Analysis of Anterior Segment Dynamics Using Anterior Segment Optical Coherence Tomography Before and After Laser Peripheral Iridotomy

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Objective: To evaluate changes in the speed of pupil constriction and in anterior segment parameters after laser peripheral iridotomy (LPI) in patients with angle closure using anterior segment optical coherence tomography.

Methods: In this prospective observational study, videos of pupil and anterior segment changes in response to illumination were captured with real-time video recording using anterior segment optical coherence tomography and were analyzed frame by frame before and after LPI. Customized software was used to measure the speed of pupil constriction and changes in anterior chamber depth and anterior chamber area, as well as iris thickness at 750 μm from the scleral spur, at the sphincter muscle region (0.75 mm from the pupillary margin), and at the mid-iris location (half the distance between the scleral spur and the pupillary margin). Pupil diameter, angle opening distance, and trabecular–iris space area at 500 μm from the scleral spur were determined. The speed of pupil constriction was defined as the rate of pupil diameter change in response to illumination.

Results: Twenty-nine patients were included. Most were Chinese (26 of 29 [90%]) and female (18 of 29 [62%]). The anterior chamber area, angle opening distance at 500 μm from the scleral spur, and trabecular–iris space area at 500 μm from the scleral spur were significantly higher after LPI (P < .001). A significant increase was observed in the speed of pupil constriction after LPI (P < .005). In response to illumination, the rate of change in iris thickness at the sphincter muscle region and at 750 μm from the scleral spur was faster after LPI (P < .05). Similarly, an increase was observed in the speed of change of angle-opening distance at 500 μm from the scleral spur in response to illumination after LPI (P < .05).

Conclusions: In patients with angle closure, changes in dynamic iridopupillary behavior are observed after LPI. The speed of pupillary constriction is faster after LPI.


Primary Angle-Closure Glaucoma (PACG) is a significant cause of ocular morbidity worldwide, particularly in Asia.1,10 Because of the blinding nature of this disease, the identification of individuals at risk is essential for early diagnosis. Although indentation gonioscopy is still considered the reference standard for the examination of the anterior chamber angle, more sophisticated and objective methods, including ultrasonographic biomicroscopy and anterior segment optical coherence tomography (ASOCT), have been introduced in the past decade.11-16 Anterior segment optical coherence tomography allows objective high-resolution visualization and reproducible measurement of the anterior segment structures.15-17 Using ASOCT, novel anatomical factors associated with angle closure, including smaller anterior chamber width, area, and volume, as well as increased lens vault, have recently been described.18-20

Other recent publications indicate that dynamic changes in the iris during physiological conditions may also have a role in the pathogenesis of PACG.10,21,22 Several studies15-17 have been conducted to evaluate dynamic changes in the anterior segment in response to illumination and to laser peripheral iridotomy (LPI), and it was reported that increased illumination15-17 and increased LPI13,15 significantly widened the angle. Using ASOCT to investigate the speed of iridopupillary changes in response to illumination, it was recently found that the pupil constricts more slowly in patients having angle closure compared with those having open angles; however, all patients with angle closure had previously undergone LPI.21

Laser peripheral iridotomy is the recommended first-line treatment in the management of PACG.24-27 After LPI, changes

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in morphologic anterior chamber angle in PACG eyes have been described in several studies,\textsuperscript{13,17,28} using ultrasonographic biomicroscopy and ASOCT. Although these anatomical characteristics were evaluated on 2-dimensional static images, dynamic changes have not been studied to date. Therefore, the objective of this study was to evaluate changes in the speed of pupil constriction (SPC) and in anterior segment parameters after LPI in patients with angle closure using ASOCT.

METHODS

This prospective observational study adhered to the tenets of the Declaration of Helsinki and was approved by the institutional review board of the Singapore Eye Research Institute. Written informed consent was obtained from each study participant.

STUDY PARTICIPANTS

Patients were prospectively recruited from the outpatient glaucoma clinics of the Singapore National Eye Centre. Eligible patients were older than 40 years, were scheduled for LPI, and were diagnosed as having PACG, primary angle closure, or primary angle closure suspect (PACS).

The diagnosis of PACS was made in eyes with peripheral anterior synchiae (PAS), intraocular pressure of 21 mm Hg or less in the absence of glaucomatous optic neuropathy, or narrow angles (defined as eyes in which at least 180° of the posterior pigmented trabecular meshwork was not visible on viewing with a gonioscopy lens in the primary position of gaze without indentation). Periphereal anterior synchiae were defined as abnormal adhesions of the iris to the angle that were at least half a clock hour in width and were present to the level of the anterior trabecular meshwork or higher.

The diagnosis of PACG was made in eyes with narrow angles, normal optic disc and visual fields, and elevated intraocular pressure or the presence of PAS. Elevated intraocular pressure was defined as an intraocular pressure exceeding 21 mm Hg.

The diagnosis of PACS was made on the basis of narrow angles with glaucomatous optic neuropathy. Evidence of glaucomatous optic neuropathy was defined as a vertical cup-disc ratio of 0.7 or higher, cup-risk ratio asymmetry exceeding 0.2, or focal notching with compatible visual field loss on static automated perimetry (standard Swedish interactive thresholding algorithm with a 24-2 test pattern [Humphrey Visual Field Analyzer II; Carl Zeiss Meditec]). This was defined as glaucoma hemifield test results outside normal limits, an abnormal pattern SD with \( P < 0.05 \) occurring in the normal population and fulfilling the test reliability criteria (fixation losses \(<20\%\), false-positive results \(<33\%\), or false-negative results \(<33\%\), or a cluster of 3 or more nonedge contiguous points on the pattern deviation plot, not crossing the horizontal meridian, with a probability of less than 5% for being present in age-matched healthy individuals (one of which was \(<1\%\)).

Patients with a history of any intraocular surgery or secondary glaucoma were excluded from the study. Eyes with posterior synechiae, extensive PAS (\( >180^\circ \)), and gross iris atrophy were also excluded from the study.

Each patient underwent a standardized ophthalmic examination that included fundus examination, visual acuity determination with a Snellen chart, ultrasonographic pachymetry (Echoscan US-1800; Nidek Co Ltd), gonioscopy with a 4-mirror lens (Sussman; Ocular Instruments Inc), and intraocular pressure measurement using Goldmann applanation tonometry. Axial length and anterior chamber depth were also measured (IOLMaster; Carl Zeiss Meditec).

LASER PERIPHERAL IRIDOTOMY

Laser peripheral iridotomy was performed in the superior region of the iris (from the 10-o’clock to the 2-o’clock position) using topical anesthesia with sequential argon (400–1000 mW, 50 milliseconds, 50 μm, and 10-20 shots) and Nd:Yag (1-3 mJ and 2-10 shots) lasers at the given settings. Prednisolone acetate, 1%, eyedrops were prescribed 4 times a day for 10 days after the procedure. Patients were evaluated at least 7 days after LPI, and a repeat ASOCT and analysis of images were performed.

ASOCT VIDEOGRAPHY

Eyes were imaged with ASOCT (model 1000, Visante computer and software, version 2.1; Carl Zeiss Meditec), which allows real-time imaging of the anterior chamber with an imaging speed of 2000 A-scans per second. Images of the anterior chamber angles were obtained using ASOCT anterior segment single imaging protocol of the nasal and temporal quadrants by one of us (C.Z.) who was masked to other test measurements. The image acquisition time was 0.125 seconds per line. The examiner adjusted the saturation and noise and optimized the polarization for each image during the examination to obtain the best-quality images. Video recording software (Camtasia 6.0; TechSmith Corporation) was installed on the computer to capture dynamic changes of the iris in response to dark-light illumination at the default recording rate of 14 frames per second.

Two ASOCT examinations were performed, one at the initial baseline visit before LPI and another 1 to 2 weeks after LPI. The video recording using ASOCT was standardized and began once the patient had been dark adapted for 1 minute (20 lux). A handheld pen torch light, kept at an approximate angulation of 45° and a distance of 23 cm, was then shone from the temporal aspect on the fellow eye (the light intensity at the patient’s sitting position was 1700lux [as measured by Studio Deluxe II L-308; Sekonic]). Care was taken to prevent light from crossing the nasal bridge. Changes in the iris and anterior segment from dilatation in the dark to constriction in the light were recorded. If any eye movements were observed during video capture, the process was repeated but not more than 3 times to prevent iris muscle fatigue.

Each video file was exported as a frame sequence using video editing software (VirtualDub 1.8.5; Avery Lee). The frame series in each eye was then reviewed by one of us (C.Z.) frame by frame, starting from a fully dilated pupil (described as the largest pupil diameter [PD] observed in the video) to a constricted pupil (described as the smallest PD observed in the video) to exclude poor-quality videos (such as those with excessive eye movements). The method of SPC measurement has been reported previously.\textsuperscript{23,29} In brief, the speed of each frame (instant velocity) was calculated based on the PD in a time series. Because the image resolution of ASOCT is 26.6 μm/pixel (300 × 600 pixels for 8 × 16 mm) and because the videography recording rate was 14 frames per second in this study, we required the measured speed to be at least 0.364 mm/s (Figure 1). This minimum speed is intended to eliminate random changes in PD due to hippus. The start frame was defined as the fully dilated pupil in the dark, and the end frame was defined as the fully constricted pupil in the light. The start and end frames were selected for iris and anterior segment measurements. The dark-light response time was defined as the number of frames between the start and the end frames times 0.071.
to the anterior iris surface \[AOD_{500}\]), and trabecular–iris space the trabecular meshwork at 500 (the inner scleral wall to the opposing iris, superiorly by the in-
line drawn from the scleral spur perpendicular to the plane of area (an area bounded anteriorly by the AOD, posteriorly by a divided by the time from the start frame to the end frame (in
millimeters per second). The rate of each of the anterior seg-
ment parameters in response to illumination was derived from
the slope of parameters vs a time graph. The reproducibility of
this program has been reported previously. In brief, ASOCT measurements were performed in 2 sessions separated by an
interval of 1 week using the Anterior Segment Analysis Pro-
gram software in 30 healthy individuals. The reproducibility
of the ASOCT measurements was excellent, with the intra-
class correlation coefficient ranging from 0.89 to 0.97.

The estimated sample size was calculated to detect a 20% (approximately 0.22 mm/s) difference in the SPC after LPI, with
80% power and \(\alpha = .05\), assuming a precision of 0.4 SD. It was
estimated that 26 participants were required.

**STATISTICAL ANALYSIS**

A software program (Statistical Package for Social Sciences, version 17.0; SPSS Inc) was used in the statistical analysis. Com-
parisons of the ASOCT findings in the dark-light dynamic changes before and after LPI were performed using paired \(t\) tests. \(P < .05\) was considered statistically significant.

**RESULTS**

A total of 33 patients with angle closure were recruited for the study. Four patients (12%) were excluded because
of poor visibility of the scleral spur on ASOCT video images \((n = 2)\) and because of excessive eye movement during video capture \((n = 2)\). Table 1 summarizes the demographic and clinical data of the participants. They
included 21 patients with PACS, 5 patients with primary
angle closure, and 3 patients with PACG (the di-
agnoses for the fellow eyes were 22 PACS, 5 primary angle
closure, and 2 PACG). No difference was observed in the
extent of glaucomatous damage (as measured by visual
field indexes) between fellow eyes in the study \((P > .05)\).
Most patients were Chinese \((26 of 29 [90%])\) and fe-
male \((18 of 29 [62%])\), and the mean \((SD)\) age was 63.0
\((8.8) years \((age range, 43-76) years.\)

Compared with baseline, the angle measurements (in
the dark), including \(AOD_{500}\), anterior chamber area, and
trabecular–iris space area at 500 \(\mu m\) from the scleral spur,
were significantly greater after LPI \((P < .001)\) (Table 2).
Iris curvature decreased, whereas iris area, iris thick-
ness at the mid-iris location, and iris thickness at 750 \(\mu m\)
from the scleral spur increased \((P < .05)\). However, PD,
lengthy, and anterior chamber depth remained the same
after LPI \((P > .10)\).

A statistically significant increase was observed in the
SPC in response to illumination after LPI \((P < .05)\) (Table 3). We also observed an increase in the rate of change in iris thickness in the sphincter muscle region \((–0.00 mm/s before LPI vs 0.03 mm/s after LPI, P = .005)\)
and a decrease in the rate of change in iris thickness at
750 \(\mu m\) from the scleral spur \((–0.04 mm/s before LPI vs −0.06 mm/s after LPI, P = .02)\) in response to illumina-
tion. After LPI, a significant increase \((P < .05)\) in the
rate of change in \(AOD_{300}\) in response to illumination was
also found. However, no significant change was found
for the rate of change in iris curvature, iris area, or iris
thickness at the mid-iris location in response to illumina-
tion.
Anterior segment optical coherence tomography not only allows evaluation of static biometric parameters of the anterior segment but also with real-time video analysis software enables observation of dynamic irido-pupillary changes in response to illumination. Our study of static biometric findings before and after LPI, which showed that PD, lens vault, and anterior chamber depth did not change after LPI but that AOD500 and trabecular–iris space area at 500 µm from the scleral spur increased considerably, is consistent with previous studies. Therefore, LPI results in significant widening of the angle but without changes in the anterior segment dimensions.

A recent study based on ASOCT videography identified a novel association of slower SPC with angle closure in Asian eyes. The present study further demonstrates increased SPC and angle widening after LPI. This is understandable because LPI may facilitate iris mobility by relieving pupillary block and flattening the iris contour and would be expected to increase the SPC. These findings provide further evidence to support the importance of pupillary block mechanism in angle closure, as well as the effectiveness of LPI in reducing pupillary block and widening the angle.

While it was previously reported that greater iris curvature and iris thickness are independently associated with angle closure, in the present study, we found that LPI resulted in an increase in iris thickness at the iris root (iris thickness at 750 µm from the scleral spur of 0.39 mm before LPI vs 0.42 mm after LPI, P < .001) while a decrease in iris thickness at the pupil edge was observed (iris thickness in the sphincter muscle region of 0.49 mm before LPI vs 0.47 mm after LPI, P = .01). These findings agree with the results by He et al in their study of 72 patients with PACS using ultrasonographic biomicroscopy. They noted that after LPI the iris thickness increased at 750 and 1000 µm from the scleral spur and suggested that the iris flattens and increases in thickness when pupillary block is eliminated.

Notably, LPI also alters how the iris functions. We found that the speed of decrease in pupil size in response to illumination increased after LPI. We hypothesize that iridotomy reduces the tension on the iris caused by relative pupillary block and that this allows more rapid movement of the pupil. Tiedeman noted that the dilator and sphincter muscles with the iris root create forces within the iris that stabilize the iris at the iris root and pupillary border. The presence of a posterior to anterior pressure differential destabilizes the iris at these locations, which results in a convex shape of the iris in pupillary block. Whether this will ultimately lead to angle closure depends on several factors, including iris position, iris stiffness, size of the pressure differential, and iris–lens channel resistance. Laser iridotomy equalizes the angle by reducing pupillary block.
the pressure across the iris, bypasses iris channel resistance, and decreases iris tension. This results in resolution of the pupillary block, with a decrease in iris curvature. Therefore, the increase in iris mobility may be associated with the faster pupillary constriction that we noted in this study.

As already noted, the iris thickness at the root increased after LPI, while the iris thickness at the pupillary border decreased after LPI. Both parameters also showed dynamic differences in terms of speed of response to illumination after LPI. This again may be associated with increased iris mobility after LPI.

While we found that AOD continued to increase significantly after LPI in the dark, we observed that in response to illumination the rate of change in AOD was faster after LPI. In separate studies of Asian eyes using ultrasonographic biomicroscopy and ASOCT, Gazzard et al and See et al reported that the increase in angle width when going from dark to light conditions was significantly greater after LPI. Their studies demonstrated that LPI and increased illumination significantly widened the angle and that such changes were greater after LPI. We not only found that this trend was present in our study but also noted that angle widening in response to illumination was faster after LPI.

This study has some limitations. Study patients were Asian (predominantly Chinese), and it is unknown if the changes found can be applied to other populations. Only the nasal and temporal angles were used for analysis because videography of the superior and inferior angles could not be recorded without manipulation of the eyelid. Some patients (8 of 29 [27.6%]) with angle closure in this study had PAS, which may have affected the pupil dynamics and introduced variability of unknown significance into the results. Additional prospective studies are needed to confirm the present findings in individuals with PAS and to determine the effect of PAS on iris velocity.

In summary, we evaluated the dynamics of the pupil and iris in response to illumination in patients with angle closure before and after LPI. After LPI, the pupil constricts faster in response to illumination in patients with...
angle closure. Moreover, dynamic changes in the iris, particularly in iris thickness, were faster after LPI, and more rapid widening of the angle was likewise noted after the procedure. These findings are likely due to relief of pupillary block after LPI.

Submitted for Publication: March 26, 2012; final revision received June 9, 2012; accepted July 6, 2012.

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Author Contributions: Drs Zheng and Guzman contributed equally to this work.

Conflict of Interest Disclosures: Dr Aung has received research funding, travel support, and honoraria from Carl Zeiss Meditec.

Funding/Support: This study was supported by grants from the National Research Foundation and the National Medical Research Council of Singapore. Dr Aung’s research was supported by grant NMRC/TCR/002-SERI/2008 from the Singapore Ministry of Health’s National Medical Research Council under its Translational and Clinical Research Flagship Programme.

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