) images and to quantify the areas using ImageJ software (National Institutes of Health, Bethesda, MD, USA) with high repeatability. Therefore, it should be possible to determine the changes in the choroidal structures after an elevation of the IOP. As best we know, there has not been a study on the effects of the IOP on the choroidal blood flow and the morphology of the choroid before, during, and after the IOP is elevated. Investigating the relationship of changes between the blood flow and the morphology should determine whether autoregulation of the choroidal occurs for changes in the OPP induced by IOP elevation.

Thus, the purpose of this study was to determine the regulation of choroidal blood flow by measuring the changes in the blood flow and morphology of the choroid in response to changes in the OPP induced by an artificial elevation of the IOP in healthy eyes. The choroidal blood flow was determined by LSFG and the choroidal morphology by analyses of the SD-OCT images.

**METHODS**

**Ethics Statement**
The procedures used were approved by the Ethics Committee of the Nagoya University Hospital and registered with the University Hospital Medical Network (UMIN) clinical trials registry (UMIN0000024980). The study was conducted at the Nagoya University Hospital. The procedures conformed to the tenets of the Declaration of Helsinki, and informed consent was obtained from all subjects after an explanation of the procedures to be used and the possible complications.

**Experimental Protocol**
Twenty-nine healthy Japanese individuals were recruited. Eyes were excluded if the best-corrected visual acuity was <20/20, macular abnormalities such as choroidal neovascularization or asymptomatic pigment epithelial detachment were present; a history of ophthalmic or systemic disorders; previous ocular laser or incisional surgery in the experimental eye; systolic blood pressure (SBP) >150 mm Hg; diastolic blood pressure (DBP) >90 mm Hg; axial length >27.0 mm; and medical conditions that could influence the hemodynamics of the eye such as diabetes, hypertension, arrhythmia, and vascular diseases.

All volunteers were asked to abstain from alcoholic and caffeinated beverages on the morning of the examination. The pupil was dilated 30 minutes before the examinations, and the subject rested in a quiet dark room for 10 to 15 minutes before the measurements to achieve stable hemodynamic conditions. All examinations were performed in the sitting position at approximately 1200 hours to avoid diurnal variations.

The axial lengths were measured by partial optical coherence interferometry (IOLMaster; Carl Zeiss Meditec, La Jolla, CA, USA), and the IOP was measured with a handheld tonometer (Icare; Tiolat Oy, Helsinki, Finland). The SBP and DBP were measured with an automatic sphygmomanometer (CH-483C; Citizen, Tokyo, Japan). The mean arterial blood pressure (MAP) and OPP were calculated as: MAP = DBP + 1/3(SBP - DBP) and OPP = 2/3MAP - IOP.

**Experimental Elevation of IOP**
An ophthalmodynamometer (Inami, Tokyo, Japan) was used to elevate the IOP. The ophthalmodynamometer was used to apply a fixed external pressure on the eye through the lower lid with the device held perpendicular to the globe (Fig. 1A). According to the ophthalmodynamometer scale, the force applied increased the IOP by a fixed amount. In addition, the IOP was measured with the Icare tonometer (Icare; Tiolat Oy) before, during, and after the IOP was elevated. One experimenter kept the ophthalmodynamometer in place and another experimenter recorded the LSFG images and then recorded SD-OCT images after the subjects moved to the SD-OCT instrument. The time courses of the changes in the IOP are shown in Figure 2.

For the experiments, the IOP was increased by 20 mm Hg for 2 minutes in experiment 1 and for 10 minutes in experiment 2. The IOP was then increased by 30 mm Hg for 2 minutes in experiment 1 and for 10 minutes in experiment 2 after a resting period of at least 20 minutes. The LSFG and SD-OCT images were recorded at 1 minute before the IOP elevation, at 1 minute after the 20 and 30 mm Hg IOP elevations, and at 1 minute after the release of the pressure (experiment 1). For another 10 volunteers, the IOP was increased by 30 mm Hg from the baseline for 10 minutes. The LSFG and SD-OCT images were recorded before, immediately after the IOP elevation (time 0), and at 1, 3, 5, 7, and 10 minutes during the IOP elevation. The IOP was measured again at 1, 3, and 5 minutes after a release of the pressure on the eye (experiment 2).

**LSFG**
The LSFG-navigation (NAVI) was used to determine the relative choroidal blood flow. The principles of LSFG have been described in detail. Briefly, the choroidal blood flow was determined by the changes in the speckle contrast pattern produced by the interference of the observation laser light by the movement of erythrocytes in the blood vessels. The changes in the speckle pattern represent the changes in the blood flow rate in the vessels, which is expressed by the MBR. The interference images were acquired at a rate of 30 frames/s over a 4-second period. The embedded analysis software synchronized all of the images of each cardiac cycle, and the averaged images of a heartbeat were displayed as a composite map. These images were used to determine the MBR.

The MBR was determined at the center of a square (6.31 × 6.31; 250 × 250 pixels) that was centered on the fovea (Fig. 1B). The MBR was measured three times at each time point in all eyes, and the average was used for the statistical analyses.

**Measurements of Thickness of Subfoveal Choroid and Areas of Luminal and Stromal Choroid**
The choroidal images were obtained by SD-OCT (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany), and the
choroidal thickness was measured in the SD-OCT images using the enhanced depth imaging (EDI) technique (Fig. 3A). The subfoveal choroidal thickness (SFCT) was measured as the distance between the hyperreflective RPE line to the choroid–sclera border with the caliper tool on the SD-OCT device.

The choroidal areas in the EDI-OCT image were binarized by the modified Niblack’s method. The EDI-OCT images were analysed with the ImageJ software (ImageJ version 1.47; National Institutes of Health). The examined subfoveal choroid area was 1500 \( \mu \text{m} \) wide and extended vertically from the RPE to the chorioscleral border (Fig. 3). This choroidal area of interest was selected by the ImageJ ROI Manager (Fig. 3B, top), and it was converted to 8-bit images by the program. The vitreous cavity anterior to the macular area was selected by the Oval Selection Tool on the ImageJ tool bar, and the maximum reflectivity of this area was determined. The maximum brightness was set as the minimum value to minimize noise in the OCT images (Fig. 3B, middle). After adjusting by the Niblack Auto Local Threshold, the luminal area was determined using the threshold tool (Fig. 3B, bottom). The light pixels were taken to be the stromal areas, and the dark pixels were taken to be the luminal areas. Finally, the areas represented by pixel on ImageJ software were converted to actual distance (\( \mu \text{m} \)) using a conversion ratio embedded in the Spectralis, and the luminal and stromal areas were calculated. Two clinicians who were masked to the other findings measured the areas.

**Statistical Analyses**

The values are presented as the means ± SDs. Independent \( t \) tests were used to determine the significance of differences in the normally distributed data. Spearman analyses were used to determine the correlation coefficients between the variables. A mixed model was used to incorporate the appropriate covariates between repeated-measured values over time. Multiple stepwise regression analyses were used to determine the association between choroidal MBR or the luminal area and the variables. All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 23 (IBM Corp., Armonk, NY, USA). The significance level was set at \( P < 0.05 \).

**RESULTS**

**Subject Disposition, Demographics, and Baseline Characteristics**

Two subjects dropped out of the study because they could not tolerate the application of the ophthalmodynamometer on the lower lid in experiment 1. Seventeen volunteers completed all phases of the examinations in experiment 1 (33.2 ± 8.3 years old) and 10 volunteers completed all phases of experiment 2 (28.6 ± 1.0 years old). No adverse events were observed in any of the volunteers, and the demographics of the participating volunteers are shown in Tables 1 (experiment 1) and 2 (experiment 2).

**Changes in IOP and OPP**

A significant increase in the IOP was observed after applying the ophthalmodynamometer in both experiments, but no significant changes in the SBP, DBP, and MAP were observed. These results indicated that the application of the ophthalmodynamometer caused a significant increase in IOP of 20 (±142.4%) and 30 mm Hg (±217.9%), and the MAP was not
significantly changed in experiment 1 (Table 3). These increases in the IOP reduced the OPP significantly by \(-52.0\%\) with 20 mm Hg and \(-77.9\%\) with 30 mm Hg (both \(P < 0.001\)).

In experiment 2, the application of the ophthalmodynamometer caused a stable and significant increase in IOP by 30 mm Hg for 10 minutes, and the MAP did not change (see Fig. 5A). Hence, the OPP was significantly decreased during the IOP elevation. After the release of the pressure, the IOP and MOPP returned to around the baseline.

### Changes in Choroidal MBR

The mean macular choroidal MBR was 11.6 ± 4.1 AU before, 7.7 ± 2.8 AU (−32.5%) during the 20 mm Hg elevation, and 6.1 ± 2.8 AU (−46.6%) during the 30 mm Hg elevation. The MBR returned to 11.2 ± 4.1 AU after the IOP elevation (Fig. 1C). The reduction of the macular choroidal MBR during both levels of IOP elevation was significant (both \(P < 0.001\)).

In experiment 2, the MBR was 13.0 ± 3.7 AU before the IOP elevation, and it was significantly reduced to 6.7 ± 2.0 AU (−47.1%) immediately after the IOP elevation by 30 mm Hg. The MBR was significantly reduced until the pressure was released (all \(P < 0.001\); see Fig. 5B). During the 30 mm Hg IOP elevation, the MBR significantly recovered by 7 minutes to 8.2 ± 2.9 AU (−35.5%; \(P = 0.022\)) and 10 minutes to 8.3 ± 2.9 AU (−35.5%; \(P = 0.022\)) compared with that immediately after the IOP elevation. The MBR returned to 13.2 ± 4.1 AU (+1.5%) at 1 minute, 12.9 ± 3.9 AU (−0.7%) at 3 minutes, and 12.6 ± 3.9 AU (−3.1%) at 5 minutes after the release of the pressure. All values were not significantly different from that at the baseline.

### Morphologic Changes of Choroid

The pressure applied by the ophthalmodynamometer caused a significant decrease in the mean SFCT; a 20 mm Hg elevation decreased the SFCT by 9.3 \(\mu\)m or 3.8%, and a 30 mm Hg elevation decreased the SFCT by 16.2 \(\mu\)m or 7.7% in experiment 1 (Fig. 4B). The mean SFCT during the IOP elevation was significantly thinner than that before the IOP elevation (\(P = 0.014\) and \(P < 0.001\), respectively).

The mean SFCT was significantly correlated with the luminal area during the elevation of 20 (\(r = 0.941\), \(P < 0.001\)) and 30 mm Hg (\(r = 0.975\), \(P < 0.001\)). The mean overall choroidal and luminal areas were significantly reduced during the IOP elevation of 20 (\(P = 0.001\)) and 30 mm Hg (\(P < 0.001\)). However, the stromal area was not changed significantly (Fig. 4).

In experiment 2, the mean SFCT and the overall choroidal and luminal area were significantly reduced immediately after the IOP elevation compared with that at the baseline (all \(P < 0.001\)). The SFCT was reduced, and the overall choroidal and luminal areas were not changed during the IOP elevation for 10 minutes.
Heart rate, BPM 69.7
Diastolic blood pressure, mm Hg 72.3
Systolic blood pressure, mm Hg 116.9

Figure 3. Representative binarized image of the choroidal area in an EDI OCT image. The area of interest of the choroid is demarcated (top). The EDI-OCT image is converted to a binary image using ImageJ software. The rectangle surrounded by the red line was excised, and the dark areas were traced by the modified Niblack method (middle). The binarized image and the margin of the traced area are merged, which demonstrates that the traced area is consistent with the dark areas of the choroidal areas of the OCT image (bottom).

minutes, and these values returned to around the baseline 1 minute after the release of the pressure (Fig. 5). The stromal area was not changed significantly. The coefficient of variation was 0.7 for the SFCT, 2.5 for the choroidal area, 1.4 for the luminal area, and 5.6 for the stromal area.

Correlation Between MBR and Other Parameters

The correlations between the percentage reduction of the OPP and the choroidal MBR and the SFCT during the IOP elevation are presented in Figure 6. The percentage reduction of the choroidal MBR was positively correlated with that of the OPP during the elevation of the IOP by 30 mm Hg ($r = 0.58$, $P = 0.014$) in experiment 1. However, the correlation between the percentage reduction of the choroidal MBR and the SFCT during the 20 mm Hg elevation was not significant. In addition, the correlations between the percent reduction of the OPP and other factors during the 20 mm Hg IOP elevation were not significant. The correlations between the percentage reduction of the choroidal MBR and the SFCT during the IOP elevation were not significant.

In experiment 2, the correlation coefficient between the percentage reduction of the choroidal MBR and OPP was similar to that in experiment 1 immediately after the 30 mm Hg IOP elevation ($r = 0.58$, $P = 0.080$), but it was reduced during the IOP elevation for 10 minutes (Fig. 7).

Discussion

Our results showed that the macular choroidal MBR, the OPP, the SFCT, and the luminal area of the choroid were significantly reduced during the IOP elevation. The correlations between the reduction of the OPP and other factors during the 20 mm Hg IOP elevation were not significant, but the correlation between the reduction of the OPP and the choroidal MBR during the 30 mm Hg IOP elevation was significant. In addition, during the 30 mm Hg IOP elevation for 10 minutes, the choroidal MBR changed slightly but recovered significantly.

The OPP is calculated as $2/3(SBP - C0)$, and because the MAP was not altered by the IOP elevation by the application of the ophthalmodynamometer, the decrease in the OPP during the elevation in the IOP caused a reduction of the choroidal MBR. Thus, the IOP elevation appears to be the major factor causing the decrease in the choroidal MBR.

It has been generally assumed that the choroid is not autoregulated. Animal experiments have demonstrated a linear relationship between the OPP and choroidal blood flow using a variety of techniques.7–9 Recently, however, investigations in rabbits strongly suggested that the choroid has some ability to autoregulate, which is particularly pronounced when the OPP is decreased by increasing the IOP at a constant MAP.26 In addition, there is evidence in humans that the choroidal blood flow is regulated during changes in the OPP induced by artificial IOP increases.12

Our findings showed that the ratio of the reduction of the choroidal MBR was smaller (~32.5% and ~46.6%) than that of the OPP (~52.0% and ~77.9%, respectively), suggesting some degree of choroidal blood flow regulation during an increase in the IOP because the decrease in the OPP was more than the decline in the choroidal blood flow. These results corroborate some earlier studies in humans, which showed that a decrease in OPP is accompanied by a decrease in the choroidal blood flow, although it is proportionately less than the decrease in OPP. This indicated that there is some degree of autoregulation of the choroidal blood flow in response to a decrease in the OPP.12,27–30

Table 2. Baseline Characteristics of Subjects (Experiment 2)

The correlations between the reduction of the OPP and other factors during the 20 mm Hg IOP elevation were not significant, but the correlation between the reduction of the OPP and the choroidal MBR during the IOP elevation for 10 minutes (Fig. 7).

Table 1. Baseline Characteristics of Subjects (Experiment 1)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mean ± SD</th>
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<tbody>
<tr>
<td>Age, y</td>
<td>33.2 ± 8.3</td>
</tr>
<tr>
<td>IOP, mm Hg</td>
<td>15.7 ± 3.6</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>25.8 ± 0.94</td>
</tr>
<tr>
<td>Refractive error, D</td>
<td>−4.26 ± 2.54</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>116.9 ± 13.8</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>72.3 ± 10.6</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>69.7 ± 6.8</td>
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</table>

There was also a significant correlation between the percentage reduction of the OPP and choroidal MBR during the elevation of the IOP by 30 mm Hg but not during an elevation by 20 mm Hg. These results imply that there is an autoregulatory plateau, below which the autoregulation function of the choroid is active, but at higher levels of IOPs, the autoregulation is not operating immediately after the IOP increase leading to changes in the choroidal MBR. The results are in agreement with previous experiments. Schmidl et al.51 reported that there is an autoregulatory plateau, below which there is autoregulation but above which there is no autoregulation and the choroidal blood flow decreases linearly.

Table 2. Baseline Characteristics of Subjects (Experiment 2)

<table>
<thead>
<tr>
<th>Characteristics, n = 10</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>33.2 ± 8.3</td>
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<tr>
<td>Heart rate, bpm</td>
<td>69.7 ± 6.8</td>
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</table>
On the other hand, our result showed that during the IOP elevation by 30 mm Hg for 10 minutes, the choroidal MBR recovered to the baseline pressure. In addition, a high correlation coefficient was found between the percentage reduction of the OPP and choroidal MBR during the IOP elevation by 30 mm Hg for 10 minutes. Thus, our results are in good agreement with the findings that the blood flow in the choroid is autoregulated after relatively slight decreases in the OPP induced by an IOP elevation.11,12

There have been several reports on the morphologic changes of the choroid after trabeculectomy including a thickening of the SFCT.17–20 Chakraborty et al.32 reported a negative association between the IOP and choroidal thickness during a 12-hour observation period over 2 consecutive days in normal adult subjects. Our results are consistent with these results of a negative correlation between induced IOP increase and choroidal thickness. Because the choroid is a vascular-rich tissue, it is most likely that SFCT can be easily affected by changes in factors such as the choroidal circulation and OPP, but the percentage reduction was smaller (20 mm Hg elevation, 3.8%; 30 mm Hg elevation, 7.7%) than that of the OPP (20 mm Hg elevation, 52.0%; 30 mm Hg elevation, 77.9%).

Histologically, the choroid is composed of blood vessels and extravascular tissue. The extravascular tissues form the stromal area and include smooth muscle cells, collagen, and elastic fibers.33 The stromal area, which accounts for one-third of the choroidal area, did not change during the elevated IOP, and its size was not significantly correlated with the MBR of the choroid. Thus, the thinning of the SFCT was caused by a reduction of the luminal area during the artificial IOP increase. However, the percentage reduction even of the luminal area (20 mm Hg elevation: 4.9%, 30 mm Hg elevation: 7.4%) was much smaller than that of the choroidal MBR (20 mm Hg elevation, 32.5%; 30 mm Hg elevation, 46.6%). In addition, there was no significant correlation in the percentage reduction between choroidal MBR and the luminal area during the IOP elevation. This discrepancy indicates that changes in the OPP induced by the IOP elevation caused a slight reduction in the luminal area, but mainly in the blood flow indicating a hemostasis of the choroidal blood flow.

The mechanism(s) involved in the choroidal autoregulation associated with changes in the OPP has not been determined. The choroid has rich parasympathetic, sympathetic, and sensory innervations. In addition, the intrinsic choroidal neurons receive parasympathetic and sympathetic innervations. These intrinsic choroidal neurons are assumed to play a role in choroidal blood flow regulation.34 Riva et al.11 examined the time course of the changes in the choroidal blood flow during a stepwise elevation in the IOP and they reported that a neurogenic mechanism may be involved in the choroidal autoregulation during the decrease in the OPP. They also stated that a myogenic mechanism cannot be excluded based on these findings. For the myogenic mechanism to be active, it must be assumed that if the transmural pressure is decreased, the vascular smooth muscles relax resulting in an

### Table 3. Changes in Parameters With IOP Increase

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline</th>
<th>20 mm Hg IOP Increase</th>
<th>30 mm Hg IOP Increase</th>
<th>After Release of the Pressure</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP, mm Hg (%)</td>
<td>88.4 ± 11.4</td>
<td>87.5 ± 12.9</td>
<td>88.0 ± 12.3</td>
<td>87.1 ± 10.7</td>
<td>0.989</td>
</tr>
<tr>
<td>IOP, mm Hg (%)</td>
<td>15.7 ± 3.6</td>
<td>18.2 ± 5.0</td>
<td>19.2 ± 5.2</td>
<td>16.7 ± 3.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OPP, mm Hg (%)</td>
<td>42.4 ± 8.7</td>
<td>19.3 ± 9.4</td>
<td>9.1 ± 8.8</td>
<td>42.8 ± 6.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**FIGURE 4.** The SFCT during the IOP elevation was thinner than that at the baseline and returned to baseline after IOP increase (A). Changes in the choroidal area (B) and luminal area (C) were similar to those of the SFCT. The stromal area did not change significantly (D).
FIGURE 5. Change in the systemic and ocular parameters before an increase in the IOP, during 30 mm Hg IOP increases for 10 minutes, and after IOP returned to baseline pressure. The IOP was significantly increased, and the OPP was significantly decreased during the application of the ophthalmodynamometer, although the MAP was not changed (A). The MBR was significantly reduced from immediately after the IOP elevation by 30 mm Hg to until the pressure was released (B). During the 30 mm Hg IOP elevation, the MBR significantly recovered at 7 (8.2 ± 2.9 AU; −36.7%; P = 0.016) and 10 minutes (8.3 ± 2.9 AU; −35.5%; P = 0.021) during 30 mm Hg IOP elevation compared with that immediately after IOL elevation. The mean SFCT (C), overall choroidal (D), and luminal area (F) were significantly reduced from immediately after the IOP elevation by 30 mm Hg to until the application was released. The stromal area was not changed (E). ***P < 0.001, **P < 0.01.
FIGURE 6. Relationship between the ratio of elevation of IOP between variables (e.g., OPP during IOP elevation and the choroidal MBR or the SFCT). There was no significant correlation in the ratio of 20 mm Hg increase to the baseline between the choroidal MBR and the OPP (A), whereas the choroidal MBR 30 mm Hg increase to the baseline ratio was positively and significantly correlated with that of the OPP ($r = 0.58$, $P = 0.014$) (B). There was no significant correlation in the ratio of IOP increase to the baseline between the SFCT and the OPP (C, D). There was no significant correlation in the ratio of IOP increase to the baseline between the choroidal MBR and the luminal area (E, F).

FIGURE 7. Relationship between the reduction ratio during 30 mm Hg IOP elevation between the OPP and choroidal MBR. The correlation coefficient between the percentage reduction of the choroidal MBR and OPP was 0.58 immediately after the 30 mm Hg IOP elevation ($P = 0.080$) but was reduced to 0.05 during IOP elevation for 10 minutes ($P = 0.900$).
increased vessel diameter that maintains a constant wall tension. In the rabbit, there is evidence that myogenic mechanisms contribute to the choroidal autoregulation. However, in contrast to the MBR recovery to the baseline during IOP elevation for 10 minutes, the luminal area was not significantly changed. Taken together, these results suggest that it is more likely that the neurogenic mechanism probably contributed to our results more than the myogenic mechanism. However, we did not measure the autoregulation associated with neurogenic mechanism in a strict sense. Furthermore, it has been reported that the choroidal thickness changes between light and dark, which is controlled by melanopsin. Melanopsin is reportedly expressed in the choroid, and melanopsin phototransduction contributes to the dark to light transition. We performed the measurements in a dark room, but the possibility still exists that some light stimulation (e.g., the fixation point of the LSFG body) has been reported that the choroidal thickness changes with neurogenic mechanism in a strict sense. Furthermore, it is more likely that the neurogenic mechanism probably contributed to our results more than the myogenic mechanism. Therefore, it is still not known what autoregulatory factors could have affected the choroidal blood flow after a decrease in the OPP induced by the IOP elevation.

This study has several limitations. First, the IOP was elevated by only 20 and 30 mm Hg with pressure applied by an ophthalmodynamometer. There have been many reports on the effects of stepwise elevations of the IOP by the suction cup method. Because we investigated the changes in the blood flow and morphology after an elevation of the IOP in one step, it is not easy to compare our findings to those obtained by an elevation in a stepwise way. Second, we evaluated the choroidal blood flow only at the macular area, and it is not known whether the blood flow in other parts of the choroid were affected in the same way. Third, the time of the IOP elevation was only for 10 minutes. However, times longer than 10 minutes are painful, and such problems are difficult to overcome in human studies. Fourth, the study was performed on relatively young subjects, and thus our results cannot be extrapolated to elderly subjects. Fifth, many subjects were myopic. Our results may be different from that in nonmyopic subjects because the choroidal thickness is thinner and choroidal blood flow is relatively lower in eyes with myopia than in nonmyopic eyes. Further studies with a wider range of ages and a larger number of subjects who are not myopic and IOP elevation in a step-by-step manner are needed.

In conclusion, the results indicate that the choroid has some ability to autoregulate its blood flow in response to experimental changes in the OPP induced by an elevation of the IOP in a single step. However, our results indicate that autoregulation is functioning at lower elevations of the OPP. The mechanisms involved in the autoregulation were not determined.

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References


