

Longitudinal Changes in Anterior Segment Parameters After Laser Peripheral Iridotomy Assessed by Anterior Segment Optical Coherence Tomography

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PURPOSE. To quantify long-term changes in anterior segment (AS) parameters after laser peripheral iridotomy (LPI) using AS optical coherence tomography (OCT) in primary angle-closure suspect (PACS).

METHODS. Thirty-two PACS subjects were imaged at pre-LPI and 2 weeks and 18 months post-LPI using AS OCT. Anterior chamber depth (ACD), iris curvature (IC), iris thickness at 750 and 1500 μm from the scleral spur (IT_{750, 1500}), lens vault (LV), anterior chamber area (AA), and iris area (IA) were estimated by ImageJ software (version 1.46). Anterior chamber angle (ACA) parameters (angle opening distance [AOD₇₅₀], angle recess area [ARA₇₅₀], and trabecular iris space area [TISA₇₅₀]) were provided by the manufacturer. Parameters were compared before and after LPI. Uni- and multivariate regression analysis was performed to evaluate factors associated with ACA narrowing.

RESULTS. Mean AA (14.63 vs. 15.87 mm²) and three ACA parameters (AOD₇₅₀ [0.17 vs. 0.28 mm], TISA₇₅₀ [0.07 vs. 0.11 mm²], and ARA₇₅₀ [0.08 vs. 0.13 mm²]) increased at 2 weeks post-LPI (all $P < 0.001$). The IT_{750, 1500} and IC also showed change at 2 weeks post-LPI. Eighteen months post-LPI, IC (0.34 vs. 0.16 mm, $P < 0.001$) and LV (0.88 vs. 1.01 mm, $P = 0.001$) were significantly different, while three ACA parameters were not different from their pre-LPI status. At post-LPI 18 months, LV was significantly associated with ACA narrowing ($P = 0.026$).

CONCLUSIONS. The ACA tended to be narrowed at 18 months post-LPI despite resolution of pupillary block, which may be due to LV increment. Our results warrant continuous follow-up of narrow-angle patients after LPI.

Keywords: angle closure glaucoma, anterior segment optical coherence tomography, laser peripheral iridotomy

Laser peripheral iridotomy (LPI) is used to resolve pupillary block by making a new shunt of aqueous flow from the posterior chamber to the anterior chamber (AC) and is recognized as the primary treatment modality for angle-closure glaucoma (ACG).^{1,2} However, in previous studies, the AC angles of some ACG eyes that underwent LPI remained closed.³⁻⁵ Furthermore, some eyes that underwent LPI showed progression of peripheral anterior synechiae (PAS).⁶⁻⁸ These observations raise the questions whether pupillary block is the only mechanism of ACG, and whether LPI is suitable for treating all types of ACG. Other mechanisms have been suggested for explaining ACG⁹⁻¹²; hence observation of longitudinal changes in anterior segment parameters after LPI is warranted to determine the optimal treatment of ACG.

In the past, AC angle assessment was entirely dependent on gonioscopic examination. Although direct viewing of the angle by an examiner is still the gold standard for angle evaluation, the outcomes of this method are subjective and difficult to quantify. Anterior segment optical coherence tomography (AS OCT) is an imaging device that can acquire an anterior segment image using a noncontact method with the patient in a sitting position. This device provides reproducible and quantitative measurements of the AC angle and other

anterior segment parameters.^{13,14} Recent studies using AS OCT showed that LPI substantially increased the AC angle width in ACG eyes.^{5,15-19} Lee et al. found that approximately two-thirds of patients with a narrow angle showed opening of the AC angle after LPI.⁵ However, these results were obtained early post-LPI, with post-LPI imaging performed at 1 week to 1 month. Anterior segment structures change according to aging¹⁴; thus the anterior segment and AC angle may undergo further changes from those observed early post-LPI.

Therefore, the aim of this study was to assess the longitudinal changes in anterior segment parameters after LPI using AS OCT. As far as we know, there has been no report of quantitative assessment of the long-term changes in AC angle and anterior segment configuration after LPI using AS OCT.

METHODS

Subjects

Primary angle-closure suspect (PACS) subjects examined by a single glaucoma specialist (KRS) at the glaucoma clinic of the Asan Medical Center from March 2009 to October 2010 and meeting the inclusion criteria were consecutively enrolled in

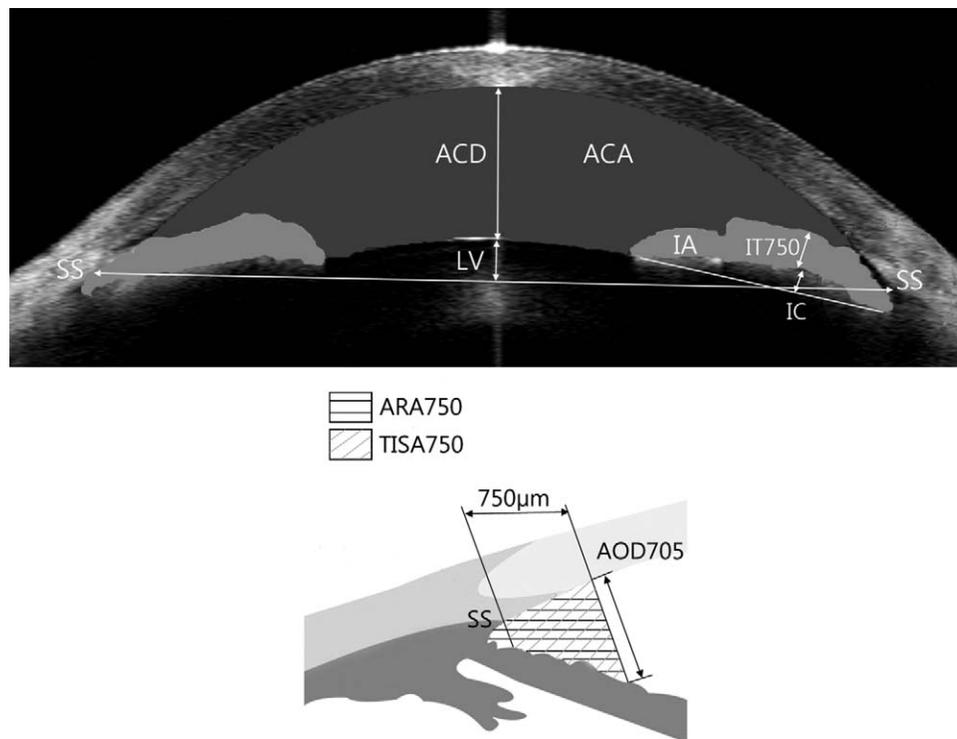


FIGURE. Anterior segment parameters measured by anterior segment optical coherence tomography and calculated using ImageJ software. AA, anterior chamber area; ACD, anterior chamber depth; IA, iris area; IC, iris curvature; IT₇₅₀, iris thickness 750 μm from the scleral spur; LV, lens vault; SS, scleral spur; AOD₇₅₀, angle opening distance; ARA₇₅₀, angle recess area; TISA₇₅₀, trabecular iris space area.

this study. Informed consent was obtained from all participants, and the study was approved by the Institutional Review Board of the Asan Medical Center; the tenets of the Declaration of Helsinki were adhered to.

PACS was diagnosed by gonioscopic exam. Subjects with appositional contact between the peripheral iris and the posterior trabecular meshwork greater than 270° were included in the PACS group.²⁰ Since the aim of this study was to evaluate the AC angle change after LPI, any eye with PAS in the AC angle at pre-LPI was excluded.

All subjects underwent a complete ophthalmic examination, including best-corrected visual acuity (BCVA) testing, slit lamp examination, Goldmann applanation tonometry, gonioscopy, and funduscopy. Subjects with any history or current use of topical or systemic medication that could affect the AC angle or pupillary reflex, history of any previous intraocular surgery, laser trabeculoplasty, laser iridoplasty or laser iridotomy, or inability to fixate for the AS OCT examination were excluded from the study. If both eyes met the inclusion criteria, one eye was randomly selected for analysis.

Slit Lamp Examination and Gonioscopy

Subjects underwent slit lamp examination and gonioscopy by an independent observer (KRS) with extensive experience in performing gonioscopy prior to AS OCT imaging. All subjects were examined with a Sussman lens in a controlled darkened room (0.5 cd/m²). A 1-mm light beam was reduced to a narrow slit. The vertical beam was offset horizontally for assessing nasal and temporal angles, and the horizontal beam was offset vertically for superior and inferior angles. Both static and dynamic gonioscopy were performed using a Sussman lens, with the eye in the primary position of gaze. Indentation gonioscopy was performed to determine if AC angle closure

was due to apposition or PAS. Care was taken to avoid light falling on the pupil.

Laser Peripheral Iridotomy

LPI was performed in the superior region of the iris (from 10 to 2 o'clock) by sequential argon and neodymium-yttrium-aluminum-garnet after pretreatment with 2% pilocarpine instilled into the eye 1 hour before LPI. Argon settings of 500 to 1000 mW power with a spot size of 50 μm for a duration of 0.05 seconds and a yttrium-aluminum-garnet setting of 2 to 5 mJ were used. All subjects were evaluated at 2 weeks after LPI, and then at 6-month intervals.

AS OCT Imaging

AS OCT imaging was performed pre-LPI and at 2 weeks and 18 months post-LPI. All imaging was performed under constant dim light (0.5 cd/m²) with the patient in a sitting position. Images were captured at the nasal and temporal angle quadrants (3 and 9 o'clock meridians, nasal-temporal angles at 0-180°) using an AS OCT operating in the enhanced AS single mode (scan length 16 mm; 256 A-scans). Internal fixation was used in all subjects, and all scans were conducted by a single well-trained operator who was blinded to other clinical findings to minimize operator-related measurement variability. Three images were acquired from each eye, and the highest-quality image, defined as showing good visibility of the scleral spur, was selected for analysis. A single examiner (KSL), who was blinded to other test results and all clinical information of the participants, analyzed all images. ImageJ software (version 1.46; National Institutes of Health, Bethesda, MD; Figure) was used to measure anterior chamber depth (ACD), iris cross-sectional area (IA), iris thickness at

TABLE 1. Comparison of Anterior Segment and Anterior Chamber Angle Parameters Before and After Laser Peripheral Iridotomy

Parameters	Pre-LPI,	2 Wk Post-LPI,	18 Mo Post-LPI,	P Value,*		P Value,*	
	Mean ± SD	Mean ± SD	Mean ± SD	Pre-LPI vs. 2 Wk Post-LPI	2 Wk Post-LPI vs. 18 Mo Post-LPI	Pre-LPI vs. 18 Mo Post-LPI	Pre-LPI vs. 18 Mo Post-LPI
AA, mm ²	14.63 ± 2.16	15.87 ± 2.20	15.36 ± 2.45	<0.001	0.038	0.005	0.005
ACD, mm	2.11 ± 0.18	2.11 ± 0.18	2.09 ± 0.18	0.292	0.228	0.381	0.381
LV, mm	0.88 ± 0.23	0.93 ± 0.24	1.01 ± 0.20	0.164	0.004	0.001	0.001
IC, mm	0.34 ± 0.09	0.15 ± 0.05	0.16 ± 0.06	<0.001	0.334	<0.001	<0.001
IA, mm ²	1.59 ± 0.26	1.68 ± 0.23	2.05 ± 2.46	0.109	0.425	0.332	0.332
IT ₇₅₀ , mm	0.39 ± 0.10	0.37 ± 0.08	0.38 ± 0.08	0.050	0.281	0.389	0.389
IT ₁₅₀₀ , mm	0.42 ± 0.08	0.40 ± 0.07	0.43 ± 0.10	0.033	0.023	0.399	0.399
AOD ₇₅₀ , mm	0.17 ± 0.11	0.28 ± 0.12	0.20 ± 0.09	<0.001	0.001	0.089	0.089
ARA ₇₅₀ , mm ²	0.08 ± 0.06	0.13 ± 0.06	0.09 ± 0.04	<0.001	<0.001	0.518	0.518
TISA ₇₅₀ , mm ²	0.07 ± 0.04	0.11 ± 0.05	0.08 ± 0.03	<0.001	0.099	0.219	0.219
PD, mm	4.41 ± 0.91	3.80 ± 1.08	4.35 ± 0.96	0.004	0.010	0.616	0.616

SS, scleral spur; PD, pupil diameter.

* Paired *t*-test.

750 and 1500 μm from the scleral spur (IT₇₅₀, 1500), iris curvature (IC), lens vault (LV), and anterior chamber area (AA). ACD was defined as the distance from the corneal endothelium to the anterior surface of the lens. The scleral spur was defined as the point at which a change in curvature of the inner surface of the angle wall became apparent; it often presented as an inward protrusion of the sclera.²¹ After locating the scleral spur, IT₇₅₀ and IT₁₅₀₀ were measured at 750 and 1500 μm from the spur²²; IA was defined as the cross-sectional area of both the nasal and temporal sides; IC was defined as the maximum perpendicular distance between the iris pigment epithelium and the line connecting the most peripheral to the most central point of the epithelium; LV was defined as the perpendicular distance between the anterior pole of the crystalline lens and the horizontal line joining the two scleral spurs.¹² Three AC angle parameters, AOD₇₅₀, ARA₇₅₀, and TISA₇₅₀, which were provided by the manufacturer (Zeiss Meditec, Inc., Dublin, CA), were also analyzed. The AOD₇₅₀ was defined as the linear distance between the point of the inner corneoscleral wall (which was 750 μm anterior to the scleral spur) and the iris. The ARA₇₅₀ was defined as the triangular area formed by the AOD₇₅₀. The corners of the triangle were the angle recess (the apex), the iris surface, and the inner corneoscleral wall. The TISA₇₅₀ was defined as the trapezoidal area with the following boundaries: anteriorly, the AOD₇₅₀; posteriorly, a line drawn from the scleral spur perpendicular to the plane of the inner scleral wall to the opposing iris; superiorly, the inner corneoscleral wall; and inferiorly, the iris surface. The mean of the nasal and temporal angles was used in the measurement of IC, IT₇₅₀, 1500 and three AC angle parameters. The image acquisition procedure and analysis method are described elsewhere in detail.^{14,23}

Analysis

The AC and anterior segment parameters were compared before and after LPI using a paired *t*-test after normality of the data distribution was confirmed. Uni- and multivariate regression analysis was performed to evaluate the factors associated with AC angle narrowing. Univariate analyses were performed separately for each variable. Variables with a probability value ≤0.20 in univariate analyses were included in the multivariate analysis. AC angle narrowing was defined as AOD₇₅₀. Statistical analyses were performed using SPSS version 15.0 (SPSS, Inc., Chicago, IL).

RESULTS

Thirty-two PACS eyes from 32 subjects were included in the final analysis. The mean (± SD) age of participants was 66.1 ± 3.9 years; 26 (81.3%) were women, and all were Koreans.

Mean AA (14.63 vs. 15.87 mm², *P* < 0.001), AOD₇₅₀ (0.17 vs. 0.28 mm, *P* < 0.001), TISA₇₅₀ (0.07 vs. 0.11 mm², *P* < 0.001), and ARA₇₅₀ (0.08 vs. 0.13 mm², *P* < 0.001) significantly increased when assessed at 2 weeks post-LPI. However, there was no significant change in ACD (2.11 vs. 2.11 mm, *P* = 0.292) or LV (0.88 vs. 0.93 mm, *P* = 0.164). Among iris-related parameters, the IT₇₅₀, 1500 and IC showed significant change at 2 weeks post-LPI; however, IA was not significantly different (Table 1).

When we compared the values obtained at 2 weeks and 18 months post-LPI, LV and IT₁₅₀₀ increased and AA significantly decreased. Among three angle parameters, AOD₇₅₀ and ARA₇₅₀ were reduced (Table 1).

Overall, when estimated at 18 months post-LPI, mean AA (14.63 vs. 15.36 mm², *P* < 0.001), IC (0.34 vs. 0.16 mm, *P* < 0.001), and LV (0.88 vs. 1.01 mm, *P* = 0.001) were significantly different from their pre-LPI status. Three AC angle parameters did not show significant difference in comparison with pre-LPI status (Table 1).

When assessed by multivariate regression analysis, IC (*P* = 0.041) was a significant predictor for AC narrowing at pre-LPI status (Table 2), while none of the analyzed covariates showed association with AC narrowing at post-LPI 2 weeks (Table 3). At post-LPI 18 months, LV was significantly associated with AC narrowing (Table 4).

TABLE 2. Uni- and Multivariate Linear Regression Analysis of the Association Between Various Parameters and Anterior Chamber Angle Narrowing (AOD₇₅₀) Assessed at Pre-LPI Status

	Univariate			Multivariate		
	SE	Beta	P Value	SE	Beta	P Value
AA, mm ²	0.010	0.011	0.270			
ACD, mm	0.119	0.076	0.526			
LV, mm	0.097	-0.010	0.053	0.109	-0.071	0.522
IC, mm	0.231	-0.088	0.100	0.093	-0.235	0.041
IA, mm ²	0.083	-0.117	0.172	0.105	-0.123	0.257
IT ₇₅₀ , mm	0.216	-0.131	0.019	0.127	-0.123	0.075
IT ₁₅₀₀ , mm	0.246	-0.315	0.312			
PD, mm	0.024	0.016	0.506			

TABLE 3. Uni- and Multivariate Linear Regression Analysis of the Association Between Various Parameters and Anterior Chamber Angle Narrowing (AOD₇₅₀) Assessed at Post-LPI 2 Weeks

	Univariate			Multivariate		
	SE	Beta	P Value	SE	Beta	P Value
AA, mm ²	0.135	0.034	0.803			
ACD, mm	0.288	0.208	0.477			
LV, mm	0.498	-0.148	0.001	0.106	-0.082	0.451
IC, mm	0.264	-0.741	0.009	0.456	-0.741	0.158
IA, mm ²	0.180	-0.264	0.155	0.137	0.018	0.898
IT ₇₅₀ , mm	0.100	-0.051	0.029	0.109	-0.048	0.650
IT ₁₅₀₀ , mm	0.011	0.009	0.450			
PD, mm	0.106	0.010	0.155	0.106	-0.07	0.515

TABLE 4. Uni- and Multivariate Linear Regression Analysis of the Association Between Various Parameters and Anterior Chamber Angle Narrowing (AOD₇₅₀) Assessed at Post-LPI 18 Months

	Univariate			Multivariate		
	SE	Beta	P Value	SE	Beta	P Value
AA, mm ²	0.101	-0.010	0.919			
ACD, mm	0.020	0.010	0.610			
LV, mm	0.280	-0.057	<0.001	0.264	-0.115	0.026
IC, mm	0.217	-0.376	0.095	0.214	-0.391	0.181
IA, mm ²	0.183	-0.221	0.239	0.087	0.117	0.075
IT ₇₅₀ , mm	0.091	-0.098	0.147	0.007	0.014	0.193
IT ₁₅₀₀ , mm	0.007	-0.010	0.177			
PD, mm	0.008	-0.005	0.539			

DISCUSSION

We found that LPI substantially widened the AC angle as well as increasing AA when assessed by AS OCT at 2 weeks post-LPI. All AC angle parameters showed significant change compared with their pre-LPI status. LPI made a direct channel between the posterior chamber and AC, which reduced the pressure gradient between the two chambers and thus removed pupillary block and flattened the IC. The most dramatic change was the reduced IC, which resulted in a substantial increment of AA. We found that the increment of AC angle parameters after LPI was in line with that seen in previous reports.^{5,15-19} Peripheral IT was slightly reduced at 2 weeks post-LPI, which may be explained by a mild reduction of pupil diameter compared with the pre-LPI status. Considering that all imaging was performed with the same standardized lighting conditions, pupil diameter may be influenced by pretreatment with 2% pilocarpine, although duration of this medication is known to be several hours. When imaged at 18 months post-LPI, pupil diameter and IT were not different compared to pre-LPI.

Approximately 18 months later, we found that the AC angle and anterior segment parameters showed significant change compared with early post-LPI. Although the IC remained flat, the AC angle narrowed as shown by two AC angle parameters, AOD₇₅₀ and ARA₇₅₀. This might be induced by a change of LV. Our result showed that LV did not change at 2 weeks post-LPI, but LV significantly increased over the long term. In multivariate analysis, LV was a significant predictor for AC angle narrowing when assessed at post-LPI 18 months. Changes in LV might be explained by aging. Sun et al. evaluated aging changes of anterior segment parameters by use of AS OCT and showed that LV increment was the main change in the anterior segment as a person ages.¹⁴ We found that the rate of LV increment (mean 0.13-mm difference over 18 months) was much higher than that reported in a previous study (0.0084 mm/y).¹⁴ The reason may be that the previous study was performed with open-angled normal subjects with a wide range of age; the participants in our study were older and narrow angled. Therefore, we hypothesize that narrow-angle subjects have higher rates of LV change than open-angle subjects, probably due to weak lens zonule or increment of lens thickness. Although LV increased and the AC angle narrowed, AA remained larger when assessed long-term compared with its pre-LPI status, which may contribute to a flat IC.

To our knowledge, this was the first study to analyze quantitative changes of the AC angle and anterior segment configuration in PACS subjects over a relatively long period using AS OCT. Among other longitudinal studies in PACS

subjects, Thomas et al. found that 11 out of 50 bilateral PACS subjects (22%) progressed to primary angle closure (PAC) after a 5-year follow-up.²⁴ Ye et al., in a 6-year follow-up study with a Chinese population, showed a 4.1% PACS progression.²⁵ In an Eskimo population, 35% of PACS subjects progressed to PAC over a 10-year follow-up period.²⁶ Therefore, although the percentages were different among studies, a substantial portion of PACS subjects showed progression over time. This progression, despite LPI, was difficult to explain; however, our results suggest that increment of LV and subsequent renarrowing of the AC angle may be an explanation.

Our present is limited by relatively small sample size; thus the results should be interpreted with caution.

Our results demonstrated that LPI significantly reduced iris bowing and widened the AC angle by aborting pupillary block. This effect of pupillary block abortion was maintained until a mean of 18 months post-LPI; but the AC angle tended to be narrowed, which may stem from an increase of LV when assessed by AS OCT imaging. Thus, for our patient population, both pupillary block and lens effect may contribute to the angle-closure mechanism. Our results suggest that LPI should be a baseline treatment modality for angle closure, which should resolve the pupillary block induced by crowding of anterior segment structures. At the same time, the lens and anterior segment parameters change continuously as one gets older. Therefore, careful longitudinal observation of lens status as well as other anterior segment parameters is integral in the management of ACG.

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