

Case Report

# Iris Morphological Features in Patients with 360° Angle-Closure Neovascular Glaucoma: An Anterior Segment Optical Coherence Tomography Study

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## Keywords

Neovascular glaucoma · Angle closure · Peripheral anterior synechia · Anterior segment optical coherence tomography

## Abstract

**Purpose:** To investigate iris morphological features in 360° angle-closure neovascular glaucoma (NVG) by swept-source anterior segment optical coherence tomography (ASOCT). **Patients and Methods:** In this retrospective, clinic-based, comparative study, 14 patients with 360° angle-closure NVG and 14 healthy age-matched control subjects were enrolled. All patients enrolled had no prior glaucoma surgery but underwent cataract surgery with intraocular lens implantation. Horizontal scanning images of swept-source ASOCT were analyzed using

software calipers in temporal and nasal angle areas. The iris thickness at 1 and 2 mm from the pupil edge, iris length, trabecular meshwork length, peripheral anterior synechia (PAS) length, PAS height ratio (PAS length/trabecular meshwork length), and pupil diameter were measured.

**Results:** Between the groups, there were no statistically significant differences in iris length, trabecular meshwork length, and pupil diameter ( $p > 0.05$ ). However, the iris thickness was significantly reduced in the NVG group compared with the control group in the temporal and nasal areas (0.306 vs. 0.563 mm/0.326 vs. 0.645 mm at 1 mm, 0.278 vs. 0.523 mm/0.282 vs. 0.546 mm at 2 mm, respectively) (mean, all  $p < 0.001$ ). In the NVG group, PAS height ratios were  $1.55 \pm 0.45$  (mean  $\pm$  standard deviation) (range, 0.58–2.30) and  $1.55 \pm 0.78$  (range, 0.68–3.68) at the temporal and nasal angles, respectively. **Conclusions:** In patients with 360° angle-closure NVG, the iris thickness decreased to about 50% of that in healthy subjects, and the PAS length exceeded the trabecular meshwork length by about 1.5 times.

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## Introduction

Morphological features of the anterior ocular segment observed using anterior segment optical coherence tomography (ASOCT) have been reported in normal subjects [1–4] and in patients with angle-closure glaucoma [5, 6]. Neovascular glaucoma (NVG) is a major cause of refractory glaucoma [7]. Circumferential angle closure due to peripheral anterior synechia (PAS) both increases the intraocular pressure (IOP) and causes corneal edema, making it difficult to examine the anterior chamber and angle structures. However, ASOCT can noninvasively provide important information on ocular anterior segment; this information is occasionally useful for making treatment decisions. Therefore, the aim of the study was to explore the iris morphological features of 360° angle-closure NVG by comparing them with those of normal subjects using ASOCT.

## Methods

This study received approval from the Institutional Review Board of Saneikai Tsukazaki Hospital and was performed according to the tenets of the Declaration of Helsinki. We retrospectively recruited patients with 360° angle-closure NVG and healthy age-matched control subjects using the medical records of our hospital. All patients enrolled have no prior glaucoma surgery but underwent cataract surgery with intraocular lens implantation without any complication. All patients who had clear cross-sectional horizontal scan images already obtained using the anterior segment mode and angle mode on swept-source-ASOCT (SS-1000 CASIATM, TOMEY, Nagoya, Japan) were included because vertical scan images were often disturbed by eyelids in ASOCT.

Additional inclusion criteria for the NVG group were as follows: (1) 360° angle-closure NVG already confirmed by gonioscopic examination (evaluated by S.N). When the trabecular pigment band was invisible, the area was diagnosed as closed [8]; (2) no history of glaucoma surgery. Patients with NVG due to uveitis were excluded.

Additional inclusion criteria for the control group were as follows: patients (1) who had no ocular disease; (2) whose age was matched  $\pm 2$  years; and (3) who had clear cross-sectional images, which had already been obtained using the anterior segment mode and angle mode on ASOCT to evaluate ocular biometry after cataract surgery.

ASOCT measurements were performed in high-resolution 2D mode using software calipers in CASIA™ by E.T, Y.K, Y.F, and K.M. The clearest horizontal scan image was selected for the analysis, and each parameter was measured once.

Iris length was measured as the distance from the scleral spur (SS) to the pupil edge in control subjects. In the NVG groups, iris length was defined as horizontal iris length + PAS length (Fig. 1a). The trabecular meshwork (TM) was identified as a hyperreflective tissue [1–3], and the reproducibility was shown as good [1–3]. The TM length was measured using 200% magnification (Fig. 1b).

The iris thickness was measured at 1 and 2 mm (within  $\pm 0.005$  mm) from the pupil's edge in line with the hyperreflective line at the bottom of the iris.

## Results

All retrospective data from November 2009 to September 2016 were collected, and during this period, 139 patients were diagnosed with NVG. Among them, 14 patients with 360° angle-closure NVG met the inclusion criteria and were subsequently analyzed.

Underlying diseases of the 14 patients in the NVG group were diabetic retinopathy ( $n = 7$ ), central retinal vein occlusion ( $n = 3$ ), ocular ischemic syndrome ( $n = 3$ ), and central retinal artery occlusion ( $n = 1$ ). The mean patient age was  $59.0 \pm 16.5$  years (mean  $\pm$  standard deviation) (range 35–82 years). Eleven patients were male (78.5%), and the right eye was the affected side in 8 patients (57.1%). IOP measured by a Goldmann applanation tonometer was  $42.2 \pm 13.7$  mm Hg (range 28–76 mm Hg) at the ASOCT examination day. In the NVG group, panretinal photocoagulation (PRP) ( $n = 12$ ) and intravitreal antivascular endothelial growth factor (anti-VEGF) injection ( $n = 5$ ) were performed before the ASOCT measurements.

In the control group, the mean age of the subjects was  $59.3 \pm 16.3$  years (range 34–82 years). Ten subjects (71.4%) were male, and IOP measured by Goldmann applanation tonometer was  $13.7 \pm 3.9$  mm Hg (range 10–22 mm Hg). No significant difference was found between the groups in terms of age ( $p = 0.954$ , Student's  $t$  test), sex ( $p = 0.662$ ,  $\chi^2$  test), and affected side ( $p = 1.000$ ,  $\chi^2$  test).

ASOCT measurements and statistical comparisons between the NVG and control groups are shown in Table 1.

There was no significant difference between the NVG and control groups in iris length, TM length, and pupil diameter ( $p > 0.05$ ). However, the iris thickness was significantly less in the NVG group compared to the control group at the temporal and nasal sites ( $0.306 \pm 0.070$  vs.  $0.563 \pm 0.107$  mm/ $0.326 \pm 0.114$  vs.  $0.645 \pm 0.122$  mm at 1 mm, and  $0.278 \pm 0.096$  vs.  $0.523 \pm 0.082$  mm/ $0.282 \pm 0.078$  vs.  $0.546 \pm 0.092$  mm at 2 mm, respectively) ( $p < 0.001$ ). The iris thickness in the NVG group decreased to about 50% of the thickness in normal subjects.

The PAS length was longer than the TM length (0.842 vs. 0.548 mm at the temporal angle and 0.790 vs. 0.529 mm at the nasal angle). Therefore, the value of PAS height ratio (PAS

length/TM length) exceeded 1.5 when the TM was completely closed by PAS in most patients with 360° angle-closure NVG.

In the NVG group, there was no significant difference in the average iris thickness between anti-VEGF treated eyes ( $n = 5$ ) and nontreated eyes ( $n = 9$ ) (0.324 vs. 0.312 mm at 1 mm,  $p = 0.758$ , and 0.295 vs. 0.271 mm at 2 mm,  $p = 0.487$  by Student's  $t$  test). Additionally, there was no significant difference in the average iris thickness between PRP treated eyes ( $n = 12$ ) and nontreated eyes ( $n = 2$ ) (0.329 vs. 0.236 mm at 1 mm,  $p = 0.06$ , and 0.286 vs. 0.240 mm at 2 mm,  $p = 0.327$  by Student's  $t$  test).

Representative ASOCT images of the NVG and control groups are presented in [Figure 2](#).

## Discussion

ASOCT, which enables the visualization of the anterior segment anatomy similar to gonioscopic examination, has recently become available [1–4]. However, not every disease's morphological features have been studied well. To the best of our knowledge, this is the first report to show that a thinner iris and longer PAS length exceeding the TM length are features characterizing 360° angle-closure NVG. These findings are useful for assessing patients' NVG stage because 360° angle-closure NVG is one of the most refractory types of glaucoma, and ophthalmologists need various strategies.

Previous pathological studies of NVG were done on enucleated eyes with absolute glaucoma [9, 10] or on TM specimens after trabeculectomy [9, 10]. At the initial stages of NVG of the chamber angle, a thin layer of capillaries grows on the surface of the iris and over the meshwork. When the process is advanced, a thick band of fibrovascular tissue fuses the iris to the cornea to form a false angle [10]. In some specimens, the corneal endothelium extends across the false angle (endothelium downgrowth) and forms a secondary Descemet's membrane on the anterior surface of the iris [9, 10]. In specimen preparation for histopathological examination, specimens shrank due to the loss of water components. However, ASOCT can directly visualize morphological conditions in real time. Our results show that the iris thickness in patients with 360° angle-closure NVG is significantly decreased to about 50% of that in healthy subjects, probably because of atrophy in the iris's stroma due to ischemia. It was thought that PRP and the anti-VEGF injection might lead to cellular and ultrastructural alteration of the fibrovascular membrane and iris stromal tissue. PRP [11, 12] and the anti-VEGF injection [13] decreased choroidal thickness; however, the effect on the iris thickness has not been investigated. In our group, no statistically significant difference was found in the average iris thickness between PRP-treated eyes and nontreated eyes and also between anti-VEGF treated eyes and nontreated eyes. The anti-VEGF injection strongly inhibits vascular permeability [14] and promotes regression of immature vessels while inducing normalization and maturation of premature vessels [15]. Further studies should clarify the effect of PRP and the anti-VEGF injection on iris thickness. Another possible explanation for the decrease in iris thickness may be that the iris acts as a sponge under normal pressure; however, the high IOP and fibrovascular changes in the iris may influence its ability to act as a sponge, leading to a reduction in thickness due to reduced fluids within the iris stroma.

Our study had some limitations. First, the pupil diameter was not different between the NVG group and the control group ( $p = 0.824$ ). This was probably because under the dark room

condition in ASOCT measurements, pupils were dilated in the control group but less dilated in the NVG group due to iris stroma atrophy. The second limitation was that whether the iris thickness decreased before closing, the whole circumference of the angle was unclear. The third, further anatomical examination of the structural changes in thinner irises is also needed because ASOCT cannot reveal the microstructures of the iris.

### Conclusion

We have reported the morphological features of the iris in patients with 360° angle-closure NVG using ASOCT. The iris thickness decreased by about 50% of that in healthy subjects, and the PAS length exceeded the TM length by about 1.5 times. Further research is required to clarify the mechanism of reduction in iris thickness.

### Statement of Ethics

The authors have no ethical conflicts to disclose.

### Disclosure Statement

The authors have no financial or proprietary interest in any product, method, or material described herein. The authors have no financial disclosures and no conflicts of interest to declare.

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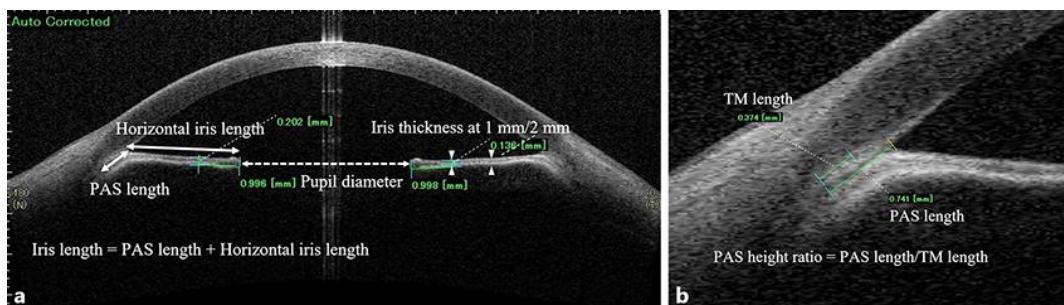
### Author Contributions

Dr. Nakakura had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Shunsuke Nakakura, Hitoshi Tabuchi, and Yoshiaki Kiuchi. *Acquisition, analysis, and interpretation of data:* All authors. *Drafting of the manuscript:* Shunsuke Nakakura, Yasuhiro Takahashi, and Yoshiaki Kiuchi. *Critical revision of the manuscript for important intellectual content:* Shunsuke Nakakura, Yasuhiro Takahashi, and Yoshiaki Kiuchi. *Statistical analysis:* Shunsuke Nakakura. *Study supervision:* Shunsuke Nakakura, Yasuhiro Takahashi, and Yoshiaki Kiuchi.

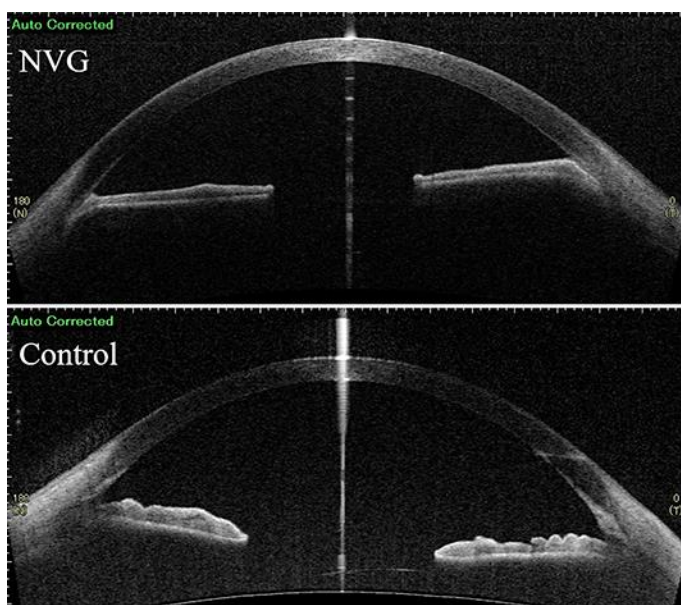
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**Fig. 1.** Morphological parameters of the iris and angle measured using swept-source anterior segment optical coherence tomography. **a** A 43-year-old male patient's left eye suffering from 360° angle-closure neovascular glaucoma as a result of central retinal vein occlusion. PAS, peripheral anterior synechia. **b** Magnification of the nasal angle of Figure 1a. TM, trabecular meshwork.



**Fig. 2.** Representative images of the iris and angles in the neovascular glaucoma (NVG) and control groups. Images were obtained from a 35-year-old male with NVG resulting from proliferative diabetic retinopathy and a 34-year-old male as a normal control. A thinner iris and completely closed trabecular meshwork due to a high peripheral anterior synechia were observed in the patient with NVG.

**Table 1.** Comparisons of anterior segment optical coherence tomography measurements between the neovascular glaucoma (NVG) group and control group

	NVG group	Control	<i>p</i> value
<i>Temporal angle</i>			
PAS length, mm	0.842±0.307 (0.361–1.328)	–	
Horizontal iris length, mm	3.292±0.699 (1.905–4.247)	–	
Iris length, mm	4.135±0.620 (2.824–5.102)	4.085±0.283 (3.633–4.646)	0.787
TM length, mm	0.548±0.158 (0.323–0.957)	0.588±0.138 (0.372–0.836)	0.491
Iris thickness at 1 mm, mm	0.306±0.070 (0.202–0.481)	0.563±0.107 (0.357–0.746)	<b>&lt;0.001</b>
Iris thickness at 2 mm, mm	0.278±0.096 (0.157–0.519)	0.523±0.082 (0.445–0.761)	<b>&lt;0.001</b>
PAS height ratio (PAS length/TM length)	1.554±0.454 (0.586–2.301)		
<i>Nasal angle</i>			
PAS length, mm	0.790±0.384 (0.391–1.779)	–	
Horizontal iris length, mm	3.217±0.470 (2.486–3.915)	–	
Iris length, mm	4.007±0.407 (3.337–4.588)	3.749±0.271 (3.272–4.101)	0.059
TM length, mm	0.529±0.137 (0.249–0.771)	0.579±0.141 (0.397–0.854)	0.348
Iris thickness at 1 mm, mm	0.326±0.114 (0.161–0.619)	0.645±0.122 (0.420–0.861)	<b>&lt;0.001</b>
Iris thickness at 2 mm, mm	0.282±0.078 (0.167–0.409)	0.546±0.092 (0.416–0.720)	<b>&lt;0.001</b>
PAS height ratio (PAS length/TM length)	1.557±0.784 (0.687–3.683)		
<i>Average of temporal and nasal angle</i>			
Iris length, mm	4.071±0.519 (2.824–5.102)	3.917±0.321 (3.272–4.646)	0.188
TM length, mm	0.539±0.145 (0.249–0.957)	0.583±0.137 (0.372–0.854)	0.242
Iris thickness at 1 mm, mm	0.316±0.093 (0.161–0.619)	0.604±0.120 (0.357–0.861)	<b>&lt;0.001</b>
Iris thickness at 2 mm, mm	0.280±0.086 (0.157–0.519)	0.534±0.086 (0.416–0.761)	<b>&lt;0.001</b>
Pupil diameter, mm	4.029±0.905 (2.831–6.169)	4.098±0.707 (2.938–5.289)	0.824

PAS, peripheral anterior synechia; TM, trabecular meshwork. Values are expressed as mean ± standard deviation with range. All *p* values were calculated using Student's *t* test.