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Comparison of anterior segment morphology following prophylactic laser peripheral iridotomy in Caucasian and Chinese eyes

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Abstract

Background—To compare anterior segment biometric parameters between Caucasians and Chinese before and after laser peripheral iridotomy (LPI).

Design—Prospective clinical cohort study

Participants—Caucasian and Chinese primary angle closure suspects.

Methods—Anterior segment optical coherence tomography images captured before and after LPI were analyzed to measure anterior segment biometric parameters. Paired Student's t-tests were used for within-ethnic group comparisons. Univariate and linear mixed-effects regression models were used for between-ethnic group comparisons.

Main Outcome Measures—angle opening distance (AOD500, AOD750); angle recess area (ARA750); iris thickness (IT750, IT2000, ITM); iris curvature (ICURV); anterior chamber area (ACA); anterior chamber volume (ACV); and anterior chamber width (ACW).

Results—Caucasians had significantly greater preoperative ARA750, ACW, and ICURV and lower preoperative IT2000 compared to Chinese ($P < 0.05$). Ethnic differences in preoperative AOD500, AOD750, IT750, ITCM, ACA, and ACV were insignificant ($P > 0.05$). Significant postoperative increases in AOD500, AOD750, ARA750, ACA, ACV, and ACW along with significant postoperative decrease in ICURV were observed within both ethnic groups ($P < 0.05$). However, the amount of LPI-induced changes in AOD500, AOD750, ARA750, ACA, ACV, ACW, and ICURV did not differ between the two ethnic groups ($P > 0.05$).

Conclusion—Both Caucasian and Chinese demonstrated opening of anterior chamber angle width (AOD500, AOD750, ARA750), expansion of anterior chamber dimensions (ACA, ACV,

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ACW), and flattening of iris convexity (ICURV) after LPI. Although certain aspects of anterior segment anatomy differed between Caucasians and Chinese preoperatively, they did not translate into significant ethnic differences in the amount of LPI-induced changes in the anterior segment biometric parameters.

Keywords

laser peripheral iridotomy; anterior segment optical coherence tomography; ethnicity; angle closure; glaucoma

INTRODUCTION

Glaucoma is the leading cause of irreversible blindness worldwide. Among people with glaucoma in developed countries, fewer than half are aware of the existence of their disease.¹ Primary angle closure glaucoma (PACG) is more likely than primary open angle glaucoma to result in bilateral blindness. An estimated 9.4 million people in China over 40 years of age have PACG.² Although not as common as in the Chinese population, the prevalence of PACG among Caucasians has seemingly been increasing at a notable rate over the past decade with population-based studies reporting a prevalence rate of up to 0.009% in 1993³, 0.1% in 1998⁴, and 0.6% in 2000⁵. In 2008, a 24-months retrospective review of consecutive Caucasian patients seen at a tertiary university hospital glaucoma service in the North East Scotland demonstrated that PACG comprised 22.9% of the glaucoma workload.⁶

Laser peripheral iridotomy (LPI) is the first-line treatment for primary angle closure suspects (PACS), primary angle closure (PAC), and PACG. Anterior segment optical coherence tomography (ASOCT) images can be analyzed using a customized software program to provide objective and reproducible quantification of anterior segment biometric parameters from a single image frame.⁷ Recent studies using ASOCT have examined anterior segment morphology before and after LPI.^{8,9} While ASOCT has been used to analyze changes in anterior segment morphology following LPI in multiethnic⁸ and Asian populations⁹, there is a lack of similar studies in Caucasian populations. Given that anterior segment morphology may substantially differ between Caucasian and Chinese eyes, investigating ethnic differences in LPI outcomes can provide useful information for clinical strategies in the treatment and management of pathology related to angle-closure. The purpose of this prospective study was to compare preoperative and LPI-induced changes in anterior segment biometric parameters between Caucasian and Chinese PACS.

METHODS

Approval for this prospective study was obtained from the University of California, San Francisco (UCSF) Committee on Human Research. The study was carried out in accordance with the tenets of the Declaration of Helsinki. Caucasian and Chinese subjects were consecutively recruited from the UCSF general ophthalmology and glaucoma clinics between April 2008 and December 2012. All enrolled subjects provided written informed consent. Inclusion criteria for subject enrollment included: (1) adult patients (age >18 years) with narrow angles as defined by the Shaffer gonioscopic classification (described below) in at least one eye; (2) self-reported Caucasian or Chinese ancestry in both parents (the term

“Caucasian” for the purposes of this study included only European-derived whites); (3) patients who consented to receiving LPI; and (4) patients who consented to undergo standardized preoperative and postoperative ophthalmic examination and ASOCT imaging. Exclusion criteria for enrollment included the following: (1) eyes with PAC, PACG, or glaucomatous optic neuropathy; (2) eyes with corneal abnormalities such as edema, abrasion or dystrophy, pterygium, and other degenerative changes; (3) eyes with irido-ciliary cysts; (4) eyes with incomplete LPI perforation; and (5) patients who could not return for follow-up in the specified time period. The International Society of Geographic and Epidemiologic Ophthalmology (ISGEO) created a classification scheme for diagnosing glaucoma in cross-sectional population based research.¹⁰ In this study, we utilized the diagnostic criteria developed by the ISGEO as the basis for diagnosis of PAC, PACG, and glaucomatous optic neuropathy. PAC was defined as eyes graded as occludable on gonioscopy with either the presence of peripheral anterior synechiae or intraocular pressure (IOP) > 21 mm Hg or both. PACG was defined as eyes with PAC and evidence of glaucomatous optic nerve damage. Glaucomatous optic nerve damage was confirmed by a glaucomatous optic nerve appearance (vertical cup:disc ratio > 0.6) and a corresponding reliable visual field defect. A glaucomatous visual field defect was considered to be present when the hemifield test was graded outside normal limits (with a probability of less than 5% based upon comparison with age-matched controls in the pattern deviation plot) and showed a cluster of three or more non-edge contiguous points that did not cross the horizontal meridian. Visual fields were defined as reliable if they fulfilled the following criteria: fixation losses < 33%, false positives < 20%, and false negatives < 20%.

Pre-operative and Post-operative Evaluation

All enrolled subjects received a standardized ophthalmic examination that included visual field testing using the 24-2 Swedish Interactive Threshold Algorithm (SITA) standard strategy with the Humphrey Visual Field Analyzer (model 750i, Carl Zeiss Meditec, Inc., Dublin, CA), IOP measurement by Goldmann applanation tonometry (model AT900, Haag-Streit AG, Koeniz, Switzerland), slit lamp examination (model BM900, Haag-Streit AG, Koeniz, Switzerland), and gonioscopy with a Zeiss-style 4-mirror lens (model OPDSG, Ocular Instruments, Inc., Bellevue, WA). A single trained ophthalmologist (S.C.L.) performed gonioscopy at ×16 magnification with slit-lamp biomicroscopy in a darkroom setting. The Shaffer gonioscopic classification was used to determine the anterior chamber angle grading in all four quadrants: an angle between the iris and the trabecular meshwork surface of 35° to 45° was classified as grade 4, between 20° and 35° was classified as grade 3, between 10° to 20° was classified as grade 2, and less than 10° was classified as grade 1. Grade 0 was assigned if angle structures were not observed.¹¹ For this study, eyes with narrow angles were defined as those with Shaffer grades of 2 or less in 3 or more quadrants. This definition of narrow angle has previously been used by other studies.^{12–17} To improve accuracy in IOP measurements, the same ophthalmologist (S.C.L.) measured IOP twice for each subject during a designated time period between 1 and 3 PM. From the two IOP measurements, an average was derived for statistical analysis. If the two IOP values differed by more than 2 mmHg, then a third measurement was performed and the median value was used.

Laser Peripheral Iridotomy

All LPIs were performed by the same ophthalmologist (S.C.L.). After pharmacological pupil constriction with topical 2% pilocarpine, topical proparacaine hydrochloride ophthalmic solution 0.5% (Alcaine, Alcon Pharmaceuticals, Fort Worth, TX) was applied to the surgical eye for anesthesia. An Abraham lens filled with Hypromellose 2.5% ophthalmic lubricant solution (Goniovise™, HUB pharmaceuticals, Rancho Cucamonga, CA) was placed on the cornea and a neodymium:yttrium aluminum garnet (Nd:YAG) laser was used to create a peripheral iridotomy approximately 1 mm from the limbus in the supero-temporal region between 10–11 and 1–2 o'clock positions on the right and left irides, respectively. Triple bursts of 7 mJ per laser shot were used initially to achieve patency, and then single bursts of 6 mJ per laser shots were used to enlarge the iridotomy. An average of 25 shots were used. At the end of every procedure, the performing physician confirmed the achievement of full-thickness perforation. The size of the iridotomy was approximately 1.5 mm in diameter. Immediately following the procedure, topical 0.1% apraclonidine (Iopidine, Alcon Pharmaceuticals, Fort Worth, TX) and 1% prednisolone acetate (Pred Forte, Allergan Pharmaceuticals, Irvine, CA) were applied. IOP was measured approximately 1 hour after the procedure. Patients with significantly elevated IOP received appropriate topical ocular hypotensives for IOP control prior to leaving the clinic. All patients were instructed to use 1% prednisolone acetate 4 times a day for 3 days. Post-LPI assessment was performed 2–3 weeks after the procedure. The post-LPI ASOCT image was obtained at this visit, gonioscopic examination was performed, and all iridotomies were examined for patency and confirmed to be of adequate size. LPI was repeated if patency could not be confirmed.

Anterior Segment Optical Coherence Tomography

All qualified study subjects received imaging in the dark with ASOCT (Visante OCT, Carl Zeiss Meditec, Inc., Dublin, CA), a non-contact optical coherence tomographic system using 1310-nm wavelength light to capture high-resolution cross-sectional images of the anterior segment of the eye. ASOCT imaging was performed under standardized dark conditions with illuminations below 1 lux as measured by EasyView Digital Light Meter (model EA30, Extech Instruments, Inc., Waltham, MA). Patients were allowed 5 minutes for dark adaptation before image acquisition. Each ASOCT scan captured both the temporal and nasal quadrants (nasal-temporal 0–180°) in a single image while the patient looked straight ahead. An experienced operator, masked to the standardized ophthalmic examination findings, performed all the ASOCT scans. Three to five images were acquired for each eye and the image with the best quality was selected for analysis using the Zhongshan Angle Assessment Program (ZAAP; Zhongshan Ophthalmic Centre, Guangzhou, China). Image quality was evaluated on the basis of a steady central fixation as judged by a clear corneal reflection, good visibility of the scleral spurs, the presence of continuity in anterior segment structures, and the absence of motion artifacts. Both eyes from the same subject were included for analysis in the ZAAP software program if the ASOCT images passed our quality threshold.

The ZAAP software program contained algorithms that automatically defined the borders and curvatures of anterior segment structures after the scleral spurs were localized manually on the ASOCT images. Measurements for both the nasal and temporal angles were

simultaneously produced. Since the peripheral iridotomies were created closer to the temporal angles, only the nasal angles were analyzed in this study. The following parameters were derived from the ZAAP software program: pupil diameter, central corneal thickness (CCT), anterior corneal curvature (ACC), posterior corneal curvature (PCC), iris thickness measured at 750 μm from the scleral spur (IT750), iris thickness measured at 2000 μm from the scleral spur (IT2000), maximal iris thickness (ITM), iris curvature (ICURV), anterior chamber area (ACA), anterior chamber volume (ACV), anterior chamber width (ACW), angle opening distance at 500 μm from the scleral spur (AOD500), angle opening distance at 750 μm from the scleral spur (AOD750), and angle recess area at 750 μm from the scleral spur (ARA750).

The ASOCT parameters listed above were defined previously in other studies. Pupil diameter was calculated by measuring the distance between the pupil edges on the cross-sectional images.¹⁸ CCT was measured from the anterior to the posterior surface of the cornea at the center of the ASOCT image.¹⁹ ACC was defined as the radius of curvature of the anterior surface of the cornea. PCC was defined as the radius of curvature of the posterior surface of the cornea.²⁰ For parameters associated with iris thickness, a circle centered at the scleral spur was drawn with a radius of 750 μm , and the point of intersection between the circle and the anterior surface of the iris was identified. The shortest distance from this point to the posterior surface of the iris was calculated as IT750. The same method was used for IT2000. ITM was defined as the highest value of iris thickness along the entire iris.²¹ To calculate ICURV, a line was drawn from the most peripheral to the most central point of the iris pigmented epithelium, and a perpendicular line was extended from this line to the iris pigmented epithelium at the point of greatest convexity.¹⁸ An illustration of the iris parameters is provided in Figure 1.²¹ ACA was defined as the cross-sectional area of the anterior chamber bounded by the corneal endothelium anteriorly, and the anterior surface of iris and the anterior surface of lens (within the pupil) posteriorly. ACV was calculated by rotating the ACA 360 degrees around a vertical axis through the mid-point of the ACA.²² ACW was defined as the horizontal scleral spur-to-spur distance.²³ An illustration of the ACA, ACV, and ACW is provided in Figure 2.²² AOD500 was defined as the length of the line drawn from the anterior iris surface to the corneal endothelium, perpendicular to the line drawn along the trabecular meshwork at 500 μm anterior to the scleral spur.²⁴ The same method was used for AOD750. ARA750 was defined as the area bordered by the anterior iris surface, corneal endothelium, and a line perpendicular to the corneal endothelium that was drawn to the iris surface from a point 750 μm anterior to the scleral spur.²⁴ An illustration of AOD500, AOD750, and ARA750 is provided in Figure 3.²⁵

Statistical Analysis

All statistical analyses were conducted with R-statistics (Ver. 2.15.1 software for Macintosh, R Foundation for Statistical Computing, Vienna, Austria) and P values <0.05 were considered to indicate statistical significance. Mean and standard deviation were calculated for all variables using data from both eyes. For comparisons of sex ratios between the two ethnic groups, the Fisher's Exact Test was used. Differences in age, preoperative pupil diameter, preoperative CCT, preoperative ACC, and preoperative PCC between the two ethnic groups were assessed with unpaired Student's t-tests. Comparisons of preoperative

and postoperative measurements for AOD500, AOD750, ARA750, IT750, IT2000, ITM, ICURV, ACA, ACV, and ACW within each ethnic group were performed with paired Student's t-tests. Preoperative and LPI-induced changes in AOD500, AOD750, ARA750, IT750, IT2000, ITM, ICURV, ACA, ACV, and ACW were modeled as a function of ethnicity using univariate and linear mixed-effects regression models, the latter adjusting for age, sex, preoperative pupil diameter, preoperative CCT, preoperative ACC, preoperative PCC, and the use of both eyes in the same subject, to determine the association of ethnicity with preoperative and LPI-induced changes in the anterior segment biometric parameters. The same statistical analysis procedure was used to compare eyes with iridotrabecular contact (ITC) between the two ethnic groups. Eyes with ITC were defined as those with a value of zero for preoperative AOD500. Change was calculated as (postoperative mean – preoperative mean). Because manual scleral spur localization is subjective in nature, to ensure consistency, a single residency-trained ophthalmologist (TK), who has had post-residency glaucoma training in Japan and the United States, manually located the scleral spurs on all ASOCT images while masked to the patient's standardized ophthalmic examination results. To evaluate intraobserver variance, 20 eyes were randomly selected and the anterior segment biometric parameters were re-measured by the same observer at a separate session. The intraobserver reproducibility was assessed with the intraclass correlation coefficient.

RESULTS

A total of 74 consecutively enrolled Caucasian and Chinese patients received LPI and agreed to participate in the study during the specified time period. Among them, 22 subjects were excluded from the study due to one or more of the following reasons: (1) the subject could not or did not complete the ASOCT examination; (2) poor ASOCT imaging quality (evaluated on the basis of corneal reflection, visibility of the scleral spurs, continuity of anterior segment structures, and motion artifacts); and (3) incomplete data in at least 1 of the analysis variables. Following exclusion, 48 eyes of 28 Caucasian subjects and 36 eyes of 24 Chinese subjects were included in the analysis. ITC (value of zero for preoperative AOD500) was observed in 4 eyes of 4 Chinese subjects and 3 eyes of 3 Caucasian subjects. Due to the small number of subjects with ITC, there is insufficient power to make meaningful inferences from the comparison of Chinese and Caucasian subjects with ITC. Therefore, results from the comparison of Chinese and Caucasian subjects with ITC will not be presented. The finding of a small number of patients with ITC may be an underestimate as our protocol for ASOCT only captures a single horizontal meridian through the temporal and nasal quadrants, and does not include any information from the superior and inferior quadrants. It is very likely that imaging of these additional quadrants would have resulted in greater numbers of eyes with ITC.

Table 1 provides the demographics and preoperative clinical characteristics of the study subjects. The Fisher's Exact Test showed no evidence of sex ratio difference between the two ethnic groups ($P=0.781$). The Caucasian and Chinese subjects also did not differ in age, preoperative pupil diameter, preoperative CCT, preoperative ACC, or preoperative PCC by unpaired Student's t-tests (all $P>0.05$).

Table 2 lists the preoperative and postoperative measurements of AOD500, AOD750, ARA750, IT750, IT2000, ITM, ICURV, ACA, ACV, and ACW as well as the differences between the two sets of measurements within each ethnic group by paired Student's t-tests. Significant postoperative increases in AOD500, AOD750, ARA750, ACA, ACV, and ACW as well as significant postoperative decrease in ICURV were observed within both ethnic groups (all $P < 0.05$). Preoperative and postoperative measurements for all iris thickness parameters (IT750, IT2000, and ITM) did not differ within both ethnic groups (all $P > 0.05$).

Table 3 summarizes the results of the univariate and linear mixed-effects regression analyses that evaluated the association of ethnicity with preoperative and LPI-induced changes in AOD500, AOD750, ARA750, IT750, IT2000, ITM, ICURV, ACA, ACV, and ACW. The linear mixed-effects regression models adjusted for age, sex, preoperative pupil diameter, preoperative CCT, preoperative ACC, preoperative PCC, and the use of both eyes in the same subject. In both univariate and linear mixed-effects regression analyses, preoperative measurements for AOD500, AOD750, IT750, ITCM, ACA, and ACV did not significantly differ by ethnicity (all $P > 0.05$), while preoperative measurements for ARA750, IT2000, and ACW demonstrated significant differences by ethnicity (all $P < 0.05$). Ethnic differences in preoperative ICURV were not significant in the univariate regression analysis ($P > 0.05$) but gained significance after adjusting for potential confounding factors in the linear mixed-effects regression analysis ($P < 0.05$). The mean preoperative ARA750, ACW, and ICURV measurements were significantly greater in Caucasian (0.147 mm^2 , 11.91 mm , and 0.36 mm , respectively) compared to Chinese (0.100 mm^2 , 11.50 mm , and 0.32 mm , respectively) subjects. In contrast, the mean preoperative IT2000 measurement was significantly greater in Chinese (0.51 mm) compared to Caucasian (0.44 mm) subjects. LPI-induced changes in AOD500, AOD750, ARA750, ACA, ACV, and ACW were not significantly associated with ethnicity in either univariate or linear mixed-effects regression analyses (all $P > 0.05$). However, although not statistically significant, the amount of LPI-induced changes in all parameters listed above was consistently greater in Caucasian compared to Chinese subjects.

Table 4 displays the intraclass correlation coefficients and confidence interval of anterior segment biometric parameters measurements in a randomly selected subset of 20 eyes. All parameters demonstrated fair to excellent intraobserver reproducibility.

DISCUSSION

This study compared preoperative and LPI-induced changes in anterior segment biometric parameters between Caucasian and Chinese PACS. Significant postoperative increases in AOD500, AOD750, ARA750, ACA, ACV, and ACW along with a significant postoperative decrease in ICURV were observed within both ethnic groups. Our results showed significantly greater preoperative ARA750, ACW, and ICURV and lower preoperative IT2000 in Caucasian compared to Chinese subjects. Preoperative AOD500, AOD750, IT750, ITCM, ACA, and ACV did not differ significantly between the two ethnic groups. Our investigation of the association between ethnicity and LPI-induced changes in AOD500, AOD750, ARA750, ACA, ACV, ACW, and ICURV did not yield statistical significance. Although not statistically significant, it is notable that Caucasians demonstrated greater changes in mean values compared to Chinese for all anterior segment biometric parameters

listed above. Overall, our analyses suggest that both Caucasian and Chinese demonstrate significant opening of anterior chamber angle width (i.e., AOD500, AOD750, and ARA750), expansion of anterior chamber dimensions (i.e., ACA, ACV, and ACW), and flattening of iris convexity (i.e., ICURV) after LPI. Although certain aspects of anterior segment anatomy differed between Caucasians and Chinese preoperatively, these preoperative differences did not translate into significant ethnic differences in the amount of LPI-induced changes in the anterior segment biometric parameters.

Our analyses indicated that Caucasians possessed significantly lower preoperative IT2000 and greater preoperative ACW compared to Chinese subjects. The associations between angle-closure related pathology and measurements of IT2000 and ACW are well characterized in the literature. In our previous study, we reported an association between increased IT2000 and angle closure with the explanation that thicker irides are associated with angle narrowing because the iris would be in closer proximity to the anterior chamber angle, thereby crowding the angle.²⁶ Nongpiur *et al.* suggested that a smaller ACW was associated with angle closure, reasoning that because the circumference of a circle is estimated through diameter $\times$ pi (a value of 3.14), a unit change in the width (diameter) of the anterior chamber of the eye (approximated as a circle) would result in a circumferential change of 3.14 units. Under such conditions, a 1-mm decrease in the ACW from an average of 12-mm would result in a 3.14-mm decrease in the circumference of the anterior chamber drainage structures, which is equivalent to an 8.3% reduction.²³ Considering that increased IT2000 and decreased ACW have previously been reported as risk factors for PAC and PACG development, the present study's finding of ethnic differences in preoperative IT2000 and ACW may explain the higher prevalence of PACS, PAC, and PACG in Chinese compared to Caucasians.^{1–6}

The combination of a decrease in ICURV and increases in ACA, ACV, AOD500, AOD750, and ARA750 following LPI within both ethnic groups supports the observation that pupillary block is the primary underlying mechanism of anterior chamber angle narrowing in the majority of our PACS study population. Increased convexity of the iris has been shown to be associated with narrowing of the anterior chamber angle width through a pupillary block mechanism.¹⁸ The contour of the iris depends in part on resistance to aqueous flow through the iris-lens channel; the zone between the iris pigment epithelium and lens capsule. In pupillary block, outflow resistance at the level of the pupil results in a build-up of pressure in the posterior chamber that results in anterior iris bowing and narrowing of the angle. In cases of iridolenticular contact resulting in closure of the iris-lens channel, modeling of channel fluid dynamics estimates posterior chamber IOP to be 1–8 mm Hg higher than that of the anterior chamber, which causes the iris to assume a convex figuration.²⁷ LPI relieves pupillary block by creating an alternative channel in the iris periphery that allows aqueous to flow into the anterior chamber. With elimination of the pressure gradient between anterior and posterior chambers, the iris flattens and falls back from the anterior chamber angle, thereby resulting in angle opening.⁸ ACA and ACV represent the overall dimensions of the anterior chamber, as these two parameters are comprised of a region that is bounded by the cornea, the iris, and the anterior surface of the

lens. Since the iris forms one of the boundaries of the anterior chamber, a decrease in the convexity of the iris should produce a corresponding increase in ACA and ACV.

Two previous studies have demonstrated in PACS subjects with pupillary block mechanism as the primary cause of narrow angle that increases in ACA, ACV, AOD500, AOD750, and ARA750 are mediated through a decrease in ICURV after LPI.^{8,9} Since ICURV has been suggested as the mediator of changes after LPI, it can be postulated that different physical and biological properties of the irides between Caucasian and Chinese individuals may play a role in determining the extent of LPI-induced changes in anterior segment biometric parameters. The elasticity of the iris is determined by the distribution and quantity of type I and III collagen in the stroma. Type I collagen decreases elasticity while type III collagen increases elasticity.²⁸ It has been shown that the total amount of collagen as well as the proportion of type I collagen are considerably greater in angle closure eyes than in normal eyes.²⁹ A study from Sun *et al.* showed that eyes with narrow angles possess thicker irides than those of normal eyes.³⁰ Given the premises of: (1) narrow angle eyes possess thicker irides than those of normal eyes; (2) a higher proportion of type I collagen in the irides of narrow angles eyes than those of normal eyes; and (3) the distribution and quantity of type I collagen determine the elasticity of the iris, it is reasonable to conclude that thicker irides are less elastic than thinner irides. Due to reduced elasticity, a thicker iris is more rigid and less malleable. A change in iris elasticity might also impact its biomechanics and affect movement compliance.³¹ When exposed to the same pressure differential between anterior and posterior chambers, in comparison to a thinner iris, a thicker iris likely exhibits more resistance to forward bowing due to its increased resistance to deformity. By the same way of thinking, a thicker iris likely also flattens less after LPI. This reasoning is supported by the results of our study in two ways. Firstly, Chinese individuals have significantly greater preoperative IT2000 but lower preoperative ICURV compared to Caucasians. Secondly, although not statistically significant, Caucasians demonstrated greater decrease in mean values for ICURV compared to Chinese. This greater postoperative decrease in ICURV in turn may be responsible for the greater postoperative increases in ACA, ACV, AOD500, AOD750, and ARA750 in Caucasians. It is probable that ethnic differences in the amount of LPI-induced changes in the anterior segment biometric parameters will reach statistical significance in the context of a larger sample size with greater power. He *et al.* reported in the Liwan Eye Study that approximately 60% of Chinese eyes with PACS exhibited persistent appositional closure in at least one quadrant after LPI.³² In contrast, in Caucasian eyes with PACS, Ang *et al.* reported that approximately 11% of such eyes were closed in at least one quadrant after LPI.³³ The potential ethnic difference in the magnitude of LPI-induced changes to the anterior segment morphology may be responsible for the increased susceptibility of persistent angle closure in Asian populations despite the presence of a patent LPI.

Our study suffers from a limitation inherent in most studies exploring ethnic differences, namely that an objective method for ethnic classification of study subjects is typically lacking. Ethnic groups in our study are not stratified according to specific anthropologically based criteria. Instead, the classification used in our study is based on the subjects' self-reported Caucasian or Chinese ancestry of both parents. A further limitation lies in the

reliance of the ZAAP software program on manual scleral spur identification as a measurement reference point for image processing. Manual scleral spur localization is subjective in nature, but our study-design controlled for this by utilizing a single ophthalmologist, masked to the patient's ethnicity and clinical examination results, to read all the ASOCT images. We also selected a random subset of 20 ASOCT images for reproducibility testing by the same ophthalmologist at a separate session. The random subset of 20 ASOCT images selected for reproducibility testing yielded fair to excellent intraobserver correlation. Additionally, our sample size was relatively small, which may have contributed to an inability to demonstrate significant differences in LPI-induced changes in anterior segment biometric parameters between Caucasians and Chinese subjects. Lastly, our subjects were PACS recruited from a university-based general ophthalmology and glaucoma clinic, so our findings may not easily extrapolate to the general population and those individuals with PAC and PACG.

In summary, this is the first study to compare preoperative and LPI-induced changes in anterior segment biometric parameters between Caucasian and Chinese PACS subjects. Our study showed that regardless of ethnic classification, LPI leads to opening of the anterior chamber angle width, expansion of anterior chamber dimensions, and flattening of iris convexity. Although certain aspects of anterior segment anatomy differed between Caucasians and Chinese preoperatively, they did not translate into significant ethnic differences in the amount of LPI-induced changes in the anterior segment biometric parameters. Based upon these results, LPI is likely equally effective in both ethnic groups, however this might be because our statistical power was insufficient due to a relatively small sample size. Since Caucasians demonstrated greater change in mean value for every parameter, despite being statistically insignificant, it can be suggested that LPI may be more beneficial for them compared to Chinese. This alternative interpretation depends upon whether significance can be reached with a larger subject population. Therefore, further studies on a larger population are warranted.

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Figure 1.

An illustration of iris curvature (ICURV), iris thickness measured at 750 μm from the scleral spur (IT750), iris thickness measured at 2000 μm from the scleral spur (IT2000), and maximal iris thickness (ITM). For parameters associated with iris thickness, a circle centered at the scleral spur was drawn with a radius of 750 μm , and the point of intersection between the circle and the anterior surface of the iris was identified. The shortest distance from this point to the posterior surface of the iris was calculated as IT750. The same method was used for IT2000. ITM was defined as the highest value of iris thickness along the entire iris. To calculate ICURV, a line was drawn from the most peripheral to the most central point of the iris pigmented epithelium, and a perpendicular line was extended from this line to the iris pigmented epithelium at the point of greatest convexity. (Graphic is a modified version of Figure 1 in Wang *et al.*²¹)

Figure 2.

An illustration of anterior chamber area (ACA), anterior chamber volume (ACV), and anterior chamber width (ACW). ACA was defined as the cross-sectional area of the anterior chamber bounded by the corneal endothelium anteriorly, and the anterior surface of iris and the anterior surface of lens (within the pupil) posteriorly. ACA is represented here as the shaded region. ACV was calculated by rotating the ACA 360 degrees around a vertical axis through the mid-point of the ACA. ACW was defined as the horizontal scleral spur-to-spur distance. (Graphic is a modified version of Figure 1 in Wu *et al.*²²)

Figure 3.

An illustration of angle opening distances at 500 μm and 750 μm from the scleral spur (AOD500, AOD750) and angle recess area at 750 μm from the scleral spur (ARA750). AOD500 was defined as the length of the line drawn from the anterior iris surface to the corneal endothelium, perpendicular to the line drawn along the trabecular meshwork at 500 μm anterior to the scleral spur [length from A to B]. [length from A to B]. The same method was used for AOD750 [length C to D]. ARA750 was defined as the area bordered by the anterior iris surface, corneal endothelium, and a line perpendicular to the corneal endothelium that was drawn to the iris surface from a point 750 μm anterior to the scleral spur [grid area]. (Graphic is a modified version of Figure 1 in Wang D *et al.*²⁵)

Table 1

Demographics and baseline clinical characteristics of the study population

	Chinese	Caucasian	P value
No. Patients/Eyes	24/36	28/48	
Sex (male:female)	11:13	15:13	0.781 ^b
Age (years)	68.3 ± 10.3 ^a	62.8 ± 12.1 ^a	0.082 ^c
Preoperative Pupil Diameter (mm)	4.12 ± 0.74 ^a	3.98 ± 0.88 ^a	0.411 ^c
Preoperative CCT (μm) ^d	546.5 ± 27.3 ^a	548.3 ± 33.9 ^a	0.791 ^c
Preoperative ACC (mm) ^d	7.36 ± 0.53 ^a	7.27 ± 0.54 ^a	0.428 ^c
Preoperative PCC (mm) ^d	6.58 ± 0.49 ^a	6.51 ± 0.50 ^a	0.529 ^c

^aData are expressed as mean value ± standard deviation.^bP-value by the Fisher's exact test.^cP values by unpaired Student's T-tests.^dCCT = central corneal thickness; ACC = anterior corneal curvature; PCC = posterior corneal curvature.

Table 2

Comparisons between preoperative and postoperative anterior segment biometric parameters related to laser peripheral iridotomy in primary angle closure suspects

Parameter ^c	Ethnicity	Preoperative Measurements ^a	Postoperative Measurements ^a	Outcome Differences	P Value ^b
AOD500 (mm)	Chinese	0.11 ± 0.07	0.18 ± 0.06	0.07	<0.0001
	Caucasian	0.13 ± 0.07	0.21 ± 0.10	0.08	<0.0001
AOD750 (mm)	Chinese	0.18 ± 0.08	0.28 ± 0.10	0.10	<0.0001
	Caucasian	0.22 ± 0.09	0.33 ± 0.12	0.11	<0.0001
ARA750 (mm ²)	Chinese	0.10 ± 0.05	0.15 ± 0.06	0.05	<0.0001
	Caucasian	0.14 ± 0.08	0.20 ± 0.09	0.06	<0.0001
IT750 (mm)	Chinese	0.50 ± 0.12	0.48 ± 0.11	0.02	0.052
	Caucasian	0.46 ± 0.08	0.44 ± 0.17	0.02	0.511
IT2000 (mm)	Chinese	0.51 ± 0.10	0.50 ± 0.09	0.01	0.441
	Caucasian	0.44 ± 0.07	0.45 ± 0.06	0.01	0.097
ITM (mm)	Chinese	0.62 ± 0.11	0.61 ± 0.09	0.01	0.641
	Caucasian	0.58 ± 0.07	0.59 ± 0.08	0.01	0.598
ICURV (mm)	Chinese	0.32 ± 0.12	0.15 ± 0.10	0.17	<0.0001
	Caucasian	0.36 ± 0.10	0.19 ± 0.14	0.18	<0.0001
ACA (mm ²)	Chinese	17.08 ± 2.58	18.14 ± 2.83	1.06	<0.0001
	Caucasian	17.68 ± 2.64	18.83 ± 2.68	1.15	<0.0001
ACV (mm ³)	Chinese	108.03 ± 19.70	121.03 ± 21.08	13.00	<0.0001
	Caucasian	116.97 ± 24.45	132.16 ± 26.22	15.19	<0.0001
ACW (mm)	Chinese	11.50 ± 0.40	11.61 ± 0.41	0.11	<0.0001
	Caucasian	11.91 ± 0.57	12.04 ± 0.54	0.13	0.005

^a Data are expressed as mean value ± standard deviation.

^b P values by paired Student's T-tests.

^c AOD500, AOD750 = angle opening distance at 500 μm and 750 μm from the scleral spur; ARA750 = angle recess area at 750 μm from the scleral spur; IT750, IT2000 = iris thickness measured at 750 μm and 2000 μm from the scleral spur; ITM = maximal iris thickness; ICURV = iris curvature; ACA = anterior chamber area; ACV = anterior chamber volume; ACW = anterior chamber width.

Table 3

Association of ethnicity with preoperative and change in anterior segment biometric parameters after laser peripheral iridotomy in primary angle closure suspects

Parameter ^b	P values of univariate regression model	P values of linear mixed-effects regression model ^a
Preoperative AOD500 (mm)	0.145	0.331
AOD500 (mm)	0.826	0.994
Preoperative AOD750 (mm)	0.055	0.136
AOD750 (mm)	0.501	0.726
Preoperative ARA750 (mm ²)	0.0213	0.011
ARA750 (mm ²)	0.939	0.755
Preoperative IT750 (mm)	0.053	0.091
IT750 (mm)	0.684	0.698
Preoperative IT2000 (mm)	0.004	0.001
IT2000 (mm)	0.156	0.320
Preoperative ITCM (mm)	0.198	0.176
ITCM (mm)	0.459	0.706
Preoperative ICURV (mm)	0.190	0.032
ICURV (mm)	0.958	0.492
Preoperative ACA (mm ²)	0.204	0.479
ACA (mm ²)	0.767	0.952
Preoperative ACV (mm ³)	0.057	0.159
ACV (mm ³)	0.386	0.444
Preoperative ACW (mm)	0.001	0.004
ACW (mm)	0.663	0.486

^a adjusted for age, sex, preoperative pupil diameter, preoperative central corneal thickness, preoperative anterior corneal curvature, preoperative posterior corneal curvature, and the use of both eyes in the same subject.

^b AOD500, AOD750 = angle opening distance at 500 μ m and 750 μ m from the scleral spur; ARA750 = angle recess area at 750 μ m from the scleral spur; IT750, IT2000 = iris thickness measured at 750 μ m and 2000 μ m from the scleral spur; ITM = maximal iris thickness; ICURV = iris curvature; ACA = anterior chamber area; ACV = anterior chamber volume; ACW = anterior chamber width.

Table 4

Reproducibility of anterior segment biometric parameter measurements in a random subset of 20 eyes

Parameters ^b	ICC ^a	Mean	Difference	95% CI ^a
PD (mm)	1.000	4.345	0.0009	1.000, 1.000
CCT (μm)	0.996	540.69	0.1	0.990, 0.998
ACC (mm)	0.982	7.489	0.0009	0.958, 0.992
PCC (mm)	0.971	6.698	0.010	0.931, 0.988
AOD500 (mm)	0.905	0.177	0.002	0.779, 0.961
AOD750 (mm)	0.933	0.266	0.023	0.841, 0.973
ARA750 (mm ²)	0.914	0.138	0.010	0.799, 0.965
IT750 (mm)	0.604	0.430	0.026	0.261, 0.813
IT2000 (mm)	0.934	0.455	0.006	0.844, 0.973
ITM (mm)	0.753	0.566	0.007	0.498, 0.889
ICURV (mm)	0.934	0.26	0.0005	0.843, 0.973
ACA (mm ²)	1.000	17.72	0.0005	1.000, 1.000
ACV (mm ³)	1.000	118.08	0.034	1.000, 1.000
ACW (mm)	0.978	11.86	0.03	0.946, 0.991

^a ICC = intraclass correlation coefficient, CI = confidence interval.

^b PD = pupil diameter; CCT = central corneal thickness; ACC = anterior corneal curvature; PCC = posterior corneal curvature; AOD500, AOD750 = angle opening distance at 500 μm and 750 μm from the scleral spur; ARA750 = angle recess area at 750 μm from the scleral spur; IT750, IT2000 = iris thickness measured at 750 μm and 2000 μm from the scleral spur; ITM = maximal iris thickness; ICURV = iris curvature; ACA = anterior chamber area; ACV = anterior chamber volume; ACW = anterior chamber width.