Correlation between lens thickness and lens density in patients with mild to moderate cataracts

Maria A Henriquez,[1] Josefina A Mejías,[1] Mirel Rincon,[1] Luis Izquierdo Jr,[1] Perry S Binder[2]

[1]Research Department, Oftalmosalud Instituto de Ojos, Lima, Peru
[2]Department of Ophthalmology, Gavin Herbert Eye Institute, Irvine, California, USA

Correspondence to
Dr Maria A Henriquez, Research Department, Oftalmosalud Instituto de Ojos, Lima 15036, Peru; mariahenriquez1610@gmail.com

Part of this study was presented as a poster at the American Academy of Ophthalmology, New Orleans, LA 2017.

Received 6 March 2019
Revised 17 October 2019
Accepted 19 December 2019

To cite: Henriquez MA, Mejías JA, Rincon M, *et al*. *Br J Ophthalmol* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/bjophthalmol-2019-314171

ABSTRACT

Purpose To determine the relationships between lens thickness (LT), lens density and anterior segment parameters in patients with mild to moderate cataracts.
Setting Oftalmosalud Instituto de Ojos, Lima, Perú.
Design Prospective, single-centre, cross-sectional study.
Methods 169 eyes with age-related mild to moderate cataracts had lens density assessed using the Lens Opacification Classification System III, the built-in Pentacam HR Nucleus Staging software and ImageJ software. LT and axial length (AL) were measured with the IOLMaster 700, and angle parameters were measured using anterior segment optical coherence tomography. Pearson correlation coefficients and Kruskal-Wallis tests were used for statistical analyses.
Results Nuclear colour score was the only clinical parameter with a weak significant correlation with LT (r=0.24, p=0.003) after accounting for age, AL, gender and anterior chamber depth (ACD). The maximum value of average lens density and the mean nuclear density were significantly correlated with LT (r=0.24, p=0.003 and −0.17, p=0.03, respectively) after controlling for the same factors. Central LT greater than 4.48 mm was present in 54.5% of the eyes with a nuclear opalescence grade 1.
Conclusions LT is independent of lens density in mild to moderate cataracts after accounting for age, AL, ACD and gender contrary to previous studies.

SUMMARY

This study objectively analysed lens thickness (LT) and lens density in mild to moderate cataracts and found that LT is independent of lens density in early stages after accounting for age, axial length (AL) and anterior chamber depth (ACD).

INTRODUCTION

Primary angle closure glaucoma (PACG) is an important eye health problem affecting an estimated 79.6 million people in 2020, of whom 5.3 million will be blind.[1] In many countries, cataract surgery remains one of the most commonly performed procedures.[2 3] LT impacts both situations: a thick crystalline lens has been associated with some forms of primary angle closure[4] and in cataract surgery, LT or parameters related to lens geometry[5–7] have become strong indicators, in addition to corneal curvature, on the effective ACD and subsequent intraocular lens (IOL) position calculation.[5–10]

Historical methods used to measure LT were less accurate compared with current technology and were for the most part subjective.[11–14] The variability of LT measurements between individuals has been attributed to several factors such as age, gender, body habits, body mass index, central corneal thickness, ACD, hyperopic refractive error, cigarette smoking and diabetes.[11–15] The increase in LT in association with the severity of a cataract is uncertain; controversial results have been reported analysing different types and grades of cataract in relation to LT using subjective or poorly reproducible methods such as slit-lamp photographs and callipers.[11 12]

The subjective Lens Opacification Classification System III (LOCS III) is a well-established system for cataract grading;[16] however, it remains a subjective method. Several objective methods used to grade cataracts have been developed among them, Scheimpflug imaging which has shown a good correlation with LOCS III[17–19] as well as ImageJ software that allows lens density and dimensions to be quantitatively graded.[18] To avoid bias for cataract grading that used subjective measures, we decided to use currently available objective methods, the Pentacam Nucleus Staging (PNS) software and ImageJ software. We also decided to objectively assess LT using swept source optical coherence tomography (OCT) based biometry.[20]

Since LT can influence effective IOL location after surgery,[8–10] IOL power calculation formulas,[10 21] as well as affect ACD measurements,[22–24] correlations between LT and lens density need to be objectively determined. The aim of our study was to evaluate and quantitatively document correlations between LT and lens density using contemporary objective and subjective techniques as well as to evaluate and define any relationships between anterior segment parameters and LT measurements according the degree of cataract formation.

METHODS

This was a prospective, single-centre, cross-sectional study that included 169 eyes of 169 patients with mild to moderate cataract who were treated at the Instituto de Ojos Oftalmosalud (Lima, Peru) from August 2016 to February 2017 and agree to participate in the study protocol. All patients underwent Optical Biometry (IOLMaster 700, Carl Zeiss Meditec AG, Jena, Germany), Scheimpflug analysis (Pentacam High Resolution (HR model 1.21r51), Oculus, Wetzlar, Germany), time-domain anterior segment optical coherence tomography (AS-OCT Visante; Carl Zeiss Meditec, Dublin, California, USA), slit-lamp examination and lens grading and best-corrected visual acuity (BCVA). All examinations were performed by the same researcher. Visual acuity was measured at 6 m using standard Snellen

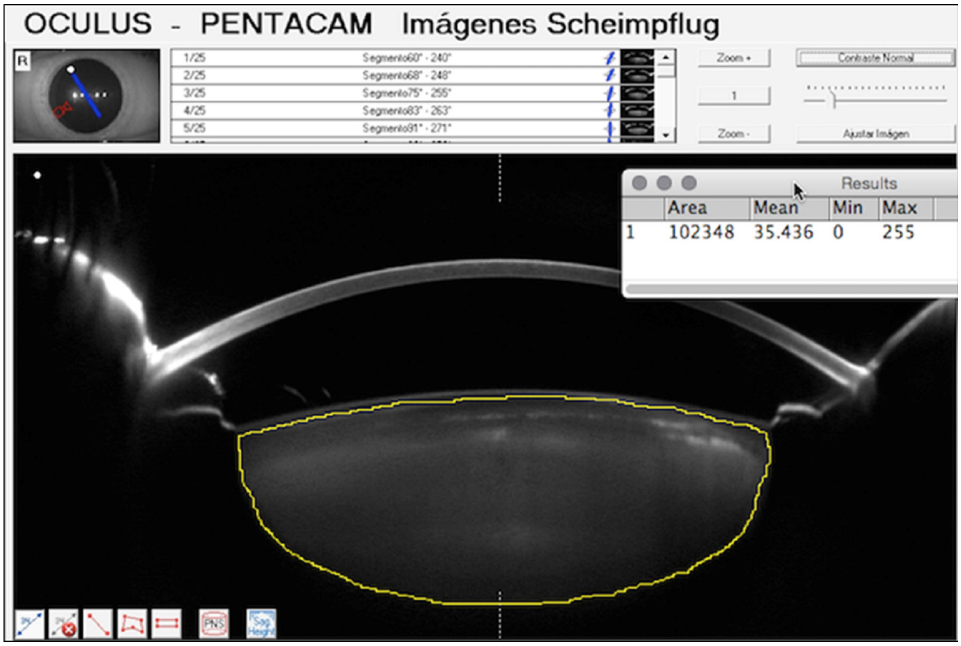

Figure 1 Pentacam Scheimpflug image exported to ImageJ analysis in a patient with incipient cataract in whom ALDavg was 35.43 pixels and NLD avg was 38.52 pixels and lens thickness was 5.01 mm according to the IOL master measurement. The yellow line represents the area of interest analysed. ALD avg, average lens density mean; NLD avg, nuclear lens density .

acuity charts. If bilateral cataracts were present, only one eye of each patient was selected randomly (random number chart) for the analysis. Inclusion criteria were an age-related cataract no greater than LOCS IV for nuclear colour, nuclear opalescence, cortical and/or subcapsular using LOCS III classification, age 45 years or older, no previous ocular surgeries or laser treatments, no history of diabetes and a no smoking history. The study complied with the Declaration of Helsinki. The ethics committee and Institutional Review Board of Oftalmosalud approved the study. Written informed consent was obtained from all patients.

All participants underwent the following same day measurements in the following order: visual acuity and refraction, slit lamp examination, IOL Master, AS-OCT and Scheimpflug imaging analysis. To assess cataract density using Scheimplug analysis, two drops given 5 min apart of 1% Tropicamide (Midilar-T, Roster Laboratories) was administered to dilate the pupil 30 min before the test was taken.

Lens density

Lens density was assessed subjectively by using LOCS III and objectively by using Scheimpflug imaging analysis with the built-in PNS software and ImageJ software V.34 (National Institutes of Health, Bethesda, Maryland, USA; available as a free download (http://rsb.info.nih.gov/ij/download.html, Accessed 15 January 2009). For LOCS III, two masked reviewers (MAH and JAM) independently assessed slit-lamp and retro-illumination images of the cataract; any disagreements were resolved by consensus or arbitration by a third party (LI). The scale ranged from 0.1 (clear or colourless) to 5.9 (very opaque in case of cortical and subcapsular posterior) or 6.9 (very opaque and/or brunescent in cases of combined nuclear opalescence and nuclear colour). The following cataract parameter scores were obtained from LOCS III: nuclear opalescence (NO), nuclear colour (NC), cortical (C) and subcapsular posterior (P) opacity.

Room lights were switched off for all Scheimpflug image examinations (PNS recording) to obtain a reflex-free image. Three images were assessed by the same ophthalmologist and the image with the highest quality factor was used; only scans with a quality of over 95% were included in the study. The PNS software has a grading system that is based on the pixel intensity measurement within the nucleus, which provides data on the mean density value, the SD and maximum nuclear density and is measured in a three-dimensional template volume and optical density array that generate a nuclear cataract grade in five stages (PNS cataract grading score). Three parameters were obtained from each PNS recording: PNS average (mean nuclear density), PNS maximum (maximum nuclear density) and PNS cataract grading score (from 0 to 4, with 4 indicating highest nuclear density).

Scheimpflug images were exported to ImageJ software for analysis of the region of interest (ROI) according to the procedure described by Grewal *et al*.[18] The ImageJ software allowed the placement of the ROI standard elliptical mask to be automated in all 50 images of each eye. The average lens density (ALD) was calculated by marking the edges of the lens using the ImageJ software (figure 1). The density of the selected area was measured in pixel intensity units on a scale of 0–255. Lens density was measured on each of the 50 Scheimpflug images and the mean value was obtained to provide a global lens density value for the average and nuclear lens density (NLD) measurements. The operator was also allowed to adjust the ROI if he felt the alignment of the image was wrong. The following parameters were obtained (in pixels units): average lens density mean (ALD avg), average lens density maximum (ALD max), nuclear lens density mean (NLD avg) and nuclear lens density maximum (NLD max).

Lens thickness, anterior chamber depth and axial length

LT, ACD and AL were measured by the same ophthalmologist (MAH) who also performed measurements with the IOLMaster 700 (Carl Zeiss Meditec AG, Jena, Germany). ACD was measured from the corneal epithelium to the posterior lens surface using the calliper software in the instrument.

Anterior segment parameters and chamber angle

The angle opening distance (AOD), the angle recess area (ARA), the trabecular-iris space area (TISA) and the lens vault (LV) were

Table 1 Baseline patients' characteristics of lens thickness, axial length and anterior chamber depth according to LOCS III classification

	N	Age (Years)	Lens thickness (mm)	Axial length (mm)	Anterior chamber depth (mm)
Nuclear colour					
NC1	16	65.5±7.1 (50-77)	4.3±0.6 (3.4–5.5)	23.9±1.8 (21.5–26.6)	3.4±0.5 (2.3–4.1)
NC2	83	64.7±10.9 (40-84)	4.5±±0.4 (3.6–5.2)	24.8±2.5 (21.8–33.2)	3.2±0.4 (2.4–4.1)
NC3	55	68.1±10.51 (40-87)	4.7±0.3 (3.9–5.4)	24.9±2.1 (21.9–31.4)	3.1±0.4 (2.4–3.9)
NC4	15	74.0±8.1 (62-87)	4.8±0.3 (4.3–5.2)	24.7±2.1 (22.3–31.3)	3.1±0.5 (2.3–3.9)
Nuclear opalescence					
NO1	11	63.7±4.8 (58-73)	4.4±0.6 (3.4–5.4)	24.7±2.5 (21.5–28.7)	3.3±0.6 (2.3–4.1)
NO2	89	65.1±10.2 (40-84)	4.5±0.4 (3.6–5.5)	24.7±2.4 (21.8–33.2)	3.2±0.4 (2.4–4.1)
NO3	52	67.9±10.5 (42-85)	4.6±0.4 (3.8–5.4)	24.8±2.1 (21.9–31.8)	3.2±0.4 (2.4–3.9)
NO4	17	73.8±12.0 (40-87)	4.9±0.3 (4.3–5.2)	24.5±1.9 (22.3–31.3)	2.9±0.3 (2.3–3.5)
Cortical					
C1	27	62.4±9.9 (40-85)	4.7±0.4 (4.1–5.3)	25±3.0 (22.1–33.2)	2.9±0.4 (2.3–3.9)
C2	55	65.3±9.9 (42-87)	4.5±0.4 (3.3–5.5)	25.5±2.3 (21.5–31.8)	3.3±0.4 (2.3–3.9)
C3	58	69.7±10.2 (40-87)	4.6±0.4 (3.4–5.2)	24.3±1.6 (21.8–30.2)	3.2±0.4 (2.2–4.1)
C4	17	73±9.4 (53-87)	4.6±0.4 (3.6–5.2)	24.1±1.4 (22.0–27.2)	3.2±0.4 (2.4–3.8)
Subcapsular posterior					
P1	78	67.7±9.9 (40-87)	4.6±0.4 (3.6–5.3)	24.1±1.7 (21.8–31.4)	3.1±0.3 (2.4–3.8)
P2	28	65.4±10.7 (40-85)	4.5±0.4 (3.6–5.3)	25.4±2.6 (21.8–33.1)	3.3±0.5 (2.4–4.1)
P3	8	70.1±11.8 (58-87)	4.6±0.3 (4.2–5.0)	24.8±2.3 (23.2–30.4)	3.2±0.0 (2.8–3.6)
P4	4	54±12.6 (40-67)	4.3±0.8 (3.4–5.2)	29.0±5.2 (21.5–33.2)	3.3±0.4 (2.8–3.7)

C, cortical cataract; LOCS III, Lens Opacification Classification System III; NC, nuclear colour;NO, nuclear opalescence; P, Subcapsular posterior cataract.

measured using anterior segment OCT and the calliper software.[22 23 25 26] Measurements were assessed at 0° and 180°, and the mean between them was recorded. The AOD is the perpendicular distance between a point 500 µm anterior to the scleral spur and the opposing iris (expressed in mm). The ARA (ARA 500 and ARA 750) is the triangular area demarcated by the anterior iris surface, corneal endothelium and a line perpendicular to the corneal endothelium drawn from a point 500 or 750 µm anterior to the scleral spur to the iris surface (expressed in μm). The TISA (TISA 500, TISA 750) is a trapezoidal area measuring the filtering area; the defining boundaries are: anteriorly, the AOD; 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 (expressed in μm).

Table 2 Mean lens thickness and lens density according to the Cataract grading score of the PNS software

PNS Cataract grading score	N	PNS average	PNS maximum	ALD average	ALD maximum	NLD average	NLD maximum	Lens thickness
0	14	10.5±4.1 (8.1–24)	30.1±26.3 (1.8–100)	28.3±3.8 (23.2–37.8)	172.2±73.1 (44–255)	28.9±2.2 (24.5–32.7)	38.8±2.8 (35–44)	4.3±0.5 (3.6–5.5)
1	93	10.8±2.2 (7.6–23.6)	31.3±23.9 (6.5–100)	34.6±5.2 (17.5–47.7)	160.8±74.1 (52–255)	43.2±11.2 (13.3–72.2)	81.1±58.5 (29–255)	4.5±0.4 (3.4–5.4)
2	55	12.2±3.3 (9.1–29.5)	35.5±23.5 (16.1–100)	44.5±6.1 (34.7–67.4)	176.8±54.6 (97–255)	62.5±15.6 (36.3–104)	100.9±44.9 (53–255)	4.7±0.31 (4.1–5.4)
3	7	11.1±1.4 (9.4–12.9)	38.9±33.5 (15.7–100)	53.0±7.5 (42.7–65.2)	209.3±54.7 (141–255)	79.6±17.9 (54.4–107.1)	143±79.9 (68–255)	4.7±0.3 (4.1–5.1)
4	0							

ALD average, average lens density mean given by the ImageJ software;ALD maximum, average lens density maximum given by the ImageJ software; NLD average, nuclear lens density mean given by the ImageJ software; NLD maximum, nuclear lens density maximum given by the ImageJ software; PNS, Pentacam Nucleus Staging software; PNS average, mean nuclear density given by the PNS; PNS maximum, maximum nuclear density given by the PNS.

Table 3 Correlation between lens thickness and lens density measured objective and subjectively

Lens density parameters	R_{xy}	P value*	$R_{xy.zw}$	P value**
Objectively assessment (Scheimpflug)				
PNS average	−0.041	0.616	−0.177	0.032
PNS max	−0.035	0.666	−0.008	0.925
NLD, mean	0.291	0.000	0.053	0.527
NLD, maximum	0.372	<0.001	0.122	0.141
ALD, mean	0.356	<0.001	0.112	0.177
ALD, max	0.198	0.013	0.241	**0.003**
Subjective assessment (LOCS III)				
NO	0.333	<0.001	0.159	0.054
NC	0.360	<0.001	0.240	**0.003**
C	−0.103	0.201	−0.119	0.152
P	−0.068	0.399	0.093	0.262

P value * for Pearson correlation coefficient without adjusting for age, AL, gender and ACD. P value ** for Pearson correlation coefficient adjusting for age, AL, gender and ACD.
Bold typeface indicates statistical significance.
ACD, anterior chamber depth; AL, axial length; ALD average, average lens density given by the ImageJ software; ALD maximum, average lens density maximum given by the ImageJ software; C, cortical cataract; NC, nuclear colour; NLD average, nuclear lens density mean given by the ImageJ software; NLD maximum, nuclear lens density maximum given by the ImageJ software; NO, nuclear opalescence; P, subcapsular posterior cataract; PNS, Pentacam Nucleus Staging software; PNS average, mean nuclear density given by the PNS; PNS maximum, maximum nuclear density given by the PNS; R_{xy}, Pearson correlation coefficient without adjusting for age, AL, gender and ACD; $R_{xy.z}$, Pearson correlation coefficient adjusting for age, AL, gender and ACD.

The LV is the perpendicular distance between anterior pole of the crystalline lens and the horizontal line joining the two scleral spurs (expressed in μm).

Statistical analysis

The R version statistical package 3.4.1 (freely available software under the terms of the Free Software Foundation's General Public License [https://www.r-project.org/]) was used for the statistical analysis. The linear correlation between the variables was evaluated using Spearman's correlation coefficient. For the comparison of independent groups, the Kruskal–Wallis test was used. The Dunn test was used for multiple comparison tests after the Kruskal–Wallis test. Differences were considered statistically significant at a p<0.05. For statistical analysis, we divided LT into four groups: 3.5–4.0 mm; 4.1–4.5 mm; 4.6–5.0 mm and 5.1–5.5 mm.

RESULTS

The average patient age was 66.8 years (range, 45–87 years). There were 72 males (42.60%), the mean BCVA was 0.28 LogMAR (SD: 0.415), the mean nuclear opalescence score was 2.54 (SD: 0.85) and the mean nuclear colour score was 2.49 (SD: 0.87). The patients' baseline characteristics of age, LT, AL and ACD according to the subjective classification LOCS III are given in table 1 according to the objective method used, and the Cataract grading scores (PNS software) are given in table 2.

Linear correlations were analysed between lens density and LT (table 3). From the subjective analysis, nuclear opalescence and nuclear colour from the LOCS III had significant correlation with LT, but after controlling for age, AL, gender and ACD, only the nuclear colour remained significant but with a weak correlation (r=0.24, p=0.003). From the objective analysis, using the Scheimpflug images, only the maximum value of ALD remained significant but with a weak correlation after accounting for the same factors (r=0.24, p=0.003).

Figure 2 shows the correlation between LT and objective measurements for lens density. As an example, grade I for nuclear opalescence had a LT that varied from 3.4 to 5.4 mm (figure 2A) and incipient cataract, grade I for nuclear colour had a LT range from 3.4 to 5.5 (figure 2B). Figure 2A,B shows the weak correlation between average and maximum PNS and LT, respectively. Figure 2C,D shows the weak correlation between mean and maximum NLD assessed with the ImageJ software and LT. Figure 2E,F shows a weak correlation between mean and maximum ALD assessed by the ImageJ software and LT, respectively, which means that regardless of the increment in the density of the cataract (expressed in pixels), whether nuclear or based on the pixel average of the entire lens, there is not a proportional increase in the thickness of the lens, having controlled for age, AL, gender and ACD.

Figure 3 also shows the correlations between the subjective cataract grading system and LT. Specifically, figure 3A shows a weak correlation between nuclear opalescence and LT. Figure 3B shows a weak correlation between nuclear colour and LT, figure 3C shows a weak correlation between cortical cataract and LT and figure 3D shows a weak correlation between subcapsular cataract and LT. These findings suggest that regardless of the degree of nuclear, cortical or subcapsular cataract, there is not a significant correlation with LT which is more evident in cataracts grade 1 and 2, where the range in LT is much wider than in grades 3 and 4.

Table 4 compares different variables obtained using OCT in eyes stratified by AL. There were statistically significant differences in the AOD500, TISA 750 and LVs between the groups with different LT. Table 5 shows the percentage of eyes for each grade and type of cataract that has a higher risk of developing primary angle closure or phacomorphic glaucoma according to cut-points suggested by previously published literature.[4 23] LT greater than 4.48 mm was present in 31% of the eyes with a nuclear colour grade 1, in 54.5% of the eyes with a nuclear opalescence grade 1, in 74.1% of the eyes with cortical cataract grade 1 and in 65.4% of the eyes with posterior subcapsular cataract grade 1.

DISCUSSION

The demographics from our study (table 1) are in agreement with the literature, which assumes cataracts advance with ageing.[27 28] Our objective methods for grading cataract (table 2), using pixel density, also agrees with the literature.[11–15] These results confirm that our study population is representative of the normal cataract population.

Previous studies suggest that there is an association of LT with greater age, gender, body stature, body mass index, central cornea, ACD, hyperopic refractive error, cigarette smoking and diabetes.[11–15] There is an assumption that LT is directly associated with lens density. However, contradictory results have been reported when analysing the relationship between LT and lens density[11–13 27] probably because lens density was assessed subjectively whereas LT was assessed using slit-lamp photographs and callipers. LT is important in cataract surgery because when it has been included in IOL power calculations, it has been associated with lower predicted error prediction and lower absolute error postsurgery.[21 24] LT is also important in angle closure, because it is a risk factor for developing phacomorphic glaucoma[23] and for incipient angle closure.[4 27]

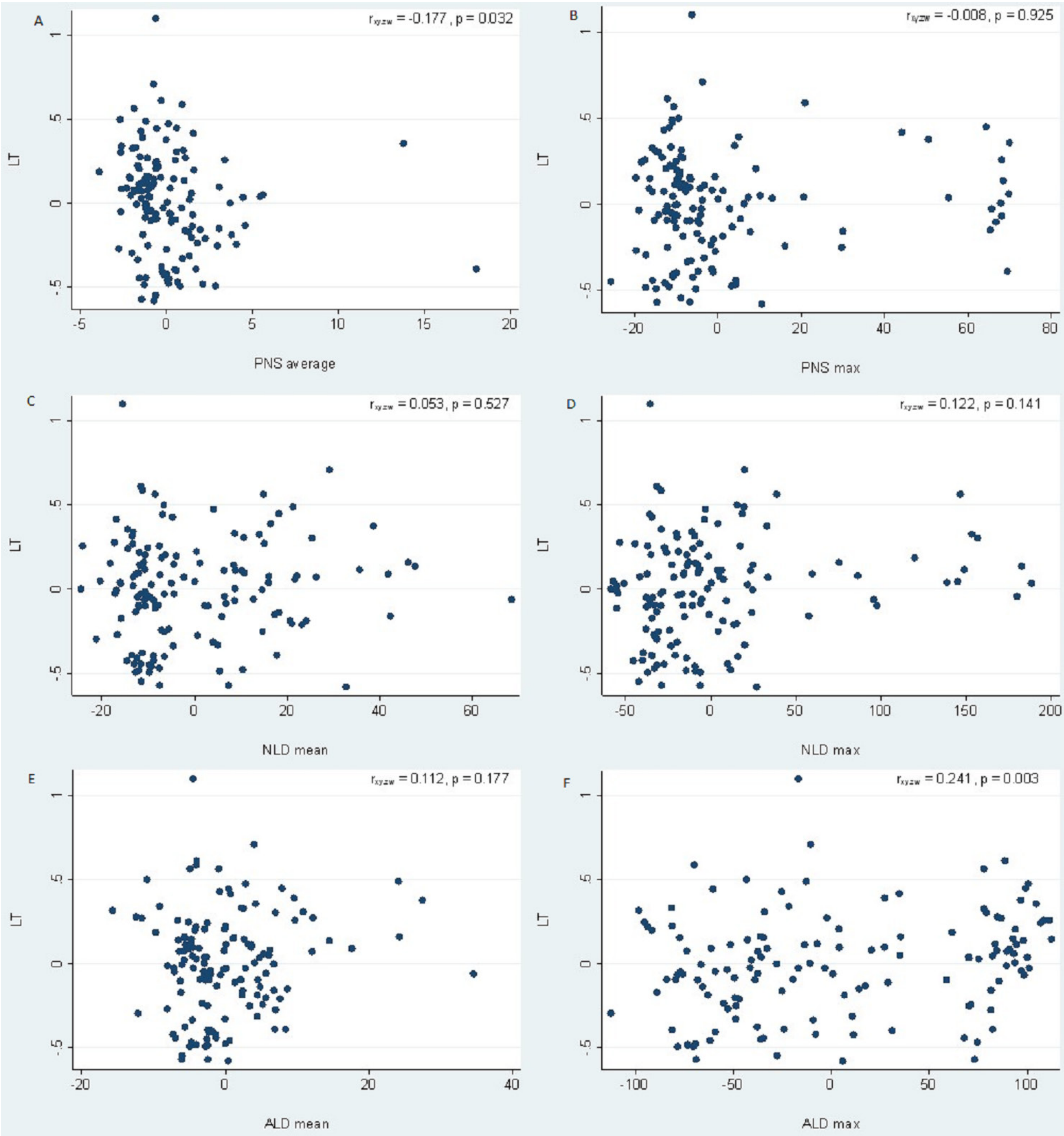

Figure 2 Two-way scatter plots showing the correlation between lens thickness and lens density measured objectively with the Pentacam and the ImageJ software. It shows a weak correlation between all objective measurements of cataract density expressed in pixels and LT, meaning that regardless of the increment in the density of the cataract, there is not a proportional increase in the thickness of the lens, having controlled for age, AL, gender and ACD. (A) Correlation between average PNS and LT. (B) Correlation between maximum PNS and LT. (C) Correlation between mean NLD and LT. (D) Correlation between maximum NLD and LT. (E) Correlation between mean ALD and LT. (F) Correlation between maximum ALD and LT. *PNS: Pentacam Nucleus Staging (mean nuclear density) assessed directly by the Pentacam, expressed in pixels; ALD: average lens density obtained after Scheimpflug images were exported to ImageJ software, expressed in pixels; NLD: nuclear lens density obtained after Scheimpflug images were exported to ImageJ software, expressed in pixels. ACD, anterior chamber depth; AL, axial length; LT, lens thickness.

Correlations between LT and lens density measured objectively and subjectively are presented in table 3. Our results show that there is not a strong correlation between LT and lens density in patients with cataract, after accounting for age, gender, ACD and AL; therefore, the increase in the LT appears to be independent of lens density and the type cataract in mild to moderate cases. This finding is more evident at the early stages of cataract formation where LTs can be greater than expected. This also means

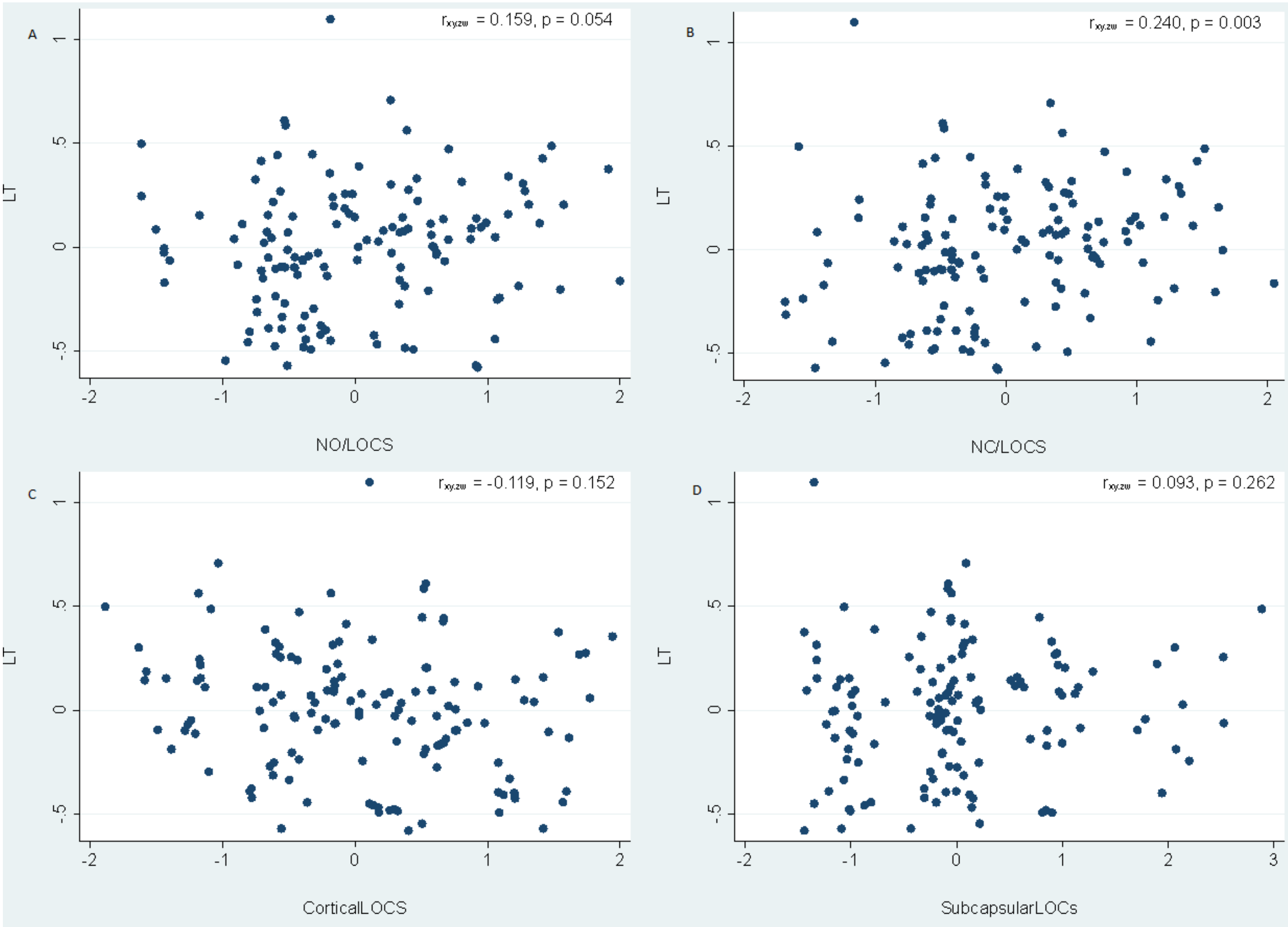

Figure 3 Two-way scatter plots showing the correlation between LT and lens density assessed by LOCS III. There is not a significant correlation between the degree of nuclear, cortical or subcapsular cataract and LT. (A) Correlation between nuclear opalescence and LT in different grades of cataract. (B) Correlation between nuclear colour and LT in different grades of cataract. (C) Correlation between different grades of cortical cataract and LT. (D) Correlation between different grades of subcapsular cataract and LT. LOC III, Lens Opacification Classification System III; LT, lens thickness.

that we do not have to wait for an advanced degree of cataract to find an increase in LT. Figure 2 shows that an incipient cataract (lower pixel density) has a high variability in measurements of LTs that are very similar to advanced cases (higher pixel density). Figure 3 shows how LT exceeds 4.5 mm regardless of the type (nuclear, cortical, subcapsular) or the degree of cataract (grades 1 to 4).

The type of cataract has been reported to be associated with different LTs, but contradictory information has been published. Nuclear cataracts have been associated with a thinner or a thicker lens. Jonas *et al*[13] found that LT decreased with a higher degree of nuclear cataract, but in contrast, Klein *et al*[11 12] reported that LT was positively associated with incipient nuclear cataracts. Shammas and Shammas[27] reported that nuclear thickness did not show a positive correlation with overall LT. In our study, after adjustment for age, gender, ACD and AL, objective analyses (maximum value of ALD (figure 2F) and subjective analysis (the nuclear colour from LOCS III (figure 3B) were the only parameters with significant correlations, but both these correlations were weak (r=0.24). A cortical cataract has been reported to be associated with thinner lens, as described by Wong *et al*[15] and Warrier *et al*.[28] We also found a significant negative correlation of –0.11 between cortical cataract and LT, but this too had a weak correlation (figure 3B).

Table 4 Angle measurements assessed by anterior segment OCT according to lens thickness

LT (mm)	AOD 500	ARA 500	ARA 750	TISA 500	TISA 750	Lens vault	ACD
3.5–4	0.4 (0.3)	0.1 (0.1)	0.3 (0.2)	0.1 (0.1)	0.2 (0.1)	0.3 (0.3)	3.2 (0.3)
4.1–4.5	0.4 (0.2)	0.1 (0.1)	0.3 (0.1)	0.1 (0.1)	0.2 (0.1)	0.1 (0.2)	3.1 (0.3)
4.6–5.0	0.3 (0.1)	0.1 (0.1)	0.2 (0.1)	0.1 (0.1)	0.2 (0.1)	0.5 (0.2)	3.0 (0.4)
5.1–5.5	0.3 (0.2)	0.1 (0.1)	0.2 (0.2)	0.1 (0.1)	0.2 (0.2)	0.7 (0.2)	3.0 (0.4)
P value*	0.006	0.26	0.06	0.07	0.007	0.0001	0.144

*P value using Kruskal-Wallis test and the Dunn test.
ACD, anterior chamber depth;AOD, angle opening distance; ARA, angle recess area;LT, lens thickness; OCT, optical coherence tomography; TISA, trabecular-iris space area.

Table 5 Percentage of eyes for each grade and type of cataract that has a higher risk of developing primary angular closure or phacomorphic glaucoma according to cut-points suggested by previously published articles

	N	LT>4.48 mm	LT>4.72 mm	TISA 500 <0.09 um at 0°	TISA 500 <0.09 um at 180°	LT>4.37 mm
Nuclear colour						
NC1	16	31% (5/16)	12.5% (2/16)	37.5% (6/16)	50% (8/16)	50% (8/16)
NC2	72	55.55% (40/72)	25% (18/72)	29.16% (21/72)	52.8% (38/72)	65.2% (47/72)
NC3	55	69.1% (38/55)	45.45% (25/5)	29.1% (16/55)	41.8% (23/55)	78.2% (43/55)
NC4	15	80% (12/15)	53.3% (8/15)	26.7% (4/15)	66.7% (10/15)	80% (12/15)
Nuclear opalescence						
NO1	11	54.5% (6/11)	18.1% (2/11)	45.5% (5/11)	36.4% (4/11)	54.5% (6/11)
NO2	78	51.2% (40/78)	24.4% (19/78)	28.2% (22/78)	50% (39/78)	64.1% (50/78)
NO3	52	63.5% (33/52)	40.4% (21/52)	34.6% (18/52	44.2% (23/52)	73.1% (38/52)
NO4	17	94.1% (16/17)	64.7% (11/17)	11.7% (2/17)	70.6% (12/17)	94.1% (16/17)
Cortical						
C1	27	74.1% (20/27)	44.4% (12/27)	14.8% (4/27)	51.9% (14/27)	77.8% (21/27)
C2	55	47.2% (26/55)	30.9% (17/55)	43.6% (24/55)	47.2% (26/55)	63.6% (35/55)
C3	58	65.5% (38/58)	32.8% (19/58)	22.4% (13/58)	50% (29/58)	70.7% (41/58)
C4	17	64.7% (11/17)	29.4% (5/17)	35.3% (6/17)	47.1% (8/17)	70.6% (12/17)
Subcapsular posterior						
P1	78	65.4% (51/78)	33.3% (26/78)	24.4% (19/78)	48.7% (38/78)	76.9% (60/78)
P2	28	53.6% (15/28)	42.9% (12/28)	50% (14/28)	50% (14/28)	64.3% (18/28)
P3	8	62.5% (5/8)	37.5% (3/8)	25% (2/8)	87.5% (7/8)	76% (6/8)
P4	4	50% (2/4)	25% (1/4)	0	50% (2/4)	50% (2/4)

LT>4.48 and TISA 500<0.009 risk factor for developing phacomorphic angle closure.[20]
LT>4.72 risk factor for 10-year incidence for any primary angle closure disease.[4]
LT>4.37 risk factor for 10-year incidence for any primary angle closure glaucoma.[4]
Grades expressed as numbers.
C, cortical cataract; LT, lens thickness; n, number of eyes in each category; NC, Nuclear colour;; NO, Nuclear opalescence; P, Subcapsular posterior cataract.

Our results could be important under two scenarios. First, almost all formulas for estimating IOL power are essentially based on a simplified model eye that assumes a thin lens,[5 10 29] but in recent years, lens geometry is considered to be an important factor in newly developed IOL power calculation methods, such as the Olsen-C[8 9] formula and the new Shammas formula[9 10] and Holladay formula.[24] We think that given the wide range of LT in different types and densities of cataract determined by our current study, this metrics is highly variable in the early stages of cataract formation and therefore could not always be assumed to be directly related to the age-related thickening of the crystalline lens.

Controversial results have been reported about LT and IOL position prediction. Some authors suggested that parameters such as anterior and posterior surface depths of crystalline lenses,[5] crystalline lens equatorial plane[6] and intracrystalline interphase point[7] are better parameters for predicting the postoperative IOL position than LT. Contrary to these studies, other authors have confirmed the importance of LT on IOL power calculations. In a comparative study about the accuracy of intraocular lens calculation formulas, Melles *et al*[21] analysed the performance across ocular dimensions of the most common IOL calculation formulas in the prediction of postoperative refraction. They found that the Haigis formula was most affected by variation in LT between 3 and 6 mm, with a mean prediction error of 0.70 Dioptres. Therefore, using the Haigis formula including an objective measure of LT should lead to a lower predicted error prediction. Lam *et al*[24] also analysed the effect of measured LT as compared with age-based LT estimate on IOL power calculation. They found that the mean absolute refractive error with measured LT was statistically significant lower when compared with IOL power prediction based on an age-based estimation.

Considering that our results exhibit a great variability in this particular measurement independent of age, gender, ACD, AL and cataract density (table 3), it seems prudent not to infer, estimate or indirectly calculate LT when today we have the technology to measure LT or points related to the geometry of the lens accurately. Knowing that LT has implications on the predictive refractive error, we cannot ignore the thickness of the lens.

The second reason we suggest measurement of LT in patients with cataract is because it is an assumed association between LT and primary angle closure suspects, PAC, PACG and phacomorphic glaucoma.[4] For example, Mansouri *et al*[23] and Wang *et al*[4] proposed a risk factor for phacomorphic glaucoma and for any PAC disease to be a LT greater than 4.48 mm and 4.72 mm, respectively. In our sample size, a LT greater than 4.48 mm was present in 54.5% of the eyes with a cataract grade of 1 based on nuclear opalescence. This large proportion of patients with such a thick lens could suggest that one could miss potential cases at risk of developing phacomorphic glaucoma or PACG and/or that more eyes are at risk than previously thought. In addition, some anterior segment parameters influenced by a thick crystalline lens have been suggested as risk factors for phacomorphic glaucoma and primary angle closure.[4 22 23 25 30] Guzman *et al*,[22] for example, proposed using a TISA of 500 um less than 0.09 mm^2 as risk factor for phacomorphic glaucoma. Our study found that 50% of the cataracts with nuclear colour grade 1 had TISA lower than 0.09 um (table 5).

Some limitations in our study include that we did not evaluate the incidence of open or narrow angle glaucoma in the study sample. Also, we did not include advanced cases of cataract (grade V and VI) where the increase in the thickness of the lens is more evident in relation to the density of the cataract. In addition, although ImageJ has been used in several studies for crystalline lens density analysis,[18] one limitation could be related to the limited information about the repeatability of the ImageJ software. However, we performed two objective methods to address the density of the crystalline lens: The ImageJ software and the PNS software which have been reported to have an excellent repeatability,[17–19 31] in order to avoid bias. Using both methods, weak correlations were found between LT and lens density (figures 2 and 3, respectively), making our results stronger.

Our study has evaluated the association between LTs and crystalline lens density using subjective and objective methods in patients with a cataract. Our results have demonstrated that, after controlling for age, AL, ACD and gender, quantitatively determined crystalline LT is independent of lens density and the type of cataract in mild to moderate cases. We also noted a large scatter of LT values in early-stages of cataract formation and this finding may be taken into account when using IOL formulas that estimate LT or when evaluating the angle in patients with suspected narrow angle glaucoma.

Acknowledgements We thank Jose Chauca, MSc, for helping with the statistical analysis and Carmen Maldonado, MSc, for technical support and data collection and Or Ben-Shaul for English grammar edition.

Contributors MAH has contributed to the planning, conduct and reporting of the work described in the article. LI and PSB have contributed to the conduct and reporting of the work described in the article. JAM has contributed to the conduct and reporting of the work described in the article. MR has contributed to the conduct of the work described in the article. JAM has contributed to the conduct and reporting of the work described in the article.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on request. No data are available.

ORCID iD
Maria A Henriquez http://orcid.org/0000-0001-9392-5536

REFERENCES

1 Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol* 2006;90:262–7.
2 Busbee BG, Brown MM, Brown GC, *et al*. Incremental cost-effectiveness of initial cataract surgery. *Ophthalmology* 2002;109:606–12.
3 Lundström M, Wendel E. Duration of self assessed benefit of cataract extraction: a long term study. *Br J Ophthalmol* 2005;89:1017–20.
4 Wang L, Huang W, Huang S, *et al*. Ten-Year incidence of primary angle closure in elderly Chinese: the Liwan eye study. *Br J Ophthalmol* 2018:pii: bjophthalmol-2018-311808.
5 Satou T, Shimizu K, Tsunehiro S, *et al*. Relationship between crystalline lens thickness and shape and the identification of anterior ocular segment parameters for predicting the intraocular lens position after cataract surgery. *Biomed Res Int* 2019;2019:1–9.
6 Yoo Y-S, Whang W-J, Hwang K-Y, *et al*. Use of the crystalline lens equatorial plane as a new parameter for predicting postoperative intraocular lens position. *Am J Ophthalmol* 2019;198:17–24.
7 Castro-Alonso FJ, Bordonaba-Bosque D, Piñero DP, *et al*. Predictive value of intracrystalline interphase point measured by optical low-coherence reflectometry for the estimation of the anatomical position of an intraocular lens after cataract surgery. *J Cataract Refract Surg* 2019;45:1294–304.
8 Olsen T. Prediction of the effective postoperative (intraocular lens) anterior chamber depth. *J Cataract Refract Surg* 2006;32:419–24.
9 Olsen T, Hoffmann P. C constant: new concept for ray tracing-assisted intraocular lens power calculation. *J Cataract Refract Surg* 2014;40:764–73.
10 Shammas HJ, Shammas MC. Improving the preoperative prediction of the anterior pseudophakic distance for intraocular lens power calculation. *J Cataract Refract Surg* 2015;41:2379–86.
11 Klein BEK, Klein R, Moss SE. Lens thickness and five-year cumulative incidence of cataracts: the Beaver dam eye study. *Ophthalmic Epidemiol* 2000;7:243–8.
12 Klein BE, Klein R, Moss SE. Correlates of lens thickness: the Beaver dam eye study. *Invest Ophthalmol Vis Sci* 1998;39:1507–10.
13 Jonas JB, Nangia V, Gupta R, *et al*. Lens thickness and associated factors. *Clin Experiment Ophthalmol* 2012;40:583–90.
14 Logstrup N, Sjolie AK, Kyvik KO, *et al*. Lens thickness and insulin dependent diabetes mellitus: a population based twin study. *British Journal of Ophthalmology* 1996;80:405–8.
15 Wong TY, Foster PJ, Johnson GJ, *et al*. Refractive errors, axial ocular dimensions, and age-related cataracts: the Tanjong Pagar survey. *Invest Ophthalmol Vis Sci* 2003;44:1479–85.
16 Chylack LT, Wolfe JK, Singer DM, *et al*. The lens opacities classification system III. The longitudinal study of cataract Study Group. *Arch Ophthalmol* 1993;111:831–6.
17 Pan A-P, Wang Q-M, Huang F, *et al*. Correlation among lens opacities classification system III grading, visual function index-14, Pentacam nucleus staging, and objective scatter index for cataract assessment. *Am J Ophthalmol* 2015;159:241–7.
18 Grewal DS, Brar GS, Grewal SPS. Correlation of nuclear cataract lens density using scheimpflug images with lens opacities classification system III and visual function. *Ophthalmology* 2009;116:1436–43.
19 Domínguez-Vicent A, Birkeldh U, Carl-Gustaf L, *et al*. Objective assessment of nuclear and cortical cataracts through scheimpflug images: agreement with the LOCS III scale. *PLoS One* 2016;11:e0149249.
20 Akman A, Asena L, Güngör SG. Evaluation and comparison of the new swept source OCT-based IOLMaster 700 with the IOLMaster 500. *Br J Ophthalmol* 2016;100:1201–5.
21 Melles RB, Holladay JT, Chang WJ. Accuracy of intraocular lens calculation formulas. *Ophthalmology* 2018;125:169–78.
22 Guzman CP, Gong T, Nongpiur ME, *et al*. Anterior segment optical coherence tomography parameters in subtypes of primary angle closure. *Invest Ophthalmol Vis Sci* 2013;54:5281–6.
23 Mansouri M, Ramezani F, Moghimi S, *et al*. Anterior segment optical coherence tomography parameters in phacomorphic angle closure and mature cataracts. *Invest Ophthalmol Vis Sci* 2014;55:7403–9.
24 Lam S. Comparison of age-derived lens thickness to optically measured lens thickness in IOL power calculation: a clinical study. *J Refract Surg* 2012;28:154–5.
25 Maslin JS, Barkana Y, Dorairaj SK. Anterior segment imaging in glaucoma: an updated review. *Indian J Ophthalmol* 2015;63:630–40.
26 Wang D, Qi M, He M, *et al*. Ethnic difference of the anterior chamber area and volume and its association with angle width. *Invest Ophthalmol Vis Sci* 2012;53:3139–44.
27 Shammas HJ, Shammas MC. Measuring the cataractous lens. *J Cataract Refract Surg* 2015;41:1875–9.
28 Warrier S, Wu HM, Newland HS, *et al*. Ocular biometry and determinants of refractive error in rural Myanmar: the Meiktila eye study. *Br J Ophthalmol* 2008;92:1591–4.
29 Olsen T. Calculation of intraocular lens power: a review. *Acta Ophthalmol Scand* 2007;85:472–85.
30 Moghimi S, Vahedian Z, Fakhraie G, *et al*. Ocular biometry in the subtypes of angle closure: an anterior segment optical coherence tomography study. *Am J Ophthalmol* 2013;155:664–73.
31 Pei X, Bao Y, Chen Y, *et al*. Correlation of lens density measured using the Pentacam scheimpflug system with the lens opacities classification system III grading score and visual acuity in age-related nuclear cataract. *Br J Ophthalmol* 2008;92:1471–5.