

## **OPEN**

# Choroidal area assessment in various fundus sectors of patients at different stages of primary open-angle glaucoma by using enhanced depth imaging optical coherence tomography

Mu Li, PhD, Xiao-Qin Yan, PhD, Yin-Wei Song, PhD, Jing-Min Guo, PhD, Hong Zhang, MD<sup>∗</sup>

#### Abstract

To compare the choroidal area in different eye fundus sectors of subjects with normal eyes, early-stage primary open-angle glaucoma (POAG) eyes, and 10° tubular visual field POAG eyes using enhanced depth imaging optical coherence tomography.

Twenty-five normal, 25 early-stage POAG, and 25 ten-degree tubular visual field POAG eyes were recruited. Enhanced depth imaging optical coherence tomography was used to measure the choroidal area in different fundus sectors (fovea; 10° superior, inferior, temporal, and 24° superior, inferior, temporal, nasal to the fovea) and the peripapillary sector.

There were neither significant differences in the choroidal area at any of the 8 measured fundus sectors, nor significant differences in the percentage change between the choroidal area of the fovea and other  $7$  measured fundus sectors among the  $3$  groups (all  $P$ ) 0.05). For the total peripapillary choroidal area, no significant difference was found among the 3 groups  $(P>0.05)$ ; however, the temporal peripapillary choroidal area of 10° tubular visual field POAG eyes was significantly thicker than that of normal eyes (4,46,213  $\pm$ 1,16,267 vs 3,74,164 $\pm$ 1,21,658 $\mu$ m<sup>2</sup>; P=0.048).

Our study showed that there was no significant difference in the choroidal area of the 8 measured fundus sectors among normal, early-stage POAG, and 10° tubular visual field POAG eyes, suggesting that there might be no blood redistribution from the peripheral choroid to the subfoveal choroid. However, the thicker temporal peripapillary choroidal area might play a role in the central visual acuity protection in patients with POAG.

Abbreviations: BCVA = best corrected visual acuity, DBP = diastolic blood pressure, EDI-OCT = enhanced depth imaging optic coherence tomography, IOP = intraocular pressure, MD = mean deviation, POAG = primary open-angle glaucoma, RNFL = retinal nerve fiber layer, RPE = retinal pigment epithelium, SBP = systolic blood pressure, SD-OCT = spectral domain optic coherence tomography.

**Keywords:** choroidal area, optical coherence tomography, primary open-angle glaucoma

#### 1. Introduction

Primary open-angle glaucoma (POAG) is characterized by progressive degeneration of retinal ganglion cells and their axons, leading to the glaucomatous changes of the optic disc and corresponding defect of visual field. Elevated intraocular pressure (IOP) was thought to be the main risk factor for  $POAG<sub>1</sub><sup>[1]</sup>$  $POAG<sub>1</sub><sup>[1]</sup>$  $POAG<sub>1</sub><sup>[1]</sup>$  but it has limitations to explain the phenomenon of normal tension glaucoma (NTG). Therefore, apart from mechanical damage, ischemic and reperfusion injuries resulting from a diminished

Department of Ophthalmology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

Medicine (2017) 96:10(e6293)

Received: 10 June 2016 / Received in final form: 31 December 2016 / Accepted: 13 February 2017

<http://dx.doi.org/10.1097/MD.0000000000006293>

blood supply might also play an important role in the pathogenesis of POAG.<sup>[2–4]</sup> The choroid is the main vascular layer of the eye and 1 of the main blood supplies to the retina.<sup>[\[5\]](#page-6-0)</sup> A limited number of studies using histological methods have indicated an association between POAG and choroid.<sup>[6,7]</sup> Recent in vivo studies reported no significant subfoveal choroidal thickness difference between normal, NTG, and POAG eyes by enhanced depth imaging optical coherence tomography (EDI-OCT).[8–10] Furthermore, a meta-analysis by Wang and  $Zhang<sup>[11]</sup>$  also showed no significant difference in the subfoveal choroidal thickness between normal and POAG eyes. In their study, Lamparter et  $al^{[12]}$  $al^{[12]}$  $al^{[12]}$  found a nonsignificant tendency towards thicker subfoveal choroid in patients with severe-stage glaucoma. Recent studies have also assessed peripapillary choroidal thickness in patients with POAG. Most of these studies indicated no significant difference in the mean peripapillary choroidal thickness between normal and POAG eyes.<sup>[13-15]</sup> However, those studies did not divide the patients with POAG into subgroups according to the visual field.

For most patients with POAG, the progress of visual field defect was from the periphery (eg, paracentral or arcuate scotoma) to the center. Also, the mean deviation (MD) changing rate of the visual field slows down as POAG progresses.<sup>[\[16\]](#page-7-0)</sup> Thus, the central visual acuity defect occurs later and more slowly than the peripheral visual field. Therefore, we speculated that central visual acuity is more resistant to elevated IOP compared with

Editor: Stela Vujosevic.

The authors report no conflicts of interest.

<sup>∗</sup> Correspondence: Hong Zhang, No. 1095 Jiefang Road, Wuhan, Hubei, China. (e-mail: [yksys3243@163.com\)](mailto:yksys3243@163.com).

Copyright © 2017 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the [Creative](http://creativecommons.org/licenses/by-nc/4.0) [Commons Attribution-Non Commercial License 4.0](http://creativecommons.org/licenses/by-nc/4.0) (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

peripheral visual field in patients with POAG. Moreover, based on the study results mentioned above, we could find that the patients with POAG could preserve their central visual acuity and subfoveal choroidal thickness unchanged for a long time. This led us to ask whether, given that the choroid provides the only blood supply to the fovea, the choroid of patients with POAG (especially severe-stage POAG patients with loss of peripheral visual field) redistributes blood from the peripheral sector to the fovea, and thereby making the central visual acuity more resistant to glaucomatous damage, preserving the more important central visual acuity as long as possible. This redistribution may be similar to that which occurs when blood is redistributed to certain tissues and organs after ischemia or shock. To investigate whether there is a redistribution mechanism of choroidal blood from the periphery to fovea to enhance the resistance of the central visual acuity to glaucomatous damage, we chose patients with POAG who had relatively large losses of peripheral visual field. Therefore, we recruited 10° tubular visual field POAG eyes.

Similarly, the peripapillary choroid provides the only blood supply to the prelaminar area and all the retinal nerve fibers would come through this area to the lamina cribrosa,<sup>[\[13\]](#page-6-0)</sup> including the papillomacular bundle, which locates temporal to optic papilla and transfers the nerve impulse from the fovea to the optic papilla. Nevertheless, most previous studies only assessed the total peripapillary choroidal thickness rather than the thickness in different peripapillar sector. Therefore, this led us to ask whether, in patients with POAG, the temporal peripapillary choroid (which supplies blood to the papillomacular bundle) becomes thicker than that in other sectors, to preserve the central visual acuity.

By using EDI-OCT, we aimed to answer the questions of whether there is a redistribution of the choroidal blood supply from the peripheral to the subfoveal area, and whether the temporal peripapillary choroid becomes thicker than that in other peripapillary sectors in 10° tubular visual field POAG patients. Also, we chose to assess the choroidal area, as Lamparter et al<sup>[\[12\]](#page-6-0)</sup> did in their study, due to the higher accuracy of 2-dimensional compared with 1-dimensional measurements, and the reduction in measurement bias associated with measuring the choroidal area rather than its thickness (as a result of the fluctuations in its thickness between adjoining areas).

#### 2. Methods

#### 2.1. Subjects

This observational study recruited 27 eyes of 27 normal individuals, 26 early-stage POAG eyes, and 27 ten-degree tubular visual field POAG eyes from 45 patients with POAG.

The inclusion criteria were as follows: age 18 to 60 years; bestcorrected visual acuity (BCVA) of >0.5 with refraction between 6.0 and +3.0 diopters. In addition, the patients with POAG were required to fulfill the POAG diagnostic criteria.<sup>[\[17\]](#page-7-0)</sup> Moreover, in this study, we only recruited 2 subgroups of patients with POAG: early-stage POAG and 10° tubular visual field POAG. We defined early-stage POAG as early glaucoma (stage 1) in accordance with the definition described by Mills et al $[18]$  and 10° tubular visual field POAG as severe glaucoma (stage 4),  $^{[18]}$  $^{[18]}$  $^{[18]}$  with the visual field limited in the central  $10^{\circ}$  visual field. The other (stages) POAG patients were not recruited.

The exclusion criteria included: a history of intraocular disease (eg, cataract), or systemic disease (eg, hypertension); a history of eye surgery; neurologic diseases that could affect the visual field (eg, hypophysoma); poor OCT image quality.

All the eyes were age and sex-matched, and received the same ophthalmic examinations at Tongji Hospital, Wuhan, China, from July 2015 to December 2015. The ophthalmic examinations included BCVA, slit-lamp microscopy and indirect ophthalmoscope examination, spherical equivalent diopter, IOP measurement (NIDEK RT-2100; Nidek, Co., Ltd, Gamagori, Japan), blood pressure measurement (OmronHEM-7201; Omron, Dalian, Liaoning, China), anterior chamber angle examination using gonioscopy, visual field test (30-2, SITA fast) using Humphrey Field Analyzer (Carl Zeiss Meditec, Dublin), central corneal thickness using pachymetry map (anterior segment OCT, Carl Zeiss Meditec, Dublin), axial length using IOL-master (Carl Zeiss Meditec, Dublin), choroid images, and retinal nerve fiber layer (RNFL) thickness using EDI SD-OCT (Heidelberg Engineering GmbH, Heidelberg, Germany). The examinations were conducted from 9:00 to 10:00 AM to avoid the impact of circadian fluctuation in the choroid area.

This study was conducted in accordance with the tenets of the Helsinki Declaration and was approved by the ethics committee of the Tongji Hospital, Medical College, Huazhong University of Science and Technology. Written informed consents were obtained from all the research participants before enrolling them in this study.

### 2.2. EDI-OCT

With EDI-OCT, we can visualize the full thickness of the choroid.[\[19\]](#page-7-0) In this study, we measured the choroidal area in different sectors of the enrolled eye including subfovea,  $10^{\circ}$ superior, inferior, temporal to the fovea, 24° superior, inferior, temporal, nasal to the fovea, and peripapillary zone. We excluded 10° nasal to the fovea because it is located within the peripapillary or papillary sectors and the optic papilla lacks choroid (Fig. 1).



Figure 1. The 8 fundus sectors for choroidal area measurement in the 3 enrolled groups. The center of this circle represented the fovea. The smaller circle represented the sectors 10° to the fovea, the bigger circle represented the sectors 24° to the fovea. Nos. 1, 2, 3, and 4 represented the sectors 10° superior, inferior, nasal, and temporal to the fovea. Nos. 5, 6, 7, and 8 represented the sectors 24° superior, inferior, nasal, and temporal to the fovea.

During the scans, we asked each participant to stare at an internal fixation point. To obtain the superior and inferior choroidal images, we moved the internal fixation point to the superior and inferior directions, respectively, and then took the Bscans vertically (Fig. 2). To obtain the nasal and temporal choroidal images, we used the same method but took the B-scans horizontally.

We set the scan angle to be 30°, so for every obtained imaging, the whole OCT picture represented 30°. We divided each image into 30 equal parts on both sides of the fovea, with each part representing 1°. Therefore, 10 parts from the fovea signified 10° to the fovea and 24 signified 24° to the fovea. The choroidal area

of each sector was represented by 4 contiguous parts (Figs. 3 and 4).

The choroidal area was defined as the area between the outer border of the retinal pigment epithelium (RPE) and the inner border of the sclera. For the macular and (10°, 24°) perimacular imaging, both sides (ie, the left and right border) of each measured area were perpendicular to the RPE and the inner border of the sclera (Figs.  $3$  and 4).<sup>[\[20\]](#page-7-0)</sup> For peripapillary imaging, both sides of each measured area were vertical ([Fig. 5](#page-3-0)).<sup>[\[21\]](#page-7-0)</sup>

We calculated the percentage change<sup>[\[22\]](#page-7-0)</sup> between the choroidal area of the fovea and other 7 measured fundus sectors by the formula below: percentage change=(subfoveal choroidal area



Figure 2. Example of superior direction EDI-OCT image. We took the superior choroid scanning as an example. When the enrolled individual stared at the superior internal fixation, we can get a picture which is from fovea to the superior direction. This choroid picture represented the superior choroid. EDI-OCT=enhanced depth imaging optical coherence tomography.



Figure 3. Example of choroid division and subfoveal choroidal area measurement. From the fovea to its both sides we divide the imaging into 30 parts, every part represented 1°. For fovea, the continuous 4 subfoveal parts (the red encircle zone) represented the subfoveal choroidal area. (A) The horizontal foveal scanning and (B) the vertical foveal scanning were represented. The mean subfoveal choroidal area was the mean value of subfoveal choroidal area in horizontal and vertical foveal scanning.



Figure 4. Example of choroid division and 10° and 24° superior choroidal area measurement. As described above, every part represented 1°, so 10° was 10 parts away from the fovea and 24° was 24 parts away from the fovea. We took superior choroid as an example, (A) was namely 10° superior (in Fig. 1 represented sector no. 1) and (B) was namely 24° superior (in Fig. 1 represented sector no. 5). For the measured sector, the continuous 4 parts (the red encircle zone) represented the choroidal area of the specific sector (as the same as Fig. 3).

<span id="page-3-0"></span>

Figure 5. The peripapillary choroid division. We divided peripapillary choroid into 6 sectors: temporal (311°–40°), superior-temporal (41°–80°), superior (81°–120°), nasal (121°–230°), inferior (231°–270°), and inferior-temporal (271°–310°).

10°/24° superior/inferior/nasal/temporal choroidal area)/subfoveal choroidal area.

For peripapillary imaging, the whole picture was 360°. We divided it into 6 independent sectors as below: temporal (311°–40°), superior-temporal (41°–80°), superior (81°–120°), nasal (121°–230°), inferior (231°–270°), and inferior-temporal (271°–310°) (modified sectors according to Garway-Heath et al $^{[23]}$  $^{[23]}$  $^{[23]}$ ) (Fig. 5).

We calculated the mean choroidal area of each peripapillary sector using the following formula: mean choroidal area= choroidal area/number of degrees associated with the sector.

We undertook the measurement by using the software Image J (version 1.42, National Institutes of Health, Bethesda, MD).<sup>[\[24\]](#page-7-0)</sup> Two observers (M.L. and X.Y.) were engaged in the measurement of the choroidal area and they were masked to the subject information. The P value for the interobserver of the choroidal area measurement was greater than 0.05.

#### 2.3. Statistical analyses

The statistical analyses were performed using the SPSS software package 19.0. Data are shown as mean $\pm$ standard deviation. The differences in the choroidal areas of the subfoveal area and other fundus sectors were determined using analysis of variance, and the difference in the percentage change between the subfoveal choroidal area and the choroidal area of the other fundus sectors were determined using Kruskal–Wallis H test. In addition, we also used analysis of variance to compare the choroidal areas of each peripapillary sectors among the recruited groups and the

Table 1



mean choroidal areas among different peripapillary sectors in each group.  $P < 0.05$  was considered statistically significant.

## 3. Results

This research initially included 80 eyes (27 eyes from 27 normal individuals, 26 early-stage POAG eyes, and 27 ten-degree tubular visual field POAG eyes from 45 patients with POAG). Among the recruited eyes, 2 normal eyes, 1 early-stage POAG eye, and 2 tendegree tubular visual field POAG eyes were excluded because of unclear borderline of the choroid in EDI-OCT images. Therefore, we had 25 eyes from 25 normal individuals, 25 early-stage POAG, and 25 ten-degree tubular visual field POAG eyes from 43 patients with POAG eventually. Most of the patients with POAG had been treated with IOP-control medication when they took part in this research.

#### 3.1. Subject characteristics

The demographic statistics are shown in Table 1. There were no significant differences in the mean age and axial length, which are considered the key factors associated with choroidal thickness,<sup>[25–29]</sup> among the 3 groups (both  $P > 0.05$ ). Spherical equivalent, central corneal thickness, visual acuity, IOP, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were also similar among the 3 groups (all  $P > 0.05$ ). The RNFL thickness was highest in the normal eyes followed by the earlystage POAG eyes, and then the 10° tubular visual field POAG eyes, with a significant difference between each pair of groups



AL = axial length, CCT = central corneal thickness, DBP = diastolic blood pressure, IOP = intraocular pressure, MD = mean deviation, RNFL = retinal nerve fiber layer, SBP = systolic blood pressure, SE = spherical equivalent.







I=inferior to the fovea, N=nasal to the fovea,  $P_1 = P$  value between normal eyes and early-stage POAG eyes,  $P_2 = P$  value between normal eyes and 10° tubular visual field POAG eyes,  $P_3 = P$  value between early-stage POAG and 10° tubular visual field POAG eyes,  $S=$  superior to the fovea,  $S=$  subfovea,  $T=$  temporal to the fovea.

 $(P<0.001)$ . There was no significant difference in the MD of the visual field between normal and early-stage POAG eyes; however, the MD in the 10° tubular visual field POAG eyes was significantly lower than in the other groups  $(P < 0.001)$ .

## 3.2. Comparison of the choroidal area in the different fundus sectors among the 3 groups

The subfoveal choroidal area was not significantly different among normal eyes  $(5,01,720 \pm 1,52,510 \,\mu\text{m}^2)$ , early-stage POAG eyes  $(4, 75, 923 \pm 1, 40, 616 \,\mu\text{m}^2)$ , and  $10^\circ$  tubular visual field POAG eyes  $(4,96,756 \pm 1,66,534 \,\mu m^2)$   $(P=0.820)$ . In addition, neither the choroidal areas of the sectors 10° superior, inferior, and temporal to the fovea  $(P=0.547, 0.321,$  and 0.904, respectively) nor that of the sectors 24° superior, inferior, temporal, and nasal to the fovea  $(P=0.209, 0.402, 0.704,$  and 0.402, respectively) showed significant difference among the 3 groups (Table 2).

## 3.3. Comparison of the percentage change between the choroidal area of the subfovea and other fundus sectors among the 3 groups

There were no significant differences among the 3 groups in the percentage change between the subfoveal choroidal area and that of the 3 sectors  $10^{\circ}$  to the fovea (P=0.419, 0.140, and 0.650, respectively). Furthermore, there were no significant differences among the 3 groups in the percentage change between the subfoveal choroidal area and that of the 4 sectors 24° to the fovea (P=0.326, 0.354, 0.919, and 0.865, respectively) (Table 3).

## 3.4. Comparison of peripapillary choroidal area among the 3 recruited groups and the mean choroidal area of different peripapillary sectors in each group

Significant choroidal area difference was only seen in temporal peripapillary sectors between normal and 10° tubular visual field POAG eyes  $(P=0.048)$ , but there were no other significant choroidal area differences among the groups (all  $P > 0.05$ ) ([Table 4\)](#page-5-0).

In each of the 3 groups, the mean choroidal area of the superior peripapillary sector was the thickest and that of the inferior peripapillary sector was the thinnest. In the normal group, the mean choroidal area of the superior-temporal and superior sectors was significantly thicker than those of the inferiortemporal and inferior sectors, and the nasal mean choroidal area was significantly thicker than the inferior-temporal mean choroidal area. In the early-stage POAG group, the mean choroidal area of the superior-temporal, superior, and nasal sectors was significantly thicker than that of the inferior-temporal and inferior sectors. In the 10°tubular visual field POAG group, the mean choroidal area of the temporal, superior-temporal, superior, and nasal sectors was significantly thicker than that of the inferior sector, and the superior-temporal mean choroidal area was significantly thicker than that of the inferior-temporal sector ([Fig. 6\)](#page-6-0).

## 4. Discussion

The association between POAG and choroid is incompletely understood, and there have been inconsistent research results by different means of measurement techniques. At first, in vitro

Table 3





I=inferior to the fovea, N=nasal to the fovea,  $P_1 = P$  value between normal eyes and early-stage POAG eyes,  $P_2 = P$  value between normal eyes and 10° tubular visual field POAG eyes,  $P_3 = P$  value between early-stage POAG and 10° tubular visual field POAG eyes,  $S =$  superior to the fovea,  $S =$  subfovea,  $T =$  temporal to the fovea.

<span id="page-5-0"></span>



I=inferior sector, IT=interior-temporal sector, N=nasal sector,  $P_1 = P$  value between normal eyes and early-stage POAG eyes,  $P_2 = P$  value between normal eyes and 10° tubular visual field POAG eyes,  $P_3 = P$ value between early-stage POAG and 10° tubular visual field POAG eyes, S=superior sector, ST=superior-temporal sector, T=temporal sector.

histological studies indicated a  $50 \mu m$  thinner choroid in glaucoma patients in contrast to normal individuals.<sup>[\[6\]](#page-6-0)</sup> Now, using EDI-OCT, Mwanza et al<sup>[\[25\]](#page-7-0)</sup> reported no difference in foveal, temporal, and nasal choroidal thickness between normal individuals and patients with POAG. With the same method, Park et al<sup>[\[9\]](#page-6-0)</sup> found no choroidal thickness difference in average, superior, inferior, nasal, and temporal fovea between POAG and normal eyes. Moreover, Wang and Zhang<sup>[11]</sup> indicated the same conclusion as that in the study by Park et al and conducted a meta-analysis that showed POAG was not associated with a significant changing of the choroid. However, in contrast to the earlier studies, in which patients with POAG were not divided into different stages for analysis, and the choroidal thickness measurement was limited to 3mm (about 10°) from fovea, we divided patients with POAG into different stages and then only recruited 2 subgroups: early-stage POAG and 10° tubular visual field POAG groups, and the measurement was performed at the subfovea, and 10° and 24° to the fovea. We found that neither the subfoveal choroidal area, nor the choroidal area of the sectors 10° superior, inferior, and temporal to the fovea and the sectors 24° superior, inferior, temporal, and nasal to the fovea showed significant differences among normal, early-stage POAG, and 10° tubular visual field POAG eyes. In addition, the percentage change between the choroidal area of the subfovea and other fundus sectors among the 3 groups also showed lack of significant difference.

These results indicated that there was no compensatory mechanism to redistribute blood from the peripheral to the subfoveal choroid. Cristini et al<sup>[\[30\]](#page-7-0)</sup> used echography to conclude that the density of choriocapillaris in the fovea was reduced in glaucomatous eyes, and Spraul et  $al$ ,<sup>[\[7\]](#page-6-0)</sup> on the basis of their histological research, reported that there was a significant positive correlation between the diameter of the choroidal vessels and the thickness of the choroid, and dilatation of the choroidal vessels were prominent in glaucoma patients. Reduced density of the choriocapillaris caused dilatation of the vessels because of increased perfusion gradient.<sup>[\[30\]](#page-7-0)</sup> This compensatory dilatation of the choriocapillaris in the fovea might help to preserve blood flow in the fovea<sup>[\[9\]](#page-6-0)</sup> and maintain the choroidal area and central visual acuity. By combining our results with those previous studies, we inferred that there might be a compensatory mechanism to preserve central visual acuity that involved the regulation of the subfoveal vessel diameter and blood flow rather than redistribution of the choroidal blood supply.

Although 10° tubular visual field POAG patients had lost peripheral visual field, the choroidal area of the sectors 10° and 24° to the fovea of the patients was not different from those of normal and early-stage POAG eyes. This might be due to the dual blood supply system of the retina. Except for the macula, the remaining part of retina was supplied by choroid and retinal vessels. In terms of retinal vessels in patients with POAG, Mitchell et al<sup>[\[31\]](#page-7-0)</sup> used optic disc photography and reported that the diameter of the retinal vessels of POAG patients was reduced. Moreover, using retinal vessel analyzer, Ramm et al<sup>[\[32\]](#page-7-0)</sup> confirmed that in glaucoma patients, the diameter of the retinal vessels, including the artery and vein, decreased by the progress of the disease. Researchers have confirmed, not only from structural, but also from the metabolic aspect, that retinal blood flow and oxygen demand are lower in POAG patients. Olafsdottir et al<sup>[\[33\]](#page-7-0)</sup> found, using oximetry, that greater visual field defect was associated with higher retinal venous oxygen saturation and lower arteriovenous difference in patients with POAG. These results might have been influenced by the atrophy of the nerve, resulting in low oxygen requirement owing to loss of tissue. Therefore, in glaucoma patients, the retinal vessels, which nourish the inner 5 retinal layers, including the POAG injury target point, retinal ganglion cell, and retinal nerve fiber, would be primarily affected, simultaneously with the injury of nerve tissue. The choroid would be less likely to be affected and remained relatively unchanged. This might explain the invariant choroidal area in 10° tubular visual field POAG patients.

Our peripapillary choroidal area result showed that the total peripapillary choroidal area was not different among the 3 groups, similar to that in other studies.<sup>[13,21,34]</sup> However, analyzing the 6 peripapillary sectors separately showed that there was a significant difference in the temporal peripapillary choroidal area between normal and 10° tubular visual field POAG eyes. In patients with POAG, the high IOP may put pressure on the blood supply of the retina, leading to ischemia of the nerve fiber and glaucomatous damage. Therefore, given the blood supply of the prelaminal area comes only from the choroid, a thicker peripapillary choroidal area might help preserve the retinal nerve of patients with POAG. The papillomacular bundle, which is the connection between the macula and the optic papilla and is very important to central visual acuity,<sup>[\[35\]](#page-7-0)</sup> would exactly passes through the temporal peripapillary sector to the lamina cribrosa. Therefore, we inferred that the thicker temporal peripapillary choroid in 10° tubular visual field POAG patients might have a protective effect on central visual acuity during progression of POAG by resisting nerve degeneration.

Our study showed that the superior and superior-temporal peripapillary choroidal areas were thickest, and the inferior and inferior-temporal peripapillary choroidal areas were thinnest in each of the 3 groups. This finding was consistent with the result

<span id="page-6-0"></span>

Figure 6. Comparison of the mean choroidal area of different peripapillary sectors in each group. Mean choroidal area=choroidal area of the sector/ number of degrees associated with the sector. \*Indicates a statistically significant difference. I=inferior sector, IT=inferior-temporal sector, N=nasal sector, S=superior sector, ST=superior-temporal sector, T=temporal sector.

reported by Lamparter et al. $^{[12]}$  In addition, the sector with the thinnest peripapillary choroid was found to be the most vulnerable to glaucomatous damage. As a neurovascular unit, this consistence prompted us to think that thicker regional choroidal blood would better nourish the nerve fiber and the thinner peripapillary choroidal area was related to glaucomatous damage.

## 4.1. Limitations

Several limitations of this research should be considered. First, our recruited sample size was relatively small, which may have affected our result. We hope to expand the sample size to do further research. Second, although through EDI-OCT we can measure the choroidal area, the choroidal area may sometimes not comprehensively represent the actual choroidal microcirculation, so we are expecting to use new methods and techniques, like OCT angiography, to monitor the choroidal microcirculation in vivo. Third, the use of antiglaucoma drugs may, to some degree, affect the choroidal area.

#### 5. Conclusions

In conclusion, in 10° tubular visual field POAG eyes, there might be no redistribution of choroid blood flow from the peripheral retina to the fovea, but the thickened temporal sector of the peripapillary choroid might have a protective effect on central visual acuity.

#### Acknowledgment

This article included contribution by Xiaolan Xu of Ophthalmology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology.

## **References**

- [1] Gordon MO, Beiser JA, Brandt JD, et al. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary openangle glaucoma. Arch Ophthalmol 2002;120:714–20.
- [2] Cioffi GA, Lin W, Brad F, et al. Chronic ischemia induces regional axonal damage in experimental primate optic neuropathy. Arch Ophthalmol 2004;122:1517–25.
- [3] Fuchsjäger-Mayrl G, Wally B, Georgopoulos M, et al. Ocular blood flow and systemic blood pressure in patients with primary open-angle glaucoma and ocular hypertension. Investig Ophthalmol Vis Sci 2004;45:834–9.
- [4] Duijm HF, Van den Berg TJ, Greve EL. Choroid haemodynamics in glaucoma. Br J Ophthalmol 1997;81:735–42.
- [5] Delaey C, Van de Voorde J. Regulatory mechanisms in the retinal and choroid circulation. Ophthalm Res 2000;32:249–56.
- [6] Yin ZQ, Millar TJ, Beaumont P, et al. Widespread choroidal insufficiency in primary open-angle glaucoma. J Glaucoma 1997;6: 23–32.
- [7] Spraul CW, Lang GE, Lang GK, et al. Morphometric changes of the choriocapillaris and the choroidal vasculature in eyes with advanced glaucomatous changes. Vision Res 2002;42:923–32.
- [8] Toprak I, Yaylalı V, Yildirim C. Age-based analysis of choroidal thickness and choroidal vessel diameter in primary open-angle glaucoma. Int Ophthalmol 2016;36:171–7.
- [9] Park HY, Lee NY, Shin HY, et al. Analysis of macular and peripapillary choroidal thickness in glaucoma patients by enhanced depth imaging optical coherence tomography. J Glaucoma 2014;23:225–31.
- [10] Rhew JY, Kim YT, Choi KR. Measurement of subfoveal choroidal thickness in normal-tension glaucoma in Korean patients. J Glaucoma 2014;23:46–9.
- [11] Wang W, Zhang X. Choroidal thickness and primary open-angle glaucoma: a cross-sectional study and meta-analysis. Investig Ophthalmol Vis Sci 2014;55:6007–14.
- [12] Lamparter J, Schulze A, Riedel J, et al. Peripapillary choroidal thickness and choroidal area in glaucoma, ocular hypertension and healthy subjects by SD-OCT. Klinische Monatsblätter für Augenheilkunde 2015;232:390–4.
- [13] Zhang Z, Yu M, Wang F, et al. Choroidal thickness and open-angle glaucoma: a meta-analysis and systematic review. J Glaucoma 2016;25: e446–54.
- [14] Ehrlich JR, Peterson J, Palitsis G, et al. Peripapillary choroidal thickness in glaucoma measured with optical coherence tomography. Exp Eye Res 2011;92:189–94.
- <span id="page-7-0"></span>[15] Maul EA, Friedman DS, Chang DS, et al. Choroidal thickness measured by spectral domain optical coherence tomography factors affecting thickness in glaucoma patients. Ophthalmology 2011;118:1571–9.
- [16] Rao HL, Begum VU, Khadka D, et al. Comparing glaucoma progression on 24-2 and 10-2 visual field examinations. PloS One 2015;10: e0127233.
- [17] European Glaucoma Society. Terminology and guideline for glaucoma. Dogma. 2008.
- [18] Mills RP, Budenz DL, Lee PP, et al. Categorizing the stage of glaucoma from pre-diagnosis to end-stage disease. Am J Ophthalmol 2006;141:  $24 - 30.$
- [19] Spaide RF, Koizumi H, Pozonni MC. Enhanced depth imaging spectraldomain optical coherence tomography. Am J Ophthalmol 2008;146: 496–500.
- [20] Usui S, Ikuno Y, Akiba M, et al. Circadian changes in subfoveal choroidal thickness and the relationship with circulatory factors in healthy subjects. Investig Ophthalmol Vis Sci 2012;53:2300–7.
- [21] Hosseini H, Nilforushan N, Moghimi S, et al. Peripapillary and macular choroidal thickness in glaucoma. J Ophthalm Vis Res 2014;9:154–61.
- [22] Tu YK. Testing the relation between percentage change and baseline value. Sci Rep 2016;6:23247.
- [23] Garway-Heath DF, Poinoosawmy D, Fitzke FW, et al. Mapping the visual field to the optic disc in normal tension glaucoma eyes. Ophthalmology 2000;107:1809–15.
- [24] Chen W, Wang ZT, Zhang H. Comparison of choroidal thickness measured by two methods. Int J Ophthalmol 2012;5:348–53.
- [25] Mwanza JC, Hochberg JT, Banitt MR, et al. Lack of association between glaucoma and macular choroidal thickness measured with enhanced depth-imaging optical coherence tomography. Investig Ophthalmol Vis Sci 2011;52:3430–5.
- [26] Esmaeelpour M, Považay B, Hermann B, et al. Three-dimensional 1060 nm OCT: choroidal thickness maps in normal subjects and improved posterior segment visualization in cataract patients. Investig Ophthalmol Vis Sci 2010;51:5260–6.
- [27] Margolis R, Spaide RF. A pilot study of enhanced depth imaging optical coherence tomography of the choroid in normal eyes. Am J Ophthalmol 2009;147:811–5.
- [28] Ikuno Y, Kawaguchi K, Nouchi T, et al. Choroidal thickness in healthy Japanese subjects. Investig Ophthalmol Vis Sci 2010;51:2173–6.
- [29] Fujiwara A, Shiragami C, Shirakata Y, et al. Enhanced depth imaging spectral-domain optical coherence tomography of subfoveal choroidal thickness in normal Japanese eyes. Jpn J Ophthalmol 2012;56:230–5.
- [30] Cristini G, Cennamo G, Daponte P. Choroidal thickness in primary glaucoma. Ophthalmologica 1991;202:81–5.
- [31] Mitchell P, Leung H, Wang JJ, et al. Retinal vessel diameter and openangle glaucoma: The Blue Mountains Eye Study. Ophthalmology 2005;112:245–50.
- [32] Ramm L, Jentsch S, Peters S, et al. Dependence of diameters and oxygen saturation of retinal vessels on visual field damage and age in primary open-angle glaucoma. Acta Ophthalmol 2016;94:276–81.
- [33] Olafsdottir OB, Hardarson SH, Gottfredsdottir MS, et al. Retinal oximetry in primary open-angle glaucoma. Invest Ophthalmol Vis Sci 2011;52:6409–13.
- [34] Chunwei Z, Tatham AJ, Medeiros FA, et al. Assessment of choroidal thickness in healthy and glaucomatous eyes using swept source optical coherence tomography. PloS One 2014;9:e109683.
- [35] Kobayashi W, Kunikata H, Omodaka K, et al. Correlation of papillomacular nerve fiber bundle thickness with central visual function in open-angle glaucoma. J Ophthalmol 2015;2015:460918.