Clinical and Epidemiologic Research

Anterior Segment Optical Coherence Tomography Study of the Cornea and Anterior Segment in Adult Ethnic South Asian Indian Eyes

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Purpose. To report normative results of anterior segment and corneal biometric parameters and their associations in ethnic South Asian Indian adults.

Methods. The Singapore Indian Eye Study is a cross-sectional, population-based study of ethnic South Asian Indians ranging in age from 40 to 80 years. Subjects underwent ophthalmic and systemic examination, including imaging with anterior segment optical coherence tomography. Parameters were derived using the Zhongshan Assessment Program: anterior chamber depth (ACD), central corneal thickness (CCT), and anterior and posterior corneal curvatures (ACC and PCC). Posterior corneal arc length (PCAL) is a novel parameter defined as the arc distance between scleral spurs on the posterior border of the cornea. The authors studied correlations between PCAL with various anterior segment parameters and systemic parameters using univariate and multivariate analyses.

Results. The authors studied 438 subjects whose mean age was 58.5 ± 9.9 years and of whom 50.7% were male. Parameters (mean ± SD) included central ACD 2.72 ± 0.37 mm, PCC 6.45 ± 0.35 mm, CCT 561.4 ± 34.1 μm, ACC 7.17 ± 0.35 mm, and PCAL 13.85 ± 0.54 mm. The authors found significant correlations between PCAL and ACD ($r = 0.46$, $P < 0.001$), PCC ($r = 0.31$, $P < 0.001$), and ACC ($r = 0.16$, $P < 0.001$), whereas they found poor correlations between PCAL and age, height, weight, blood pressure, and glucose levels. Multivariate analysis showed a significant association between PCAL and both ACD ($P < 0.001$) and PCC ($P < 0.001$).

Conclusions. The authors have described useful baseline anterior segment parameters from this population-based study of ethnic South Indian adults. These data may be useful for corneal and anterior segment procedures such as endothelial keratoplasty and anterior chamber intraocular lens insertion. (*Invest Ophthalmol Vis Sci.* 2012;53:120–125) DOI:10.1167/iovs.11-8386

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Supported in part by National Research Foundation Translational and Clinical Research Programme Grant TCR R621/42/2008.

Submitted for publication August 9, 2011; revised September 22, 2011; accepted October 15, 2011.

Disclosure: **M. Ang**, None; **W. Chong**, None; **W.T. Tay**, None; **L. Yuen**, None; **T.Y. Wong**, None; **M.-G. He**, None; **S.M. Saw**, None; **T. Aung**, None; **J.S. Mehta**, None

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Accurate assessment of the anterior segment of the eye is crucial for surgical planning, diagnosing, and monitoring progress of ocular disease.[1] Since its introduction to ophthalmic use in 1995, anterior segment optical coherence tomography (AS-OCT, Visante; Carl Zeiss Meditec, Dublin, CA) has provided rapid, objective, and quantitative imaging of the cornea, anterior segment, and angle configuration.[2,3] The AS-OCT relies on using a longer wavelength (1310 nm), to allow greater penetration of tissues that scatter light, such as the sclera and limbus, and low coherence interferometry to measure the delay and intensity of backscattered light by comparing it with light that has traveled a known reference path.[4]

The Zhongshan Angle Assessment Program (ZAP, Guangzhou, China) has been developed to quantitatively assess anterior segment parameters in AS-OCT images, with high inter- and intraobserver agreement and reproducibility.[5–7] The program essentially extracts the gray-scale images from the AS-OCT images and uses algorithms to define the anatomic structures and measurements from the scleral spur as points of reference. The corneal thickness and morphology measurements play an essential role in assessment for keratorefractive procedures or corneal transplantation.[8] Anterior chamber depth and angle assessment are important for diagnosing mechanisms of glaucoma, and planning for surgical interventions such as intraocular lens implantations.[9] Recently, parameters such as anterior chamber width and posterior corneal arc length (PCAL) have been shown to be useful in assessment for angle closure and biometric measurements for endothelial keratoplasty surgery.[6,10]

Interracial differences have been described for corneal parameters such as central corneal thickness (CCT), anterior chamber depth (ACD), axial length, and angle parameters.[11,12] Singapore provides an opportunity to describe these anterior segment parameters in adult ethnic South Asian Indians, which form a significant proportion of the population, with a potential for comparison with other major ethnic groups (Chinese and Malay), who reside in a relatively common geographic and socioeconomic environment.[13] Thus, we report results of our study of anterior segment parameters such as PCAL, ACD, and CCT in ethnic, adult Indians residing in urban Singapore.

Methods

Study Population

The Singapore Indian Eye Study (SINDI) is a population-based study of ethnic South Asian Indians in Singapore, and part of a multiethnic study in Singapore that has been described previously.[14] In brief, we used age-stratified random sampling to select ethnic Indians ranging in age

Investigative Ophthalmology & Visual Science, January 2012, Vol. 53, No. 1

from 40 to 80 years, enrolled June 2007 to March 2009 at the Singapore Eye Research Institute, and followed the principles of the Declaration of Helsinki, with ethics approval obtained from our Institutional Review Board. Written informed consent was obtained from all subjects before enrollment.

Study Examinations

Details of our study design and methodology have been described.[14] For this substudy, we included subjects by systematically sampling (every fifth subject) who met the study eligibility criteria. Exclusion criteria included previous intraocular surgery or laser treatment, penetrating eye injury, or corneal disorders preventing anterior chamber assessment. A detailed interviewer-administered questionnaire was used to collect relevant sociodemographic data and medical history from all participants. Study ophthalmologists performed standardized slit-lamp examinations and images of anterior segments were taken under slit-lamp microscope by a digital camera (Topcon SL-D7; Topcon Medical Systems, Tokyo, Japan). Blood pressure was measured with a digital automatic blood pressure monitor (Dinamap model Pro Series DP110X-RW, 100V2; GE Medical Systems Information Technologies, Inc.) after the participants were seated for at least 5 minutes. Hypertension was defined as systolic blood pressure (BP) ≥ 140 mm Hg, diastolic BP ≥ 90 mm Hg, or use of antihypertensive medication. We also collected nonfasting venous blood samples for biochemistry tests, including serum lipids, glycosylated hemoglobin A1c (HbA1C), and random glucose. These variables were analyzed in participants on a continuous scale. Diabetes was defined as random glucose ≥ 11.1 mM, use of diabetic medication, or a physician diagnosis of diabetes mellitus.

Anterior Segment Optical Coherence Tomography Imaging

We obtained consecutive, anterior segment scans of the right eye from each participant using the AS-OCT (Visante; Carl Zeiss Meditec) under standardized conditions of light (20 lux) by an operator who was masked to the results of the clinical ophthalmic examinations.[15] Scans were centered on the pupil and taken along the horizontal axis (nasal–temporal angles at 0–180°) using the standard anterior segment single-scan protocol to maximize visibility of anatomic location and repeatability.[4] It provides anterior segment scans, high-resolution corneal and angle scans, and pachymetry maps at a rate of up to 2048 A-scans per second, with an optical axial resolution of up to 18 mm and optical transverse resolution of up to 60 mm (Carl Zeiss Meditec; www.meditec.zeiss.com). We chose the best-quality images with the fewest artifacts for analysis.

Image Processing

The Zhongshan Angle Assessment Program (Guangzhou, China) was used to assess all AS-OCT images using an algorithm previously described,[6] where the only observer input was to determine the location of the two scleral spurs in each image (WC). The scleral spur was defined as the anatomic junction between the inner wall of the trabecular meshwork and the sclera.[16] In the AS-OCT images, they appear as a prominent inner extension of the sclera at its thickest part and a change in curvature of the inner surface of the angle wall. The algorithm then automatically calculated the anterior segment and corneal parameters: ACD, CCT, anterior and posterior corneal curvatures (ACC and PCC), and PCAL (Fig. 1),[5,6] which is a novel parameter defined as

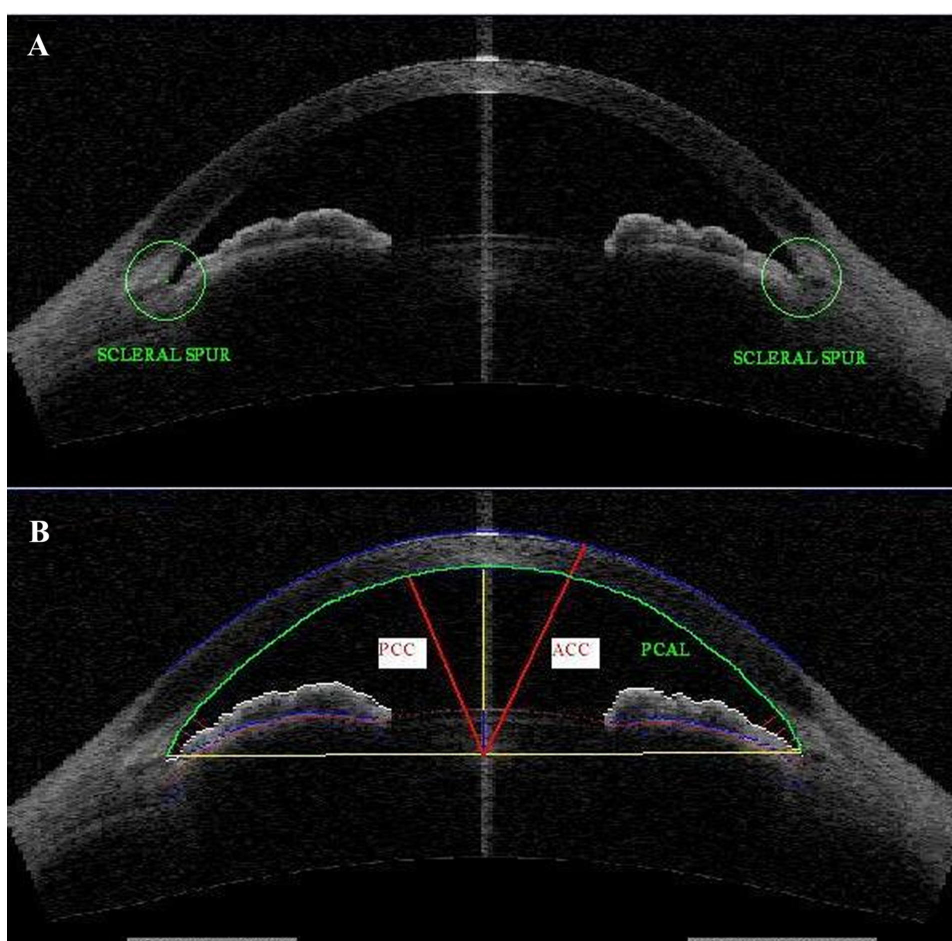

Figure 1. The ZAP software measuring corneal parameters from AS-OCT images after identification of the scleral spurs (**A**), which automatically calculates the anterior corneal curvatures (ACC), posterior corneal curvatures (PCC), and posterior corneal arc length (PCAL; **B**).

Table 1. Posterior Corneal Arc Length and Corneal Parameters Analyzed by Age and Sex

		ACD (mm)		CCT (μm)		PCC (mm)		ACC (mm)		PCAL (mm)	
Group (y)	*n*	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
All persons: all ages	438	2.72	0.37	561.37	34.07	6.45	0.35	7.17	0.35	13.85	0.54
40–49	103	2.77	0.37	557.61	35.27	6.47	0.30	7.24	0.30	13.88	0.56
50–59	140	2.76	0.37	562.98	34.69	6.46	0.33	7.18	0.31	13.82	0.53
60–69	130	2.66	0.38	560.95	32.22	6.40	0.38	7.09	0.38	13.85	0.52
70–80	65	2.67	0.32	564.73	34.58	6.49	0.38	7.18	0.41	13.85	0.55
P for trend		**0.03**		0.248		0.974		0.096		0.814	
P value*		0.916		0.310		0.933		0.928		0.908	
Males: all ages	222	2.72	0.39	559.74	35.40	6.45	0.35	7.16	0.35	13.85	0.55
40–49	54	2.80	0.38	553.37	35.61	6.47	0.28	7.25	0.29	13.86	0.52
50–59	68	2.74	0.41	557.97	36.17	6.46	0.36	7.18	0.34	13.81	0.57
60–69	67	2.66	0.40	566.64	31.56	6.39	0.40	7.04	0.37	13.86	0.56
70–80	33	2.65	0.35	559.82	39.80	6.50	0.33	7.22	0.39	13.87	0.58
P for trend		0.051		0.247		0.924		0.289		0.855	
Females: all ages	216	2.72	0.34	563.05	32.64	6.45	0.34	7.17	0.35	13.85	0.52
40–49	49	2.74	0.36	562.28	34.66	6.47	0.31	7.22	0.32	13.90	0.61
50–59	72	2.77	0.34	567.70	32.79	6.45	0.30	7.17	0.29	13.84	0.49
60–69	63	2.65	0.36	554.90	32.05	6.41	0.36	7.13	0.39	13.85	0.48
70–80	32	2.70	0.29	569.80	27.95	6.47	0.43	7.13	0.44	13.83	0.53
P for trend		0.303		0.669		0.884		0.203		0.585	

**P* value for differences between sexes. Value in bold represents significance.

the arc distance between scleral spurs on the posterior border of the cornea.[6,7]

Statistical Methods

Statistical analysis included descriptive statistics, where the mean and SD were calculated for the continuous anterior segment variables. Differences in the mean values between age groups and between males and females were assessed with the ANOVA and *t*-test, respectively. The Pearson correlation coefficient was performed to test the strength of the linear relationship between PCAL and the various anterior segment parameters and systemic parameters. Linear regression was used to assess factors relating to the PCAL. Primary adjustments included age and sex, and multivariate adjustments included age, sex, ACD, and PCC. All reported *P* values were compared with a significance level of 5%. All analyses were performed using commercial analytical software (SPSS version 17; SPSS Inc., Chicago, IL).

Results

A total of 443 eyes of subjects from the SINDI cohort were included in our study, of which we obtained 438 (99.0%) reliable anterior segment measurements (five images did not have identifiable scleral spurs). The mean age of our subjects was 58.5 ± 9.9 years and 50.7% were male. We summarized the demographics and corneal parameters of our study subjects in Table 1.

The mean (± SD) values of the anterior segment parameters of our cohort respectively were central ACD 2.72 ± 0.37 mm, PCC 6.45 ± 0.35 mm; CCT 561.4 ± 34.1 μm, ACC 7.17 ± 0.35 mm, and PCAL 13.85 ± 0.54 mm. PCC and ACC were strongly correlated ($r = 0.80$, $P < 0.001$), with a ratio of 0.88. We summarized the relationship of PCAL to the other measured corneal and anterior segment parameters in Table 2. We also found weak to moderately strong correlations between our measured anterior segment parameters, but no correlations with refractive and systemic variables such as height, weight, intraocular pressure, blood glucose, and blood pressure (Table 3). The significant positive correlations were ACD ($r = 0.46$, $P < 0.001$), PCC ($r = 0.31$, $P < 0.001$), and ACC ($r = 0.16$, $P < 0.001$) (Fig. 2).

On univariate analysis, we found significant associations with PCAL to include ACD, PCC, and ACC. Using these variables to form a multivariate model, we found a significant association between PCAL and ACD ($P < 0.001$) as well as PCC ($P < 0.001$), which was independent of age and sex (Table 4).

Discussion

The PCAL is a relatively novel anterior segment parameter developed from the ZAP software, which has been found to be reproducible and reliable.[7] The ZAP software also uses image processing and algorithms to identify anatomic landmarks such as the borders of the cornea endothelium and anterior surface of the iris to derive other corneal parameters such as ACD and PCC.[5] This reduces potential inaccuracies that can arise from subjective placement of the measurement tools on the AS-OCT

Table 2. Relationship of PCAL with Measured Corneal and Anterior Segment Parameters*

		ACD (mm)		CCT (μm)		PCC (mm)		ACC (mm)	
PCAL (mm)	*n*	Mean	SD	Mean	SD	Mean	SD	Mean	SD
1st quartile (<13.49)	113	2.47	0.33	564.60	34.49	6.29	0.38	7.06	0.39
2nd quartile (13.490 to 13.860)	109	2.61	0.32	565.24	37.22	6.42	0.29	7.17	0.33
3rd quartile (13.861 to 14.240)	114	2.81	0.30	556.81	32.00	6.48	0.30	7.19	0.33
4th quartile (>14.240)	107	3.01	0.55	558.66	31.77	6.60	0.37	7.24	0.37
P for trend		**<0.001**		0.07		**<0.001**		**<0.001**	

* PCAL in quartiles. Values in bold represent significance.

TABLE 3. Pearson's Correlations between Posterior Corneal Arc Length and Corneal Parameters

Factor	PCAL	ACD	CCT	PCC	ACC
PCAL					
Pearson's correlation	1	0.459	−0.082	0.305	0.161
Significant positive correlations (two-tailed)		**<0.001**	0.085	**<0.001**	**<0.001**
n	443	443	443	443	443

Values in bold represent significance.

image compared with this user-friendly software where identification of the sclera spur is the only input required. Using this population-based study, we confirmed the significant positive correlations of PCAL with ACD, PCC, and ACC in ethnic Indian adults, which can be used as a normative database for future studies. This association is also consistent with a previous report in adult ethnic Chinese.[6]

We have previously established that we are able to use the ZAP software to reliably derive PCAL in both normal and diseased corneas.[7] Compared with a previous study on Chinese, the PCAL in Indians was higher despite comparable dependent variables such as ACD and PCC (previous study on Chinese, PCAL = 12.92 ± 0.54 mm; ACD 2.68 ± 0.30; and PCC 6.65 ± 0.34).[6] However, this needs to be confirmed in larger, direct comparative studies between different ethnicities. The linear relationship and moderately strong correlation between PCAL and ACD suggest that PCAL may be useful to estimate the ACD. Although ACD varies according to the vertical location of the lens, PCAL uses scleral spurs as landmarks and thus may be a more reliable anterior segment measurement and a useful tool as a predictive parameter for anterior chamber surgery.

There are several clinical applications to which PCAL may be applied. An algorithm using PCAL could be designed to attain the optimum donor size of donor graft for endothelial keratoplasties such as Descemet's stripping automated endothelial keratoplasty (DSAEK) or Descemet's membrane endothelial keratoplasty (DMEK) surgery.[6] Currently, there is no method for optimal selection of donor graft size for either

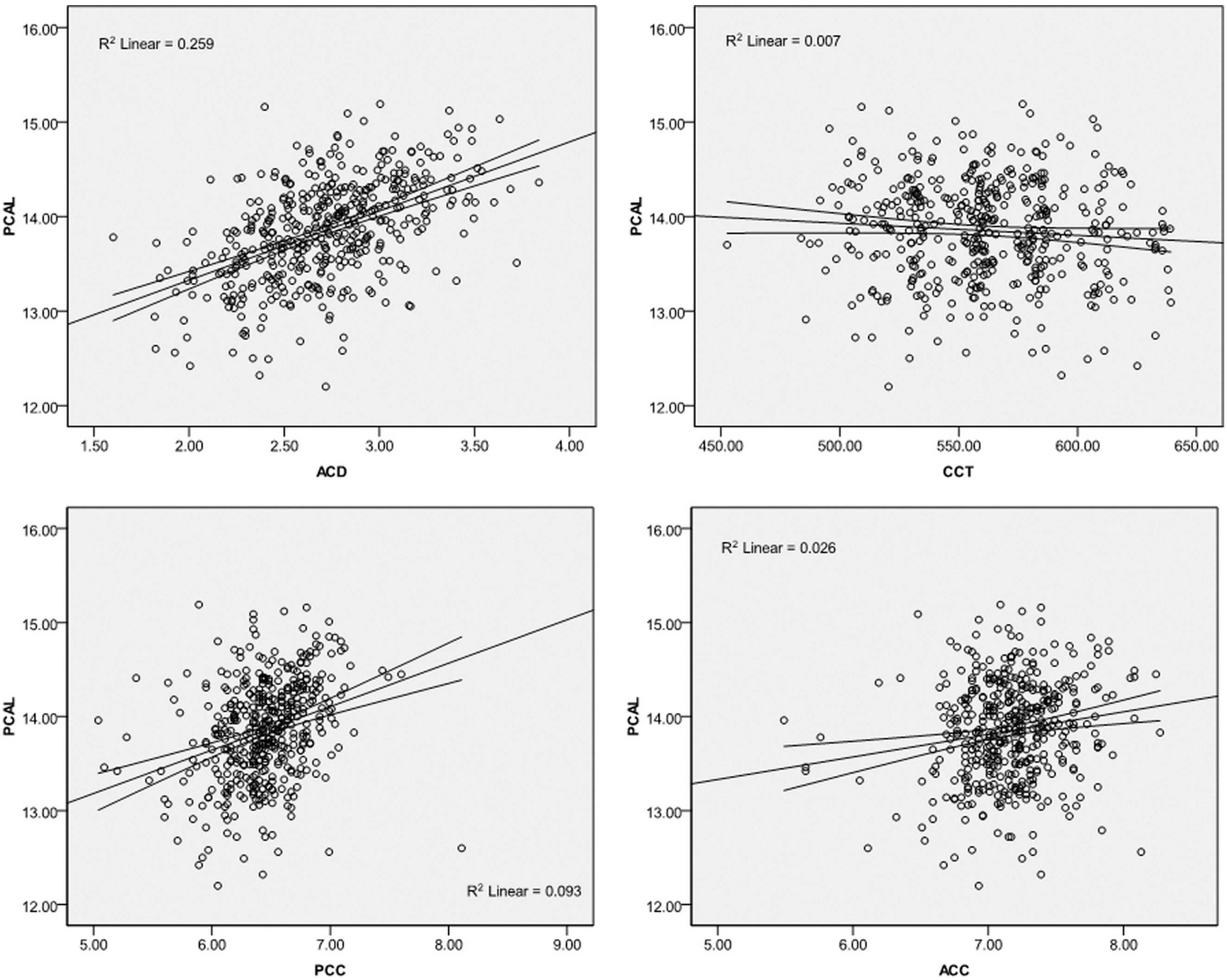

FIGURE 2. Scatterplots with best fit regression line and confidence intervals between PCAL and corneal parameters: ACD (r = 0.46, P < 0.001), CCT (r = −0.08, P = 0.09), PCC (r = 0.31, P < 0.001), and ACC (r = 0.16, P < 0.001).

Table 4. Univariate and Multivariate Analyses of Posterior Corneal Arc Length and Parameters

		Age-Sex Adjusted			Multivariate		
Parameter	**Unit**	**Beta Coefficient**	**SE**	***P* Value**	**Beta Coefficient**	**SE**	***P* Value**
ACD	per mm increase	0.757	0.060	**<0.001**	0.771	0.056	**<0.001**
CCT	per μm increase	−0.001	0.001	0.093			
PCC	per mm increase	0.472	0.071	**<0.001**	0.496	0.059	**<0.001**
ACC	per mm increase	0.241	0.073	**0.001**			
Age, y	per year increase	−0.001	0.003	0.705	0.003	0.002	0.176
Sex	female vs. male	0.006	0.051	0.910	0.005	0.041	0.905
Height	per cm increase	0.001	0.004	0.751			
Weight	per kg increase	0.000	0.002	0.835			
Body mass index	per kg/m^2 increase	0.000	0.006	0.947			
Spherical equivalent	per diopter increase	0.004	0.013	0.770			
IOP	per mm Hg increase	−0.011	0.009	0.199			
Systolic BP	per mm Hg increase	−0.001	0.001	0.440			
Diastolic BP	per mm Hg increase	−0.001	0.003	0.839			
Hypertension	yes vs. no	−0.062	0.054	0.253			
Blood glucose	per mM increase	−0.002	0.007	0.787			
HbA1c	per % increase	−0.011	0.021	0.601			
Diabetes	yes vs. no	−0.059	0.057	0.308			

Values in bold represent significance.

DSAEK or DMEK. Accurate preoperative measurement of the PCAL in a recipient can guide an appropriate choice of donor graft diameter to allow the largest possible graft diameter graft to be feasibly inserted. Postoperative measurements using this ZAP software may also be useful for monitoring these patients' progress. Corneal curvature measurements, CCT, and ACD allow for planning of both lamellar corneal grafts and refractive procedures as well. Another potential application of PCAL and ACD is the accurate calculation of the power and size of phakic intraocular lens implantations and postoperative follow-up in such patients.

There are few studies that have examined anterior segment and corneal parameters using this relatively novel ZAP software. Several studies have validated the software and our results from the other corneal parameter analyses are similar to previously published studies.[6,7] However, there were some interesting differences detected in our present study of adult ethnic Indians. Our study found no significant difference in ACC between sexes in adult ethnic Indians (7.16 ± 0.35 vs. 7.17 ± 0.35; $P = 0.20$). The ACC was found to be different between sexes in previous studies involving predominantly Caucasian and Chinese populations.[11] Furthermore, the PCC in our study population was 6.45 ± 0.35 mm, which was less than that of Chinese (6.6–6.7 mm), but more similar to schematic eyes in previous studies (6.4–6.5 mm).[17] We also found a poor correlation between PCC and PCAL ($r = 0.31$, $P < 0.001$), similar to that found in Chinese eyes.[6] Similar to the ZAP study in Chinese eyes, we did not find any associations of PCAL to systemic disorders that may affect corneal physiology such as hypertension ($r = 0.04$, $P = 0.90$) and diabetes mellitus ($r = 0.015$, $P = 0.76$). However, these findings need to be further studied in direct, comparative studies.

Central corneal thickness (CCT) is a clinically important parameter in the diagnosis of glaucoma,[18] which is affected by genetic as well as environmental factors.[19,20] The mean CCT from our study cohort was relatively higher than that published in other studies (561.4 ± 34.1 μm), but comparable to that found in our Chinese cohort (562.4 ± 31.9 μm).[6] Previous studies using ultrasound pachymetry have found that adult Indians (40 years of age and older) from rural Central India have markedly thinner corneas than do Caucasians or Chinese.[21] The ethnic Indians from our study come from an urban environment, thus raising further questions on the influence of socioeconomic factors on anterior segment parameters. In this study of adult Indians living in urban Singapore, albeit with a smaller sample size, we found that CCT was not significantly correlated with age, sex, refractive error, or ACD, unlike that found in Indians living in rural regions of India.[22] Anterior chamber depth in our ethnic Indian study population (2.72 ± 0.37 mm) was greater than that reported in ethnic Chinese and Caucasians.[11] Unlike that described in Chinese populations, there was no significant difference between males and females in our study (2.72 ± 0.39 vs. 2.72 ± 0.34 mm; $P = 0.92$). We did find that ACD significantly decreased with increasing age ($r = -0.12$, $P = 0.011$) and increasing hyperopia ($r = -0.11$, $P = 0.019$).

One of the limitations of our study is that we studied only one ethnicity. However, the adult ethnic Indians in our study population are comprised of mixed proportions of native, immigrant, and expatriate Indians from abroad, adding to the generalizability of our study results. Most of our study subjects (370, 84.5%) had ancestry from South India, although our ethnic Indians comprise second- and third-generation descendents of immigrants to Singapore. Although we do not have any comparative gold standard to compare our results on PCAL in ethnic Indians, the parameters we derived from our study are similar to those reported previously. The inability to detect the scleral spur, in suboptimal images and where the sclera formed a smooth continuous line, is another recognized limitation in all studies involving AS-OCT. However, we were able to reliably measure 99% of all our AS-OCT scan images. The advantage of the ZAP program is that once these scleral spurs are identified, the rest of the measurements are produced automatically. Horizontal nasal–temporal AS-OCT scans were used because these have been shown to be the most consistent with respect to obtaining high-quality images for the ZAP program to analyze.

In summary, we describe useful baseline corneal and anterior segment parameters in adult Indian eyes, adapted from a population-based study. Further studies with comparisons with Indians from rural areas or other ethnic populations would be useful.

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