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Effect of laser peripheral iridotomy on anterior chamber angle anatomy in primary angle closure spectrum eyes

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Abstract

Purpose—To evaluate the change in trabecular-iris circumference volume (TICV) after laser peripheral iridotomy (LPI) in primary angle closure (PAC) spectrum eyes

Patients and Methods—Forty-two chronic PAC spectrum eyes from 24 patients were enrolled. Eyes with anterior chamber abnormalities affecting angle measurement were excluded. Intraocular pressure, slit lamp exam, and gonioscopy were recorded at each visit. Anterior segment optical coherence tomography (ASOCT) with 3D mode angle analysis scans were taken with the CASIA SS-1000 (Tomey Corp., Nagoya, Japan) before and after LPI. Forty-two pre-LPI ASOCT scans and 34 post-LPI ASOCT scans were analyzed using the Anterior Chamber Analysis and Interpretation (ACAI, Houston, TX) software. A mixed-effect model analysis was used to compare the trabecular-iris space area (TISA) changes among 4 quadrants, as well as to identify potential factors affecting TICV.

Results—There was a significant increase in all average angle parameters after LPI (TISA500, TISA750, TICV500, and TICV750). The magnitude of change in TISA500 in the superior angle was significantly less than the other angles. The changes in TICV500 and TICV750 were not associated with any demographic or ocular characteristics.

Conclusion—TICV is a useful parameter to quantitatively measure the effectiveness of LPI in the treatment of eyes with PAC spectrum disease.

Keywords

laser peripheral iridotomy; anterior segment optical coherence tomography; trabecular-iris space area; trabecular-iris circumference volume; anterior chamber angle

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Introduction

A leading cause of bilateral blindness worldwide,^{1, 2} primary angle closure glaucoma (PACG) is estimated to affect 16-20 million people,^{3, 4} with an estimated 4 million bilaterally blind.⁴ There are 2 main mechanisms responsible for the development of the primary angle closure (PAC) spectrum of diseases (PAC, primary angle closure suspects [PACS], and primary angle closure glaucoma [PACG]⁵): pupillary block and plateau iris configuration.^{6, 7} Regardless of mechanism, angle closure prevents aqueous from leaving the eye through the trabecular meshwork, leading to elevated intraocular pressure (IOP). This rise in IOP may cause progressive loss of ganglion cells and axons at the optic nerve head, resulting in vision loss.

Laser peripheral iridotomy (LPI) is typically the first-line treatment for PAC spectrum eyes.⁶ LPI eliminates pupillary block, allowing the iris to flatten, opening the anterior chamber angle. If peripheral angle anatomy is not improved, then iridoplasty may be performed to attempt to open the angle and treat any remaining component of plateau iris.⁷ Although LPI is a known treatment and prophylaxis for PAC and PACS,^{6, 7} no single quantitative parameter has been shown to reflect its effectiveness in opening the peripheral angle.

Quantifying changes in the peripheral anterior chamber after LPI is challenging. Previous studies have evaluated the changes in anterior chamber angle anatomy after LPI using gonioscopy,⁸ ultrasound biomicroscopy (UBM),^{9, 10} and time domain anterior segment optical coherence tomography (TD-ASOCT; Visante, Carl Zeiss Meditec, Inc., Dublin, CA).^{11, 12} Clinically, gonioscopy can be used to visualize the angle structures qualitatively, but it is a challenging exam. Quantifying angle measurements or changes in those measurements is unreliable.^{13, 14} High resolution UBM can image angle structures; however, it is difficult to standardize, and obtaining reproducible angle measurements before and after LPI is difficult.

ASOCT allows for consistent and reproducible identification of anterior chamber angle landmarks, such as the scleral spur, thereby allowing reliable and reproducible measurement of parameters such as trabecular-iris space area (TISA) and angle opening distance (AOD).¹⁵ The wavelengths of the Visante and CASIA SS-1000 (Tomey Corp., Nagoya, Japan) spectral domain ASOCT instruments allow visualization of the peripheral angle. However, because of the increased scan speed provided by the swept-source Fourier domain CASIA SS-1000 ASOCT, 128 cross-sectional images (256 angles) can be obtained in less than 5 seconds. Additional data obtained from multiple cross-sectional angles may provide information not previously available regarding angle anatomy, such as information about the peripheral angle from trabecular-iris circumference volume (TICV; Figures 1 and 2).¹⁶

The purpose of this study is measure the change in TISA500 and TISA750 in 4 quadrants and TICV500 and TICV750 following LPI in PAC spectrum eyes.

Patients and Methods

This prospective cohort study was conducted at the Robert Cizik Eye Clinic of the Ruiz Department of Ophthalmology and Visual Science at The University of Texas Medical

School in Houston. Institutional Review Board approval was obtained from The University of Texas Health Science Center Committee for the Protection of Human Subjects. All research was HIPPA compliant.

Participants

PAC spectrum eyes were recruited from the Robert Cizik Eye Clinic between January 2012 and April 2013.⁷ Eyes with anterior segment abnormalities that could affect the angle measurements (i.e. significant corneal opacity) were excluded. Acute angle closure eyes were also excluded.

Procedures

After obtaining informed consent from the participant, demographics (age, race, and gender) were recorded, and an ocular examination (including slit lamp, IOP measurement, and gonioscopy) was performed before LPI treatment. IOP was measured by Goldmann applanation tonometry. Gonioscopy was performed by experienced examiners and graded using the Spaeth grading system.^{17, 18} Cataracts were graded as present or absent. Peripheral anterior synechiae (PAS) were documented as present or absent; if present, the number of clock hours was recorded. ASOCT images were taken as previously described.^{15, 16} The ASOCT operator viewed the scans to ensure that image quality was adequate, i.e. no lid obstruction, no eye movement artifact, etc.

LPI procedures were performed using the surgeon's standard technique, with the iridotomy placed temporally (in all except one eye). Administration of pilocarpine preoperatively was surgeon's choice; all preoperative images were obtained prior to the administration of pilocarpine. Slit lamp exams, IOP, gonioscopy, and ASOCT images were performed again 3 months (± 1 month) after LPI treatment.

Image Analysis

Instrumental details for the CASIA SS-1000 are previously described.^{15, 16} The image files obtained at the pre- and post-LPI visits were imported into the Anterior Chamber Analysis and Interpretation software (ACAI, Houston, Texas) and read by an experienced reader (LAB), who was masked to the gonioscopic grading. ACAI reading and image analysis have been previously described.^{15, 16}

TICV Calculation

The ACAI software calculates AOD and TISA at 500 μm and 750 μm for each angle along with radius (R), the distance from the midpoint of the 2 SSLs to the centroid of each TISA. TICV500 and TICV750 are defined as the volume bounded by the posterior corneal surface, anterior iris surface, scleral spur landmark ring, and 500 μm or 750 μm centrally the from scleral spur landmark ring, respectively (Figure 1). TICV500 and TICV750 were calculated using Pappus's centroid theorem formula¹⁶:

$$TICV=2 \pi \sum_{i=1}^{256} TISA_i \times R_i / 256$$

Data Analysis

Data were summarized using frequency (%) for discrete variables (i.e. race, gender, eye, and presence of PAS). Mean and standard deviation were used for continuous variables (i.e. age, IOP, extent of PAS, and number of IOP-lowering medications).

Pre- and post-LPI gonioscopy grades, presence or absence of PAS, and presence or absence of cataract were compared using the McNemar test. The mean and standard deviation of the changes in TICV, TISA, and clock hours of PAS and IOP before and after LPI were calculated. A mixed-effect model analysis was used to compare TISA changes among all 4 quadrants (superior, inferior, nasal, temporal) and to estimate the relationship between TICV and potential influential factors. The random effect was the study participants; the fixed effects were age, gender, race, study eye, presence or absence of cataract and PAS, number of IOP-lowering medications at the pre-LPI visit, use of pilocarpine pre-LPI, and TICV before LPI.

All statistical analysis was performed using SAS for Window v9.3 (SAS Inc., Cary, NC), with a *P* value less than 0.05 considered statistically significant.

Results

Twenty-four participants with PAC spectrum disease (42 eyes) were enrolled in the study. Two subjects (3 eyes) were lost to follow-up. Five eyes did not have acceptable post-LPI images due to eye movement/blink artifact (1 eye), eyelid blockage (3 eyes), and missing image acquisition (1 eye). As a result, images from 42 eyes (24 participants) pre-LPI and 34 eyes (19 participants) post-LPI were analyzed.

The mean age of participants was 58.7 ($\pm$ 9.6) years with 5 (21%) males, and there were 11 (46%) White, 6 (25%) Black, 5 (21%) Hispanic, and 2 (8%) Asian participants. There were no significant differences in demographics between participants with and without post-LPI images ($P=0.2278$ for age, $P=0.5440$ for sex, and $P=0.6312$ for race). Twenty-two study eyes (52%) were right eyes. Two eyes (5%) required additional LPs within 1 month postoperatively. All LPI sites were patent at 3 months. One eye required a trabeculectomy before the 3-month follow-up visit due to elevated IOP. The mean time elapsed from LPI to the 3-month follow-up examination was 123 days ($\pm$ 49 days, range 76 to 274 days).

Ocular characteristics before and after LPI are listed in Table 1. A comparison of baseline ocular characteristics between eyes that had images before and after LPI to those that only had images before LPI showed no differences ($P>0.05$). Comparisons of post-LPI ocular characteristics for eyes with and without post-LPI images found a significantly lower treated IOP ($P=0.022$) and more PAS ($P=0.016$) in eyes without adequate post-LPI images (Table 1). In the 34 eyes with both pre- and post-LPI images, pre-LPI gonioscopy showed 17 (50%) eyes open to Schwalbe's line (Grade A) and 17 (50%) eyes open anterior to the trabecular meshwork (Grade B), with average deepening of 1.5 grades post-LPI ($P<0.0001$). There was no change in the number of eyes with PAS pre- and post-LPI ($P=0.1797$ by the McNemar test). Of the eyes ($N=9$) without pre-existing lenticular opacity, 5 (57%) eyes developed cataracts during follow-up ($P=0.0253$ by the McNemar test). The mean IOP at the pre-LPI

(16.3 ± 4.1 mm Hg) visit and the mean IOP at the 3-month visit (16.2 ± 3.5 mm Hg) were found to be comparable ($P=0.8183$). The average number of IOP-lowering medications was reduced by a mean of 0.21 ± 0.48 medications ($P=0.0172$) from pre-LPI to the 3-month visit.

Angle parameters are shown in Table 2. Preoperatively, no differences were found in eyes with post-LPI images and in eyes without post-LPI images ($P>0.200$). Average TISA at 500 μ m and 750 μ m significantly increased in all 4 quadrants after LPI ($P<0.001$ for all comparisons). Average TICV at 500 μ m and 750 μ m significantly increased after LPI ($P<0.001$). The magnitude of change of TISA500 in the superior angle was significantly less than the other 3 angles ($P=0.0051$ comparing to nasal, $P=0.0176$ comparing to inferior, $P=0.0393$ comparing to temporal). Similarly, the change in TISA750 in the superior angle was significantly less than in the nasal ($P=0.001$) and inferior ($P=0.0128$) angles. However, no differences were found in the change in TISA750 between superior and temporal angles ($P=0.081$). Furthermore, the changes in TICV500 and TICV750 were not associated with any demographic or ocular characteristics, including the corresponding pre-LPI TICV value ($P=0.580$ for TICV500 and $P=0.465$ for TICV750).

Discussion

There was a significant increase in all average angle parameters as measured by ASOCT in our study before and after LPI (TISA500, TISA750, TICV500, and TICV750). This is consistent with the improvement in gonioscopic grade by 1.5. Lee et al found that the amount of angle deepening was inversely dependent on the pre-LPI angle measurement using pre-and post-LPI images taken 2-3 weeks after the treatment.¹⁹ However, in our study, the change in TICV500 and TICV750 at 3 months did not depend on pre-LPI TICV500 ($P=0.580$) or TICV750 ($P=0.465$), respectively.

Across all angle parameters, we found that the nasal angle deepened the most (TISA750 of 0.087 ± 0.072 mm²). This is consistent with a 2008 Philippine study using UBM to study post-LPI changes. The greatest AOD widening (at 250 μ m and 500 μ m) was also reported in the nasal quadrant with no clear explanation.²⁰ Interestingly, in the Philippine study, the PI was placed superiorly²⁰ with similar results to our study, where the PI was placed temporally (97%). Also in our study, the superior angle deepened the least (TISA750 of 0.047 ± 0.044 mm²). It is well documented that the superior quadrant is the narrowest,^{15, 16, 21} thought to be due to the effect of gravity, and the findings of our study support this result.

The values of TISA in the nasal and temporal angles obtained from this study were similar to those averaged values for the nasal and temporal quadrants reported by Memarzadeh et al,²² and the changes in TISA were similar to those previously observed at 1 month post-LPI by Lee et al in the nasal and temporal quadrants for TISA500.²³ However, TISA is only measured in 1 meridian and not integrated over the entire angle^{22, 23}; therefore, the results likely overestimate the effect of LPI as these 2 studies did not examine the superior and inferior angles. Other studies have also reported increased TISA500 and/or TISA750 post-LPI,^{19, 24-26} but comparison of the exact values for TISA and magnitude of change is limited by varying angle closure populations, time frame of analysis, and ASOCT methodology.

Quantitative measurement of peripheral anterior chamber angle anatomy is important for evaluating the effectiveness of a particular treatment, even if the exact clinical implications are still uncertain. ASOCT is able to provide several quantitative measurements, such as TISA and AOD, but there are limitations with using these measurements. To date, there has not been a single quantitative measurement that can accurately describe pre- and post-LPI changes over the entire peripheral anterior chamber angle. TICV is useful because it integrates the volume over the entire peripheral angle at a defined distance from the scleral spur landmark ring, allowing objective comparisons to be made. Because of the limitations of AOD and TISA, TICV may provide a better objective measurement to assess angle depth in PAC spectrum eyes.

In our study, 7 eyes (21%) were on IOP-lowering medications preoperatively, and 2 eyes (6%) not on IOP-lowering medications had IOPs greater than 21 mm Hg. Mean medically treated IOP did not change post-LPI ($P=0.8183$). However, the mean number of IOP-lowering medications was significantly reduced at 3 months of follow-up ($P=0.0172$). These findings indicate that, at least in the short term, LPI may be a useful adjunct in reducing the number of IOP-lowering medications. However, many studies have agreed that a majority of eyes with LPI will go on to further treatment, and it is unclear how long the effect of LPI will last.²⁷⁻²⁹

In our study, there was no difference in the percentage of eyes with PAS pre- and post-LPI ($P=0.1797$). Similarly, Lim et al showed that the amount of PAS remained stable post-LPI up to one year.³⁰ Our finding supports that LPI does not treat PAS. Whether LPI prevents formation of PAS remains to be seen.

Of the 9 non-cataract eyes in our study, 5 developed cataract. While there are reports of cataract formation after LPI,^{9, 31} to date there is no agreement about the causal relationship between LPI and cataract development. Since etiology of cataract formation is complex and multivariate, from trauma association to medical conditions to toxic environmental exposures, it is difficult to convincingly show that laser treatment causes increased risk of cataract formation, and our study was not powered to detect these changes.

There were some limitations to the study. First, the sample size was small (42 eyes) and only 34 eyes had both pre- and post-LPI images for comparison. Although there were no statistical differences in baseline ocular characteristics between the 34 eyes with post-LPI images and 8 eyes without post-LPI images, there is not sufficient power to conclude that the groups are not different. Interestingly, when comparing post-LPI ocular characteristics of 5 eyes without adequate images to the 34 eyes with adequate imaging, there was a significantly lower treated IOP ($P=0.022$) and more PAS ($P=0.016$) in eyes without adequate post-LPI images. It may be possible that these 5 eyes without post-LPI imaging were more difficult to adequately image because of the increased burden of PAS, but this needs further investigation. Second, the extent and location of PAS was not recorded in some participants possibly due to difficulty in identifying PAS formation in PAC eyes prior to LPI. Finally, this study only followed patients over a period of 3 months. Other studies have demonstrated progressive narrowing in patients who have had LPI with extended follow-up.^{12, 23} Although

statistically significant deepening did occur with LPI over the course of this study, the threshold of *clinically* significant angle deepening is unknown.

Our study is the first to use TICV, a measurement of the peripheral angle,¹⁶ to determine volume changes in this critical portion of the angle with LPI. TICV appears to be a useful parameter to determine the magnitude of change in the angle anatomy after LPI. This study determines that LPI is effective in deepening the anterior chamber angle for eyes with PAC spectrum disease in the short term. Further investigation is required to fully understand both the long-term effect of LPI as well as the overall clinical significance of TICV.

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Figure 1. Trabecular Iris Circumference Volume (TICV). Anterior Segment Optical Coherence Tomography (ASOCT) image exhibiting TISA750 (light green space) and TICV750 (darker green spaces), along with the scleral spur landmark (red circle), iris (yellow), and cornea (violet line) in an open angle.¹⁶

Figure 2.

Comparison images of exhibiting TISA750 in a normal eye (A), before LPI in an eye with PAC spectrum disease (B), and after LPI in the same eye (TISA is indicated by yellow asterisk). TICV is TISA integrated over the peripheral angle.

Table 1

Summary of Clinical Examinations before and after LPI

Variable	Pre-LPI (N=42)			Month 3 (N=39)		
	Without Post-LPI image (N=8)	With Post-LPI image (N=34)	P Value	Without Post-LPI image (N=5)	With Post-LPI image (N=34)	P Value
IOP, mm Hg $\pm$ SD	17.6 $\pm$ 2.7	16.3 $\pm$ 4.1	0.396	12.2 $\pm$ 3.7	16.2 $\pm$ 3.5	0.022
On IOP-lowering medications, N (%)	3 (38%)	7 (21%)	0.369	2 (40%)	2 (6%)	0.072
Number of IOP-lowering medications, mean $\pm$ SD	1.3 $\pm$ 1.8	0.3 $\pm$ 0.8	0.171	1.2 $\pm$ 1.6	0.1 $\pm$ 0.4	0.205
Presence of cataract, N (%)	5 (63%)	25 (73%)	0.668	3 (60%)	30 (88%)	0.161
Angle Assessment by Gonioscopy						
Spaeth grading, N (%)						
Open to Schwalbe's line	6 (75%)	17 (50%)	0.259	0 (0%)	2 (6%)	0.072
Open anterior to trabecular meshwork	2 (25%)	17 (50%)		3 (60%)	4 (12%)	
Open to posterior trabecular meshwork	0 (0%)	0 (0%)		2 (40%)	20 (59%)	
Open to scleral spur	0 (0%)	0 (0%)		0 (0%)	8 (24%)	
Open to ciliary body band	0 (0%)	0 (0%)		0 (0%)	0 (0%)	
Presence of PAS, N (%)	7 (88%)	15 (47%) ^{**}	0.054	5 (100%)	20 (59%)	0.139
Extent of PAS, clock hours $\pm$ SD	1.8 $\pm$ 2.5	1.0 $\pm$ 1.3 ^{**}	0.262	4.4 $\pm$ 1.8	1.3 $\pm$ 1.6	0.016

IOP=intraocular pressure; LPI=laser peripheral iridotomy; PAS=peripheral anterior synechiae; SD=standard deviation

^{**}2 eyes were unable to be assessed

Table 2

Angle Assessment before and after LPI Using ASOCT images

Variable	Baseline (N=42)			Month 3 (N=34)	Change from Baseline (N=34)	P Value**
	Without Month 3 Images (N=8)	With Month 3 Images (N=34)	P value*			
TISA500, mm ² ± SD						
Temporal	0.035 ± 0.022	0.035 ± 0.028	0.961	0.070 ± 0.037	0.034 ± 0.035	<0.001
Nasal	0.023 ± 0.016	0.034 ± 0.026	0.149	0.073 ± 0.044	0.039 ± 0.044	<0.001
Superior	0.020 ± 0.029	0.012 ± 0.014	0.470	0.031 ± 0.024	0.019 ± 0.023	<0.001
Inferior	0.013 ± 0.013	0.023 ± 0.024	0.117	0.059 ± 0.042	0.036 ± 0.035	<0.001
TISA750, mm ² ± SD						
Temporal	0.085 ± 0.038	0.081 ± 0.047	0.807	0.148 ± 0.062	0.067 ± 0.055	<0.001
Nasal	0.064 ± 0.026	0.070 ± 0.048	0.660	0.157 ± 0.081	0.087 ± 0.072	<0.001
Superior	0.050 ± 0.049	0.036 ± 0.034	0.480	0.084 ± 0.049	0.047 ± 0.044	<0.001
Inferior	0.043 ± 0.026	0.053 ± 0.047	0.403	0.129 ± 0.076	0.076 ± 0.058	<0.001
TICV500, µl ± SD	0.798 ± 0.489	0.931 ± 0.607	0.521	1.962 ± 0.985	1.031 ± 0.719	<0.001
TICV750, µl ± SD	2.020 ± 0.835	2.065 ± 1.274	0.904	4.179 ± 1.862	2.114 ± 1.203	<0.001

TISA=trabecular-iris space area; TICV=trabecular-iris circumference volume; SD=standard deviation; ASOCT=anterior segment optical coherence tomography

* Obtained from two sample *t*-test (comparing eyes with and without ASOCT images, 34 eyes vs 8 eyes)

** Obtained from paired *t*-test (comparing pre- and post-LPI in 34 eyes)