·Clinical Research·

Comparison of ultrasound biomicroscopy and spectral-domain anterior segment optical coherence tomography in evaluation of anterior segment after laser peripheral iridotomy

Xiao-Yun Ma[1,2], Dan Zhu[2], Jun Zou[3], Wen-Jie Zhang[1], Yi-Lin Cao[1]

[1]Department of Plastic and Reconstructive Surgery, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai Key Laboratory of Tissue Engineering, National Tissue Engineering Center of China, Shanghai 200011, China
[2]Department of Ophthalmology, Shanghai Guanghua Integrative Medicine Hospital, Shanghai 200052, China
[3]Department of Ophthalmology, Shanghai Tenth People's Hospital, Tongji University, Shanghai 200072, China
Correspondence to: Jun Zou. Department of Ophthalmology, Shanghai Tenth People's Hospital, Shanghai Tongji University, 301 Yanchang Middle Road, Shanghai 200072, China. zoujun70@126.com
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Abstract

• AIM: To quantitatively assess narrow anterior chamber angle using spectral-domain anterior segment optical coherence tomography (SD-AS-OCT) and ultrasound biomicroscopy (UBM), and to evaluate the correlations and consistency between SD-AS-OCT and UBM.

• METHODS: Fifty-five eyes from 40 patients were examined. Patients were diagnosed with primary angle-closure glaucoma (PACG) remission (11 eyes from 8 patients), primary angle closure (PAC, 20 eyes from 20 patients) and PAC suspect (24 eyes from 12 patients). Each eye was examined by SD-AS-OCT and UBM after laser peripheral iridotomy (LPI). The measurements of SD-AS-OCT were angle open distance (AOD), anterior chamber angle (ACA), trabecular iris angle (TIA), and trabecular iris space area (TISA). UBM measurements were AOD and TIA. Correlations of AOD500 and TIA500 between UBM and AS-OCT were assessed. All parameters were analysed by SPSS 16.0 and MedCalc.

• RESULTS: ACA, TIA and AOD measured by SD-AS-OCT reached a maximum at the temporal quadrant and minimum at the nasal quadrant. Group parameters of AOD500 and AOD750 showed a linear positive correlation, and AOD750 had less variability. UBM outcomes of AOD500 and TIA500 were significantly smaller than those of SD-AS-OCT. The results of the two techniques were correlated at the superior, nasal and inferior quadrants.

• CONCLUSION: Both UBM and SD-AS-OCT are efficient tools for follow-up during the course of PACG. We recommended using parameters at 750 μm anterior to the sclera spur for the screening and follow-up of PACG and PAC. The two methods might be alternatives to each other.

• KEYWORDS: primary angle-closure glaucoma; ultrasound biomicroscopy; spectral-domain anterior segment optical coherence tomography; laser peripheral iridotomy
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INTRODUCTION

Glaucoma is the leading cause of irreversible blindness worldwide. Quigley and Broman [1] predicted that the prevalence of primary angle-closure glaucoma (PACG) would reach 21 million (26% of all types of glaucoma) by 2020. The incidence and prevalence of PACG also differ among races [2-3]. Currently, China has the largest number of PACG patients, and is expected to have 48% of the total incidence by 2020[1].

Follow-up surveys of primary angle closure suspect (PACS) eyes showed that 22%-28% of them progress to primary angle closure (PAC) within a few years [4-5]. PACS can be diagnosed early by certain ways, such as slit-lamp, gonioscopy, ultrasound biomicroscopy (UBM) and Pentacam. If treated early and safely, some patients with PACS may not progress to PACG or blindness. In China, there is an urgent need to develop simpler, more efficient and economic examinations.

UBM has been used in imaging and quantitative evaluation of anterior ocular segments since the 1990s. It allows *in vivo* observation of the anatomy and pathology of the anterior

segments, from the conjunctiva and cornea to the iris and basal vitreous body, which provides significant information on glaucoma, cysts, neoplasms, trauma and foreign bodies. UBM also provides biometric information of anterior segment structures, such as anterior chamber (AC) depth, anterior chamber angle (ACA), and iris thickness. UBM provides more detailed information compared to slit-lamp, gonioscopy or B-scan examinations for diagnosis and follow-up of PAC eyes[6].

Optical coherence tomography (OCT) is a widely used non-invasive fundus imaging technique. Since the first application of OCT in the cornea in 2002 [7], anterior segment-optical coherence tomography (AS-OCT) has developed rapidly. There are two major OCT platforms on the market: time domain-optical coherence tomography (TD-OCT) and spectral (or Fourier) domain-optical coherence tomography (SD/FD-OCT). With a higher imaging resolution than UBM, AS-OCT makes it easier for the operator and software to identify ACA structures [8], such as: the scleral spur (SS), iris surface, Schwalbe's line, even trabecular meshwork (TM), and Schlemm's canal [9]. This provides more precise analysis of the angle opening distance (AOD) from the SS, ACA, trabecular iris angle (TIA), and trabecular iris space area (TISA).

Glaucoma research has often been conducted by TD-AS-OCT. RetinaScan-3000 OCT (NIDEK) is a high-speed SD-OCT that uses dual diode lasers with wavelengths of 880 nm. It is capable of conducting 53 000 A-scans per second with a 7 μm axial and 20 μm transverse resolution, providing high-quality imaging (4 μm OCT digital resolution) with shorter measurement time and fewer artefacts than TD-AS-OCT [10]. RetinaScan-3000 is designed mainly for ocular fundus assessment, but with a forehead attachment and a switch to the anterior segment mode, it is capable of assessing anterior segments, including corneal thickness and ACA parameters. Correlation of AC parameters between SD-AS-OCT and UBM has rarely been investigated. Therefore, we designed this study to compare the utilisation of images from UBM and SD-AS-OCT, and to assess the ACA in narrow angle patients.

SUBJECTS AND METHODS

From January to December 2014, we recruited 40 patients (29 female; mean age 67.2±9.0y) from the Department of Ophthalmology, Shanghai Tenth People's Hospital of Tongji University, who were diagnosed with PAC, PACS or PACG following systematic eye examination, including medical history, slit-lamp examination (Haag-Streit, Bern, Switzerland), non-contact tonometry (CT-80; Topcon, Tokyo, Japan), corneal thickness measurement (RetinaScan 3000; NIDEK, Gamagori, Japan), gonioscopy (Volk Optical Inc., Mentor, OH, USA) and automated perimetry (Octopus 900; Haag-Streit, Koeniz, Switzerland) measurement. All subjects were of Chinese ethnicity. Patients with severe systemic diseases, history of optical surgery or laser treatment, or diseases and pathological structures that might have interfered with observation of the cornea, AC, iris or pupil were excluded. Fifty-five eyes from 40 patients received laser peripheral iridotomy (LPI) that was performed by the same experienced doctor using the combination of argon and neodymium:yttrium-aluminum-garnet (Nd:YAG) laser. Argon laser was set at 500 to 1000 mW power with a spot size of 50 μm for a duration of 0.1s. Nd:YAG was set at 3 to 5 mJ. The study protocol was approved by the Ethics Committee of Shanghai Tenth People's Hospital of Tongji University. Written informed consent was obtained from each patient after explanation of the purpose and possible consequences of the study.

All patients underwent imaging with SD-OCT (RetinaScan 3000; NIDEK, Gamagori, Japan) under ordinary room light. Patients were asked to gaze at the inward illumination to minimise eye movement. Scans were centred on the limbus to visualise the ACA and were taken in the nasal, temporal, superior and inferior quadrants (0, 3, 6 and 9 o'clock positions) using the anterior segment programme. This programme automatically overlaid valid images selected from 50 scans of the same location. The operator repeated this process and chose the best images and calculated parameters (AOD at 500 μm and 750 μm from the SS (AOD500 and AOD750), ACA, TIA, and TISA (Figure 1) with the built-in software.

All patients underwent imaging with UBM (UD-6000; Tomey Corporation, Nagoya, Japan) under bright conditions following SD-AS-OCT. Following topical anaesthesia, an appropriately sized eye cup was placed on the sclera of the eye being examined, with normal saline as the couplant. Scans were taken in the nasal, temporal, superior and inferior quadrants. Measurements were taken three times and the operator chose the best image (when the iris was located on the reference line and its length was shortest). The mean value of three repetitions was used for statistical analysis. UBM measurements were AOD500 and TIA500.

Statistical Analysis Statistical analysis was performed using SPSS version 16.0 (Chicago, IL, USA) and MedCalc version 12.7.0.0 (Ostend, Belgium). Differences in mean values of parametric data among eyes of different patients were analysed using the independent-sample Student's t-test. Correlation between two groups of data collected by SD-AS-OCT was examined. The Pearson correlation test was used to evaluate correlations between measurements. Bland-Altman plots were used to evaluate limits of agreement of AS-OCT and UBM. $P<0.05$ was considered statistically significant.

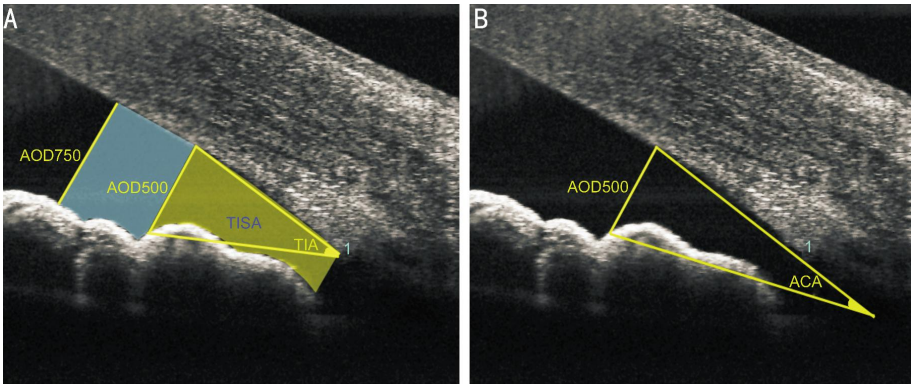

Figure 1 Anterior chamber angle in SD-AS-OCT image A: AOD: The distance from the corneal endothelium to the anterior iris perpendicular to a line drawn along the trabecular meshwork at 500 μm or 750 μm from the scleral spur; TISA: The areas bounded by the corneal endothelium, trabecular meshwork, and anterior iris surface out to a distance of 500 μm or 750 μm from the scleral spur; TIA: The angle measured with the apex in the scleral spur and the arms of the angle passing through a point on the trabecular meshwork 500 μm from the scleral spur and a perpendicular point on the iris. B: ACA: The angle measured with the apex at the angle recess and the arms of the angle passing through a point on the trabecular meshwork 500 μm from the scleral spur and a perpendicular point on the iris. 1: Scleral spur.

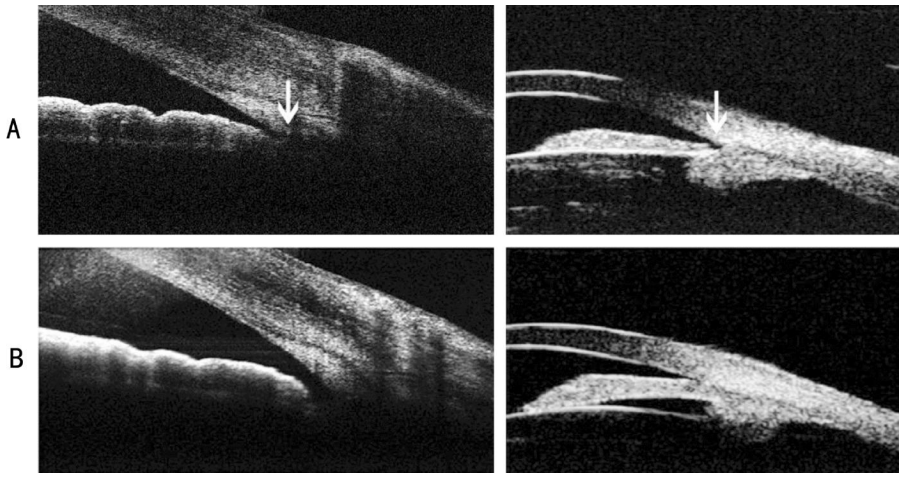

Figure 2 Images of ACA from SD-AS-OCT and UBM A: SS is clearly shown (white arrows) in both SD-AS-OCT and UBM. SD-AS-OCT (left) had a disadvantage in displaying the angle recess area and structures behind the iris; B: ACA image by SD-AS-OCT (left) and UBM (right) after LPI.

RESULTS

Fifty-five eyes from 40 patients were available for analysis. Complete ophthalmic examination revealed PACG remission in 11 eyes from 8 patients, PAC (the fellow eye of the acute PACG eye, with gonioscopy revealed peripheral anterior synechiae, 20 eyes from 20 patients) and PACS in 24 eyes from 12 patients. There was no significant difference in mean intraocular pressure (IOP) measured by non-contact tonometry before LPI (15.36±2.90 mm Hg) and after LPI (15.12 ±3.20 mm Hg; P=0.477). The corneal thickness (514 ±30.19 μm) did not differ significantly between the sexes or according to pathological stage (P>0.05). None of the patients experienced rose of IOP, acute PACG or progressive loss of vision after LPI. The SS could be identified in all SD-AS-OCT images, and 82.7% (182/220) of UBM images (Figure 2).

SD-AS-OCT measurements of ACA after LPI are summarised in Table 1. Measurements at 500 μm from SS were linearly correlated with those at 750 μm (P<0.01). ACA, TIA and AOD measured by AS-OCT reached the maximum at temporal quadrant and minimum at nasal quadrant, but for TISA, the maximum value appeared to be at the inferior quadrant and minimum value at the superior quadrant. UBM showed similar distributions of angle width to OCT. Measurements using UBM and SD-AS-OCT were correlated at the superior, temporal and inferior quadrants, but Pearson correlations were not significant in the nasal quadrant (Table 2). UBM yielded significantly smaller measurements compared with SD-AS-OCT (Paired t-test, P<0.01). No evidence of outliers from normal distribution was seen for any of the indices.

TIA500 and AOD500 were chosen to analyse consistency between UBM and SD-AS-OCT examinations (Table 3). Agreement of AOD500 and TIA500 measurements was illustrated with Bland-Altman plots (Figure 3). The mean value and mean difference of AOD500 were 0.191 μm and 0.11 μm, respectively, and 3.6% (2/55) of measurements were out with the 95% limits. The mean ratio of AOD500

Table 1 Mean values of angle parameters by AS-OCT after LPI

Parameters	Superior	Inferior	Nasal	Temporal
TIA500 (°)	24.784±7.971	25.719±10.472	23.411±8.463	26.425±7.398
TIA750 (°)	22.589±6.158	23.178±8.615	21.566±7.342	23.400±6.755
ACA500 (°)	16.046±6.641	14.739±6.320	12.913±6.312	16.449±5.866
ACA750 (°)	16.079±5.795	15.296±6.455	13.728±6.162	16.294±5.855
AOD500 (mm)	0.244±0.098	0.246±0.103	0.228±0.092	0.259±0.086
AOD750 (mm)	0.317±0.106	0.326±0.147	0.304±0.120	0.332±0.109
TISA500 (mm^2)	0.084±0.040	0.094±0.060	0.084±0.037	0.093±0.033
TISA750 (mm^2)	0.150±0.060	0.165±0.098	0.153±0.064	0.163±0.061

TIA: Trabecular iris angle; ACA: Anterior chamber angle; AOD: Angle opening distance; TISA: Trabecular iris space area.

Table 2 Mean values and Pearson correlation of TIA500 and AOD500 measured by UBM and AS-OCT

Quadrants	TIA500 (°)					AOD500 (mm)				
	UBM (SD)	AS-OCT (SD)	*t*	*P*	Pearson *P*	UBM (SD)	AS-OCT (SD)	*t*	*P*	Pearson *P*
Superior	10.109 (10.196)	24.784 (7.971)	-10.795	0.000	0.002	0.08 (0.097)	0.244 (0.098)	-10.711	0.000	0.005
Inferior	15.385 (10.979)	25.719 (10.472)	-6.308	0.000	0.007	0.148 (0.133)	0.246 (0.103)	-5.108	0.000	0.016
Nasal	17.368 (11.857)	26.425 (7.398)	-3.662	0.001	0.498	0.154 (0.104)	0.228 (0.092)	-4.248	0.000	0.333
Temporal	17.094 (10.416)	23.411 (8.463)	-6.014	0.000	0.017	0.159 (0.123)	0.259 (0.086)	-5.903	0.000	0.017

TIA: Trabecular iris angle; AOD: Angle opening distance; UBM: Ultrasound biomicroscopy; AS-OCT: Anterior segment-optical coherence tomography; SD: Standard deviation.

Table 3 Mean difference and ratio between results of UBM and AS-OCT together with 95% limits of agreement

Parameters	AS-OCT-UBM				AS-OCT/UBM			
	Mean difference	Mean (95%)	Range	1.96×SD	Mean ratio	Mean (95%)	Range	1.96×SD
AOD500	0.11±0.05	0.11 (0.01, 0.20)	0.19	0.10	1.97±0.60	1.97 (0.79, 3.14)	2.35	1.18
TIA500	10.15±4.72	10.2 (0.9, 19.4)	18.5	9.25	1.79±0.48	1.79 (0.86, 2.73)	1.87	0.94

AOD: Angle opening distance; TIA: Trabecular iris angle; SD: Standard deviation.

was 1.97, and 1.8% (1/55) of measurements were out with the 95% limits. The mean value and mean difference of TIA500 were 20.0° and 10.2° , respectively, and all measurements were within the 95% limits. The mean ratio of TIA500 was 1.79, and 5.4% (3/55) of measurements were out with the 95% limits.

Measurements of 500 μm and 750 μm from SS were analysed for coefficient of variation (Table 4). Coefficient of variation was smaller for measurements at 750 μm.

DISCUSSION

The ACA is an important structure in the diagnosis and treatment planning of PACG. It has been shown previously that there is no significant difference in ACA between Chinese and Caucasian people [3]. However, Chinese people tend to have flatter keratometry, thicker peripheral iris, and more forward iris root and ciliary body, therefore, they have a more crowded AC and narrower ACA compared to Caucasian people[3].

LPI is the first-line treatment for PAC, because it relieves pupil blockage, flattens the iris, widens ACA, and improves aqueous humour outflow[11]. It is reported that LPI results in a significant increase in ACA width in eyes with narrow angles [6,12]. However, the mechanism of PACG in Chinese people often involves non-pupillary block [13]. It was recommended that clinicians should follow the progress of PAC eyes even after successful LPI, because LPI might not resolve goniosynechia caused by non-pupillary block [14-15]. Long-term follow-up shown that, despite the presence of a patency LPI, a large proportion of PACG eyes require further treatment, such as anti-glaucoma medications, peripheral laser iridoplasty, or surgical therapy to control IOP[4,16].

Some studies have verified that OCT and UBM show excellent performance in identifying eyes with narrow angles [4,17-18]. SD-AS-OCT shows excellent reproducibility, sensitivity and ability to identify ACA structures [19-20]. However, the measurements were mostly done only at the nasal and temporal quadrants to avoid influence by the eyelids. Moreover, outward illumination was applied during the examination to achieve better image quality. Patients with narrow angles should be examined in as many orientations as possible to gain a comprehensive assessment of goniosynechia. Using SD-AS-OCT, we managed to image four quadrants of the limbus using inward illumination, which minimised eye movement and provided credible results. We found that ACA, TIA and AOD measured by SD-AS-OCT reached a maximum at the temporal quadrant and a minimum at the superior quadrant. The maximum value of TISA appeared to be at the inferior quadrant and minimum value at the nasal quadrant. Measurements by UBM and SD-AS-OCT were correlated at the superior, nasal

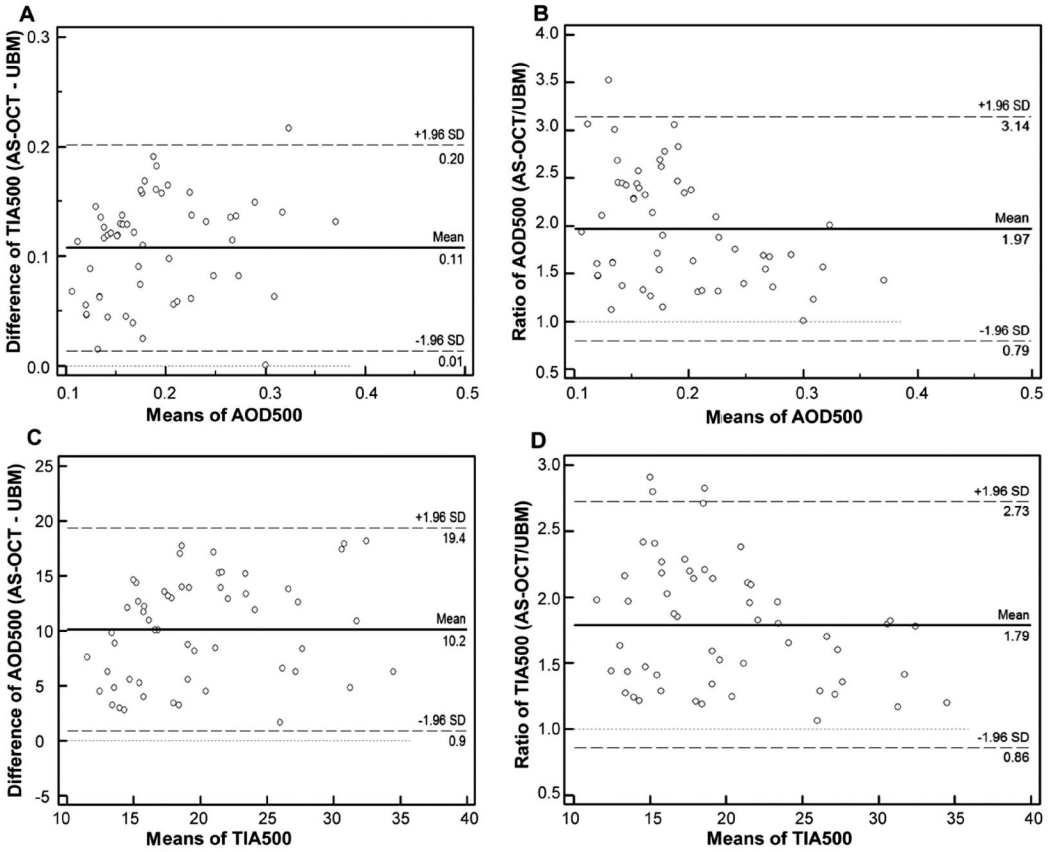

Figure 3 Bland-Altman plots of AOD500 and TIA500 measured by UBM and AS-OCT A and C: The differences of TIA500 and AOD500 measured by UBM and AS-OCT. B and D: The ratios of TIA500 and AOD 500 measured by UBM and AS-OCT. The ratio variations are much bigger when the mean values are smaller.

Table 4 Coefficient variation of 500 μm and 750 μm measurements

%

Measurements	500 μm from SS	750 μm from SS
TIA	34.26	31.83
ACA	42.20	39.77
AOD	41.41	37.71
TISA	47.75	44.66

TIA: Trabecular iris angle; ACA: Anterior chamber angle; AOD: Angle opening distance; TISA: Trabecular iris space area; SS: Sclera spur.

and inferior quadrants, which was consistent with previous findings[21-22].

The TM is the primary drainage structure for aqueous humour and is intimately related to the pathophysiology of glaucoma. The TM extends for 500-800 μm from the SS[23-24]. It is believed that there is no significant association between TM width and angle parameters [23]. In the current study, the coefficient of variation of the 500 μm group was larger than that of the 750 μm group in every quadrant. We speculated that structures like the plateau iris and recess of peripheral iris might have more influence on parameters at 500 μm, which means that AOD750 would be more steady and accurate in reflecting the scale of aqueous humour outflow blockade than AOD500, and help clinicians to estimate goniosynechia. Therefore, we recommend using parameters at 750 μm anterior to the SS for screening and follow-up of narrow angles.

Currently, TD-AS-OCT, Pentacam or Orbscan are widely used for AC measurements [3]. Some studies have compared SD-OCT and UBM in terms of the quantitative angle measurements and suggested that they do agree [8,25]. Radhakrishnan *et al* [18] have compared the specificity and sensitivity of gonioscopy, TD-AS-OCT and UBM in identifying narrow angles. The ACA parameters measured by OCT and UBM had similar mean values, reproducibility, and sensitivity and specificity profiles. Mansouri *et al*[26] compared the accuracy in measurement of the ACA by UBM and TD-AS-OCT. They found that AS-OCT measurements are significantly correlated with UBM measurements but show poor agreement with each other. They think that TD-AS-OCT cannot replace UBM for the quantitative assessment of the AC angle. In the current study, we used SD-OCT instead of TD-OCT. AOD500 and TIA500 in superior, inferior, nasal and temporal quadrants were examined, and the average values were accepted for analysis of correlation between the techniques. Bland-Altman plots were used to evaluate whether these two different techniques could be alternatives in clinical use. As demonstrated in Figure 3, for the same quadrant in the same eye, the smaller the mean value of the two methods, the greater the ratio

between them. This indicated that as the iris root approaching the TM, it was hard for UBM to discern the presence of goniosynechia or outflow block. In other words, UBM had a higher probability to underestimate TIA and AOD in narrow angles. This might explain why patients could keep a relatively low and stable IOP while UBM examinations revealed a wide range of goniosynechia.

UBM requires patients to be in the supine position. Although topical anaesthesia is applied, contact between the eye cup and couplant still make patients uncomfortable. Moreover, the eye cup and the couplant may affect the angle structure by gravity and pressure. AS-OCT is a newer instrument that requires patients to be in the seated position and there is no contact with the eyeballs, which makes it more practical and the ACA structure is more similar to the natural configuration. RS-3000 AS-OCT had the disadvantage of displaying angle recess area and structures behind the iris but could gave the precise location of the SS and identified the separation between the iris root and the TM (Figure 2). UBM was unable to resolve different tissues when the separation between them was too small. Both UBM and AS-OCT could show the SS with high reproducibility (Figure 2), which means TIA (use SS as vertice while measuring) should produce a smaller measuring error than ACA (use summit of AC as vertice while measuring). In the current study, TIA500 and AOD500 measurements by two methods were correlated in every quadrant except for the nasal quadrant. The two groups had statistically significant difference, even though they were not significantly different in clinical application [6,20]. Our findings were consistent with the study of Wang *et al* [20], they compared ACA width measurements by UBM and high and low-resolution TD-OCT, and found that low-resolution OCT was similar to UBM for most of the studied angle measurements, but high-resolution OCT tended to give larger measurements compared to low-resolution OCT and UBM. The difference in resolution between the three methods, the outer illumination of high-resolution OCT, different image processing algorithms, and the air-cornea and cornea-aqueous humour interface distortion of coherent light may have contribute to the differences. This might be an explanation to the results carried out by Mansouri *et al*[26]. Aptel *et al* [27] used SD-AS-OCT and TD-AS-OCT to measure AC parameters in healthy participants, and the two devices were consistent for all the parameters except for the AC depth and SS angle.

The extent of goniosynechia could influence the treatment choices for PAC and PACG. Comparing the images obtained from our two techniques, we believed that SD-AS-OCT has a major advantage over UBM in estimating AC width. The resolution difference between UBM and SD-AS-OCT might be responsible for the measurement error. First, the RS3000 OCT had better axial resolution of 7 μm compared to 50 μm provided by UD-6000 UBM. OCT could give the precise location of the SS, while the lack of image contrast made UBM incapable of such discernment when the separation between the TM and iris root was too small. Second, the two methods might not have scanned at the same location, which could have led to the different results. With a real-time scanning system and inward aiming light, it was much easier for SD-AS-OCT to locate the exact same target limbus position. UBM required patients to follow the external guidance light, meaning that the probe was perpendicular to the target tissue. The reproducibility depended on the operator's experience and patient's coordination. In the current study, we tried to eliminate this error by repeating UBM three times. Moreover, the UBM and SD-AS-OCT images were processed with a built-in programme, and the different analytical software of the two procedures might have accounted for the discrepancy in the results. SD-AS-OCT has better definition of interfaces between different tissues and less background noise, which might be helpful for the software to recognize and calculate. The low resolution of UBM could have caused minute differences that accumulated into a significant difference in the calculation of angle recess area.

There were some limitations to the current study that might be improved in future studies. First, all the patients had narrow ACAs. Comparison of UBM and SD-AS-OCT for evaluation of open angles needs further investigation. Second, we chose inward rather than outward guidance light to minimise eye movement and aimed for the natural configuration of the ACA. However, whether the measurements with the two type of guidance light were consistent should be validated. Third, because the coherent light was not perpendicular to the target tissue, the image clarity was not as good as in some previous studies that used outward guidance light. Improvement in analytical software and new image processing algorithms should be developed.

In conclusion, both UBM and SD-AS-OCT are efficient tools for follow-up during the course of PACG. However, SD-AS-OCT was capable of providing angle images with fine anatomical structures, which was more useful in quantitative assessment of a narrow or closed angle. ACA parameters measured by SD-AS-OCT were well correlated with those from UBM. SD-AS-OCT provided larger measurements of TIA500 and AOD500 compared to UBM in patients with narrow ACA, but this was not clinically significant. Parameters measured by SD-AS-OCT at 750 μm anterior to the SS appear to be less variable than those at 500 μm and are useful clinically. We recommend using parameters at 750 μm anterior to the SS for screening and follow-up of PACG and PAC. With real-time monitoring of imaging, SD-AS-OCT is a non-contact apparatus with high

resolution; it is user friendly and is a promising method for screening individuals at risk for developing PACG.

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