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Authors
Zhao, Tong
Zhao, Mengya
Xie, Qinghong
et al.

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Repeatability and reproducibility of anterior chamber angle measurement with Swept-Source Optical Coherence Tomography in Patients with Primary Angle Closure Suspect

Tong Zhao[1,2], **Mengya Zhao**[1,3], **Qinghong Xie**[1], **Christopher W. Fong**[1], **Jeremy Chen**[1], **Yingna Liu**[1], **Hui Feng**[4], **Shuning Li**[4], **Benjamin F. Arnold**[1,5], **Tin Aung**[6,7], **Mingguang He**[8,9], **Julius T. Oatts**[1,*], **Ying Han**[1,*]

[1]Department of Ophthalmology, University of California, San Francisco, San Francisco, CA

[2]Department of Ophthalmology, China-Japan Friendship Hospital, Beijing, China

[3]Department of Ophthalmology, Shanghai General Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China.

[4]Beijing Tongren Eye Center, Beijing Tongren Hospital, Beijing Ophthalmology & Visual Science Key Lab, Capital Medical University, Beijing, People's Republic of China

[5]Francis I. Proctor Foundation, University of California, San Francisco, San Francisco, CA

[6]Singapore Eye Research Institute, Singapore National Eye Centre

[7]Department of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore

[8]State Key Laboratory of Ophthalmology, Clinical Research Center, Zhongshan Ophthalmic Center, Sun Yat-Sen University, Guangzhou, China

[9]Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, East Melbourne, VIC, Australia

Abstract

Purpose: To evaluate the inter- and intra-observer reliability of anterior chamber (AC) angle measurements obtained by swept-source optical coherence tomography (SS-OCT).

Methods: Forty-eight consecutive patients diagnosed with primary angle closure suspect (PACS) were included. Three masked observers at different training levels (one glaucoma specialist, one ophthalmology resident and one pre-medical college student) measured 192 SS-OCT images of the PACS patients. One observer (the glaucoma specialist) repeated measurements 1 week later. SS-OCT parameters included: Anterior segment volume, including corneal, AC, and iris volume; anterior segment dimensions, including AC depth and width (ACD, ACW), and lens vault (LV); and angle parameters, including angle opening distance (AOD), angle recess area

[*]Corresponding authors: Julius T. Oatts and Ying Han, 10 Koret Way, Department of Ophthalmology, San Francisco, CA94143, USA. Tel: 1-415-476-3321, ying.han@ucsf.edu.

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(ARA), trabecular iris space area (TISA), and the trabecular iris angle (TIA). Intraclass correlation coefficients (ICCs) were used to measure reliability.

Results: For inter-observer reproducibility, ICCs of corneal, AC, and iris volumes were 0.952 to 0.998. ICCs of ACD at all axes were above 0.989. ICCs of ACW and LV were smallest in the 90 −270 axis (0.751 and 0.768) but not significantly different from other axes. ARA, TISA and TIA at all angles had significantly smallest ICCs 250 μm from the scleral spur compared with 500 μm and 750 μm. The ICCs comparing observers with different training levels had similar ranges and followed similar trends. For intra-observer repeatability, the smallest ICC was 0.843. Decreasing AC depth correlated with increased inter-observer reproducibility.

Conclusions: We found excellent intra-observer repeatability for all SS-OCT parameters. Angle measurements have more variation among the observers when taken 250 μm from the scleral spur. Shallow AC might lead to more variability for angle parameters. Non-expert observers may be recruited for high quality image grading with standard training.

Keywords

anterior chamber; ss-OCT; glaucoma; angle closure; imaging

Introduction

Anterior chamber (AC) angle evaluation is essential for the classification of glaucoma and determination of appropriate treatment. In comparison to the gold standard for angle evaluation, gonioscopy,[1–3] advanced imaging technology is able to produce objective and quantitative data necessary for research and clinical care. Traditional anterior segment optical coherence tomography (AS-OCT) allows for detailed non-contact visualization of the AC angle structures, with high repeatability and reproducibility and good agreement between AS-OCT and gonioscopy.[2, 4] Individual cross-sectional images of the angle are obtained at certain meridians, a process which can be limited by a slow A-scan rate and can fail to provide an assessment of all 360 degrees of the angle. Evaluation of the entire angle is essential when evaluating patients with primary angle closure disease (PACD).

Newer technology, swept-source optical coherence tomography (SS-OCT, CASIA SS-1000, Tomey Corporation, Nagoya, Japan), with an acquisition speed of 30,000 A-scans per second, can obtain 128 meridional scans (256 images) in 2.4 seconds. This fast scan rate decreases motion artifact and provides higher resolution images. Additionally, a larger number of cross-sectional images allows for more detailed information of the entire circumference of the angle and more accurate calculation of corneal, iris, and AC volumes.

However, in the process of image analysis, correct identification of scleral spur (SS) and angle recess (AR), the key anatomic landmarks, is crucial for both traditional AS-OCT and SS-OCT. The locations of SS and AR may vary among different graders, leading to differences in measurement of the same angle parameters. In most situations, the system-generated automatic marking of these two landmarks is not accurate and needs manual correction. Although SS-OCT has demonstrated high repeatability and reproducibility for angle measurements in healthy subjects,[5, 6] anatomic landmarks can be difficult to visualize in patients with PACD. Arguably, in terms of diagnostic and treatment value, this population would benefit most from precise measurements of AC structures using SS-OCT, where the consistency of the labeling SS-OCT images has not been studied.

The purpose of this study was to evaluate the intra- and inter- observer reliability of AC angle measurement using SS-OCT in patients with primary angle closure suspect (PACS), the most commonly encountered type of PACD.

Methods

Subject Recruitment

Fifty consecutive patients diagnosed clinically with PACS were recruited from the glaucoma clinic in the Department of Ophthalmology at Beijing Tongren Hospital. PACS was defined as iridotrabecular contact with non-visualization of the posterior trabecular meshwork for at least 180 degrees on gonioscopy without peripheral anterior synechiae or elevated intraocular pressure.[7] One eye from one patients was randomly selected for this study. Patients were excluded if they had additional ocular pathology (excluding cataract), prior iris laser treatment or intraocular surgery, a history of intraocular inflammation, trauma, congenital malformation, secondary angle closure, or a prior episode of acute primary angle closure in either eye. The study was conducted in accordance with the Declaration of Helsinki and approved by the institutional review board of both Bejing Tongren Hospital and University of California, San Francisco. Patients underwent a complete ophthalmic examination by a glaucoma specialist (LSN) including slit lamp microscopy, intraocular pressure measurement with Goldmann applanation, gonioscopy using a three-mirror gonioprism (Volk G3), and SS-OCT imaging of both eyes.

SS-OCT imaging

All patients were imaged by a masked examiner (FH) with SS-OCT (CASIA SS-1000, Tomey Corporation, Nagoya, Japan) using the AC angle scan protocol.[5] During scan acquisition, the upper eyelids were routinely retracted to decrease superior eyelid artifacts, and an eyelid speculum was used when necessary. The right eye was chosen as the study eye if both eyes met inclusion criteria.

Measurement of volumes, AC and angle parameters

The Tomey Software (Version 7M.1) was used for image analysis using a pre-specified standardized grading protocol as previously described.[8] Both the scleral spur and the angle recess were manually labeled and anterior segment traces were manually adjusted when required to correct segmentation errors. Next, the following parameters were calculated automatically: (1) anterior segment volume including corneal, AC, and iris volume (CV, ACV, IV); (2) anterior segment dimensions including AC depth and width (ACD, ACW), and lens vault (LV) at four axes: 0–180, 45–225, 90–270, and 135–315; (3) angle parameters including angle opening distance (AOD), angle recess area (ARA), trabecular iris space area (TISA), and the trabecular iris angle (TIA) at 0, 45, 90, 135, 180, 225, 270, and 315. The definition of the parameters: ACD: The perpendicular distance from the corneal endothelium at the corneal apex to the anterior lens surface. More specifically, ACW: The distance between the scleral spurs of both sides on the meridian. LV: The perpendicular distance between the anterior pole of the crystalline lens and the line drawn between the two scleral spurs (same line used to define ACW). AOD: The perpendicular distance measured from the trabecular meshwork at 250, 500, and 750 μm anterior to the scleral spur along the anterior iris surface (AOD 250, AOD 500, AOD 750). ARA: The enclosed triangular area demarcated by the anterior iris surface, trabecular meshwork, and corneal endothelium out to a distance of 250, 500, and 750 μm from the scleral spur (ARA 250, ARA 500, ARA 750). TISA: The trapezoidal area with 4 boundaries: the line segment of AOD; a line drawn from the scleral spur perpendicular to the plane of the inner scleral wall to the opposing iris; the corneoscleral wall; anterior iris surface (TISA 250, TISA 500, TISA 750). TIA: The angle measured with the apex in the angle recess and the arms of the angle passing through the two endpoints of AOD segment (TIA 250, TIA 500, TIA 750). A representation of these parameters is shown in Figure 1.

Three observers at different training levels were selected for this study: one glaucoma specialist (Observer 1), one ophthalmology resident (Observer 2), and one pre-medical college student (Observer 3). SS and AR were identified as previously described.[9] A basic overview of eye anatomy and training on SS-OCT image interpretation by a glaucoma specialist (HY) were conducted prior to the study. The training process included a one-on-one session focusing on: 1. Identification of the cornea, sclera, and iris on SS-OCT images. 2. Instruction on how to identify the SS on SS-OCT images, defined as a point shaped as inward scleral obtrusion associated with a change in the curvature of the anterior chamber angle wall. 3. Instruction on how to identify the AR, defined as the junction where the peripheral anterior iris meets the angle wall. 4. The trainee needed to correctly identify the SS and AR in 90% of the training images specifically selected for this training purpose 10 sample images to complete the training. The 10 sample images used for training were not included in the study analysis. After the training phase, the three masked observers (Observer 1, 2, 3) rated all images independently to evaluate the inter-observer reproducibility. Observer 1 re-rated images 1 week after the first grading for intra-observer repeatability assessment, masked to prior measurements.

Statistical analyses

We measured the reliability of AS-OCT measurements between each observer pair (inter-observer reproducibility) and within Observer 1 (intra-observer repeatability) using the intraclass correlation coefficient (ICC), which combines correlation and agreement between measurements into a single summary.[10, 11] We defined the ICC as: $ICC = \frac{\sigma_b - \sigma_w}{\sigma_b + (k-1)\sigma_w}$, where k is the number of raters (k=2 in all comparisons), σ_b is the between-patient variability, and σ_w is the within-patient variability. We estimated the ICC using a one-way ANOVA with a random effect for patient using the psych package in R.[12] ICC values >0.7 generally indicate high levels of agreement[13].

To study the effect of measurement angle on reliability of anterior chamber measurements, we estimated the difference in the ICC between 270 and other angles. We conducted a similar analysis to study the effect of measurement distance on reliability of angle parameters by estimating the difference in ICC between 250 μm and other distances, stratified by measurement angle. We computed percentile 95% confidence interval of ICC differences with a nonparametric bootstrap that resampled patients with replacement (1,000 replicates).

To study the effect of anterior chamber depth on SS-OCT parameters, we summarized each eye's ACD using on the average of Observer 1 ACD measurements. We modeled the difference in SS-OCT parameters between raters as a function of ACD using a linear mixed model that included a random effect for patient.[14] We assessed the assumption of linearity in each analysis with comparisons to non-parametric, locally weighted regression fits. Statistical analyses were performed using R version 3.6.1. P <0.05 was considered statistically significant, equivalent to 95% confidence intervals excluding zero.

Results

After excluding 2 patients with poor quality images, 48 eyes from 48 patients with PACS were included with a mean age of 58.3±6.8 years. Forty-two (87.5%) were female. The average ACD was 2.36±0.33 mm. Occasionally, low quality images at different meridians led to the inability to visualize SS and/or AR, so these individual scans were excluded from the study. The number of high-quality images used in analysis at each axis were 48, 39, 39, 42, 48, 47, 41 and 46 (corresponding to 0°, 45°, 90°, 135°, 180°, 225°, 270°, and 315°).

SS-OCT parameters were grouped into 3 categories: dimensions (ACD, ACW and LV), angle parameters (AOD, ARA, TISA, and TIA), and volumes (AC volume, corneal volume, and iris volume). For inter-observer reproducibility between the ophthalmology resident and pre-medical college student, high values of ICC (0.610–0.988) were observed (Supplementary table 1). As for parameters for anterior chamber dimensions, ICCs of ACD at all axes were 0.989–0.997. ICC of ACW in the 90–270 axis was 0.751 while ICCs in all other axes ranged from 0.803 to 0.992. LV also had the smallest ICCs in the 90–270 axis (0.768). There was a trend of lower measurement reliability in the 90–270 axis, though not significant at the 95% confidence level (Figure 2). As for angle parameters, ICC of ARA in the 0 axis 250 μm from the scleral spur (ARA 250) was the smallest (0.610) compared to ARA 500 and ARA 750 (0.778, 0.806) at the same axis. Similar findings were observed at all other axes. In addition, TISA 250 and TIA 250 at all axes also had the smallest ICCs when compared to corresponding measurements 500 and 750 μm from the scleral spur. When calculating the differences of ICCs at 250 and 500 or 750 μm, we found the differences below 0 at almost all angles with either TIA, ARA or TISA, and at certain angles the differences were significant at the 95% confidence level (Figure 3, Supplementary Figure1 and 2). ICCs of AOD at all angles ranged from 0.702 to 1.000 without significant differences based on distance from the scleral spur. For anterior chamber volume, ICC was high among all 3 observers for iris, corneal, and AC volumes (0.952, 0.998 and 0.998, respectively).

We then compared the ICCs between the glaucoma specialist (Observer 1) and the ophthalmology resident (Observer 2), which ranged from 0.641 to 0.985 (Supplementary table 2). When comparing the glaucoma specialist (Observer 1) and the pre-medical college student (Observer 3), the ICCs were between 0.651 and 0.999 (Supplementary table 3). In both of these two comparisons, ICCs followed all the same trends observed above.

Finally, we studied whether the inter-observer agreement depended on ACD, that is, whether a shallower anterior chamber is associated with larger difference in the SS-OCT measurements. Most of the SS-OCT parameters showed no significant relationship with ACD, except LV and ACW. The difference in LV and ACW between the ophthalmology resident (Observer 2) and the pre-medical college student (Observer 3) was negatively correlated with ACD (LV, $\beta = -0.165$, $P < 0.001$; ACW, $\beta = -0.239$, $P = 0.002$), namely the inter-observer difference increased with decreased ACD. The differences in LV and ACW between the glaucoma specialist (Observer 1) and the pre-medical college student (Observer 3) also showed the same association with ACD (LV, $\beta = -0.171$, $P < 0.001$; ACW, -0.252, $P < 0.001$) (Table 1, Figure 4). However, there was no significant association between ACD and differences in LV or ACW measured by the glaucoma specialist (Observer 1) and the ophthalmology resident (Observer 2). (Table 1, Figure 4).

Intra-observer measurements showed excellent repeatability with ICCs ranging from 0.927 to 0.998 in anterior segment volumes and dimensions. For AC angle parameters, ICCs of intra-observer repeatability ranged from 0.843 to 0.988 (Supplementary table 4).

Discussion

Our evaluation demonstrated high repeatability and reproducibility of AC angle measurements using SS-OCT among masked observers. Currently, software-enabled automatic measurement of AC angle structures relies on manual identification of the SS and AR. The AR is the apex of the angle recess, and can be challenging to be identified, particularly in patients with narrow angles. In our study, we found that TIA and ARA, parameters which depend on both SS and AR, had lower ICCs than AOD and TISA, which depend only on SS. This finding suggests that variability in labeling AR may contribute to these differences. The SS is a protrusion of the sclera into the anterior chamber connecting the base of the trabecular meshwork and ciliary muscle fibers. It is identified on SS-OCT by following the boundary between the longitudinal fibers of the ciliary muscle (hypo-reflective) and the sclera (hyper-reflective) until they meet in the anterior chamber. The newer SS-OCT provides significant improvement over time-domain OCT instruments for examination of the angle structures including excellent visibility of the scleral spur, with a detection rate as high as 98% in the nasal and temporal quadrants.[9] Notably, compared with Cirrus spectral domain AS-OCT (840 nm), the Casia SS-OCT uses a longer laser wavelength (1310 nm) which enhance tissue penetration, but reduces visualization of the angle structures.[9] A study using older time-domain AS-OCT showed that the inferior and superior angle had the worst visibility of the scleral spur.[15] We found no significant difference in ICCs comparing the 90–270 axis to other axes in spite of the fact that traditionally, the 90–270 axis is less reliable. Although eyelid position may affect quality of images, particularly superiorly and particularly in Asian patients who may have narrow palpebral fissures,[16, 17] with appropriate technique and careful attention, high quality images can be obtained along the 90–270 axis to provide detailed angle information.

Based on previous studies,[15] we investigated angle parameters 250 μm from the scleral spur, finding that measurements at this distance were less consistent among the 3 observers than measurements taken at 500 or 750 μm from the scleral spur. A few papers have studied interobserver variation and its relationship to the distance at which angle parameters are measured. Similar to our study, Console et al.[18] found higher variance of the AOD 250 compared to AOD 500 or 750, with measurements nearer to the manually labeled scleral spur leading to more variance. In our study, we found the lowest ICCs for nearly all angle parameters at all axes for measurements taken at 250 μm. This is consistent with difficulty in identifying the SS and AR, particularly in patients with narrow angles. The closer to the scleral spur the angle parameter is measured, the more dependent it is on exact identification of the scleral spur and angle recess. Our study indicated that angle parameters taken at 500 or 750 μm from the scleral spur provide more reliable measurements with less measurement variation.

Majority of the SS-OCT parameters have no relationship between grading difference of any of the two observers and AC depth, except LV and ACW. Our finding that the difference in LV or ACW measurements increased in eyes with shallower chambers is consistent with a previous study on traditional spectral AS-OCT showing that the visibility of the scleral spur was positively correlated with ACD.[15] The reasons why narrow angles tended to have invisible scleral spurs include: (1) The limited space between two high-reflectivity surfaces (the corneoscleral wall and the iris) compromises SS visualization, and (2) the structure of the SS is affected following the development of angle closure.[15] Differences in LV or ACW between the glaucoma specialist and ophthalmology resident did not correlated with ACD, while differences between them and the pre-medical colleague correlated with ACD. Specialized ophthalmology experience may aid in consistent identification of the SS to some degree, however, ICC of the LV and ACW between any of the two observers were all greater than 0.7, indicating the grading difference is minor.

Despite the varying experience levels of the 3 observers, we found excellent inter-observer reproducibility even in patients with PACS. Prior studies that unexperienced observers can be trained to the level of an expert[19, 20] are consistent with our results. Reliable SS-OCT anterior chamber measurements depend on accurate identification of the SS and AR, which is performed manually in most cases. SS-OCT produces a large number of images per eye per patient, and in order to accurately and efficiently analyze data, significant manpower is needed. This heavy workload would be difficult to cover with a trained ophthalmologist, thus non-expert observers are required to process the thousands of images. Achieving high levels of reliability relies on a strict, image-based, one-on-one training protocol with follow up checks to ensure accuracy. Additionally, the rise of artificial intelligence in ophthalmic imaging may ease the workload and make large volume angle analysis possible.

There are limitations to the study. First, only patients with PACS were included. Although this is the most common type of PACD, similar studies are needed to create more generalizable data. Second, only high-quality images were chosen for this study, and variations in image quality could change reliability. Finally, we did not record the difference before and after training for the non-expert to objectively quantify the training-related progress.

In conclusion, we found excellent agreement and intra-observer repeatability for all SS-OCT parameters. For most parameters, inter-observer reproducibility was also high. Angle measurements have more variation among the observers than volume or dimension parameters, especially when taken 250 μm from the scleral spur. Parameters measured 500 and 750 μm from the scleral spur may be chosen for future angle evaluation to improve reproducibility. Lastly, non-expert observers may be recruited for image grading with standard training.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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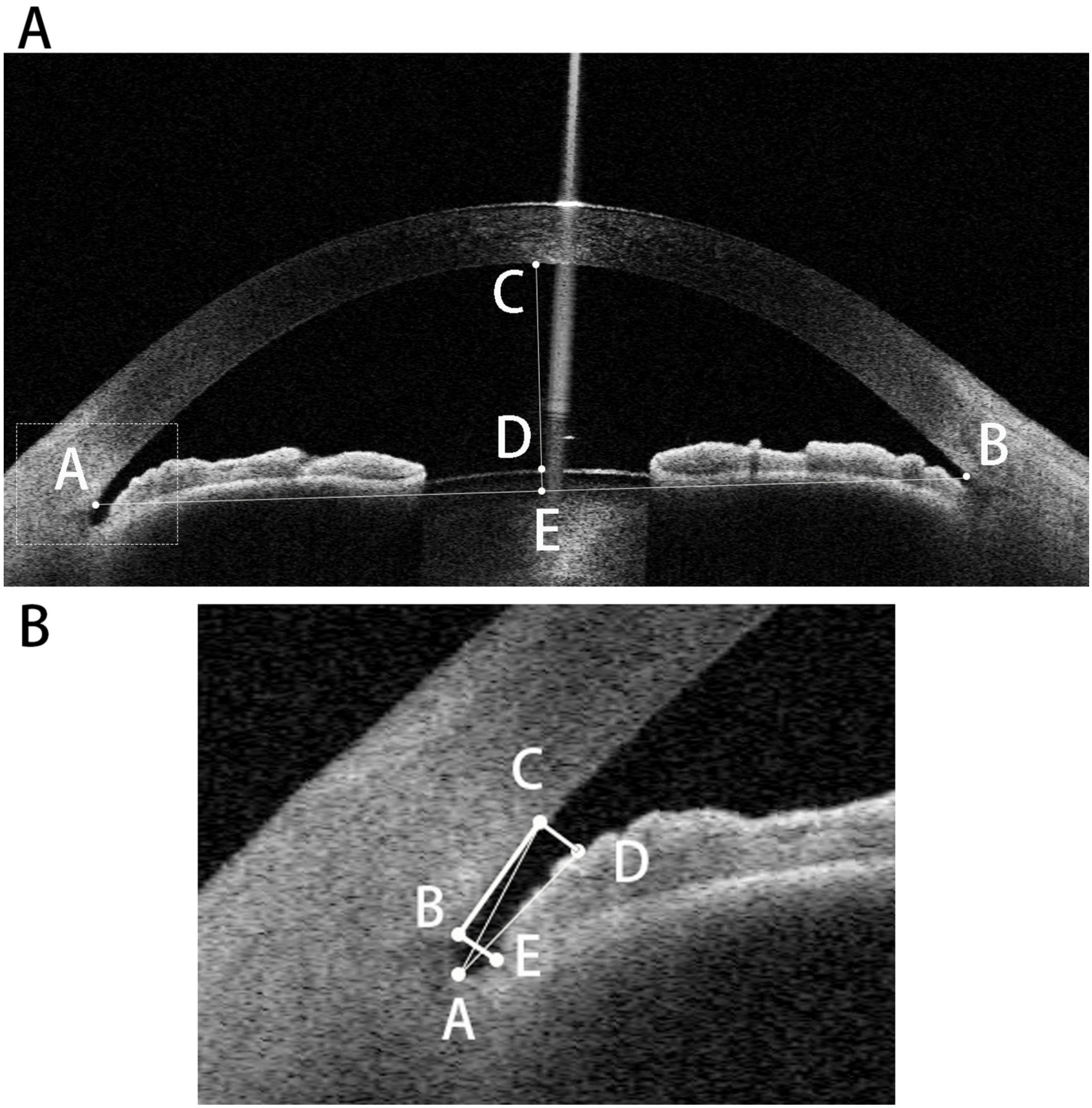

Figure 1.

Definition of the anterior segment parameters. A. The anterior segment dimensions. Point A and B, scleral spurs (SS) of both sides; point C, corneal endothelium apex; point D, the anterior lens apex; the line CDE is perpendicular to AB. The distance of line CD is anterior chamber distance (ACD); The distance of line AB is anterior chamber width (ACW); the distance of line DE is lens vault (LV), notably, the value of which is negative because of lens protrusion. B. The square part of Figure A showing the angle parameters, an example at distance of 750 μm from scleral spur. Point A, angle recess (AR); Point B, SS; Point C, 750 µm away from point A; line CD and BE are perpendicular to BC. The distance of line CD is angle opening distance (AOD); the angle CAD is trabecular iris angle (TIA); the area of trapezoid BCDE trabecular iris space area (TISA); the area of the polygon ABCDE is angle recess area (ARA).

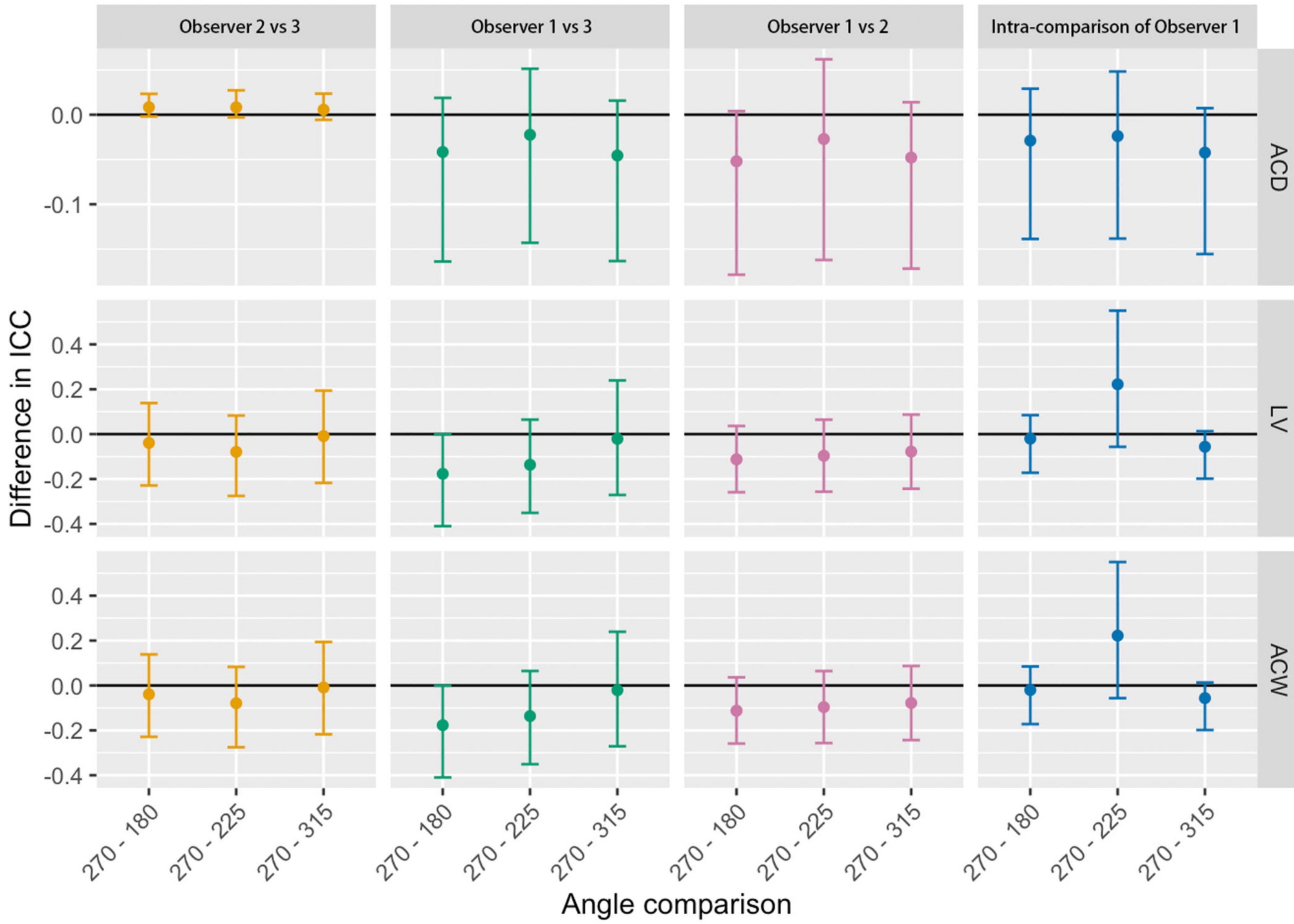

Figure 2.
Difference of ICCs between the 90–270 axis and other axes. Four columns represent paired comparisons of observers from left to right: Observer 2 vs Observer 3, Observer 1 vs Observer 3, Observer 1 vs Observer 2 and intra-comparison of Observer 1. The three rows represent anterior chamber measurements from top to bottom: anterior chamber depth (ACD), lens vault (LV) and anterior chamber width (ACW). For each chart, the horizontal coordinates "270–180", "270–225", "270–315" represent the difference between the 90–270 axis and the other corresponding axes (0–180, 45–225 and 135–315). None of the differences in ICCs were statistically significantly different at the P=0.05 level.

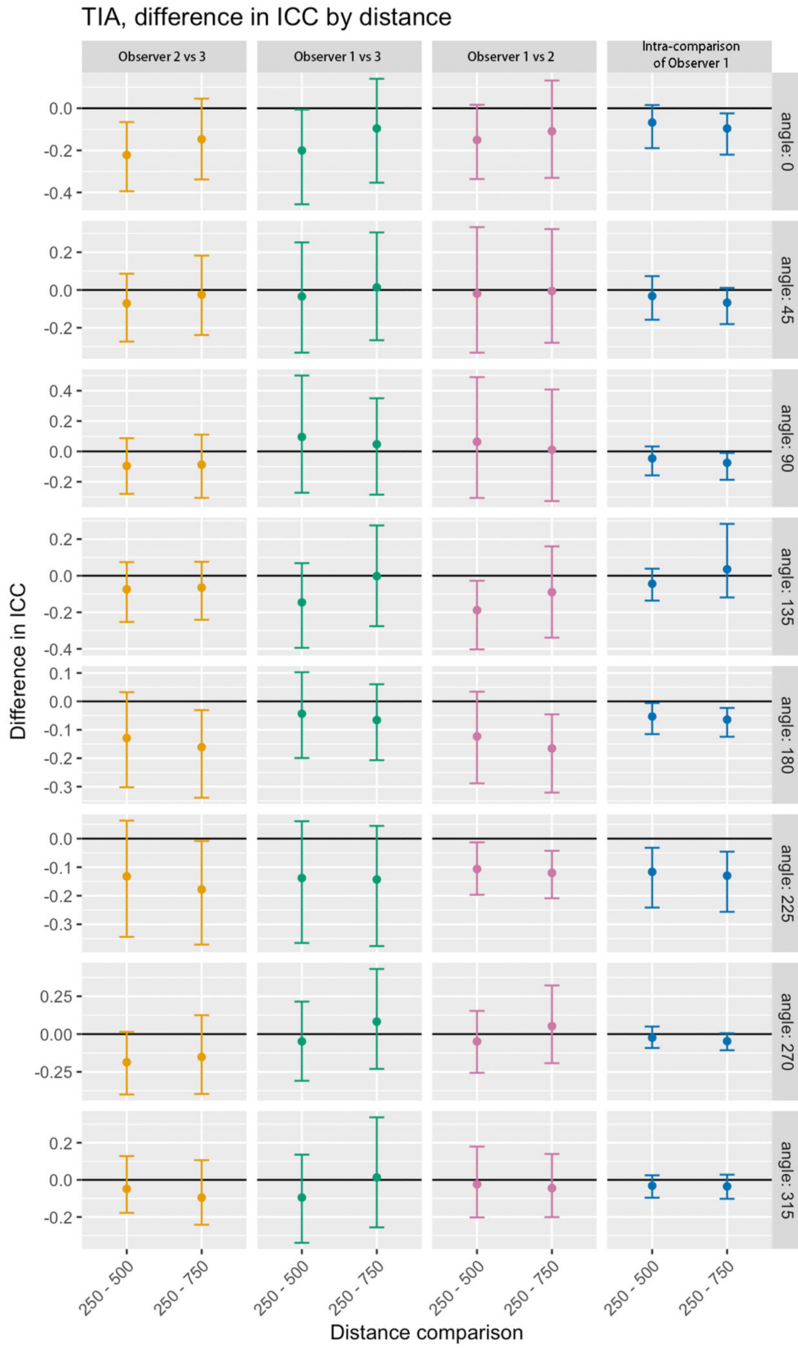

Figure 3.
Difference of ICCs of trabecular iris angle (TIA) by distance from the scleral spur. Four columns represent paired comparisons of observers from left to right: Observer 2 vs Observer 3, Observer 1 vs Observer 3, Observer 1 vs Observer 2 and intra-comparison of Observer 1. Rows represent different angles from 0 to 315. For each chart, the horizontal coordinates “250–500”, “250–750” mean the difference of 250 μm and 500, 750 μm. Most of the differences of ICCs were below 0, indicating the 250 parameters had lower ICC compared with others. Many of the confidence intervals exclude zero, which the differences

in ICCs are statistically different at the P=0.05 level, indicating statistically significantly less reliability of TIA 250 compared with other distances.

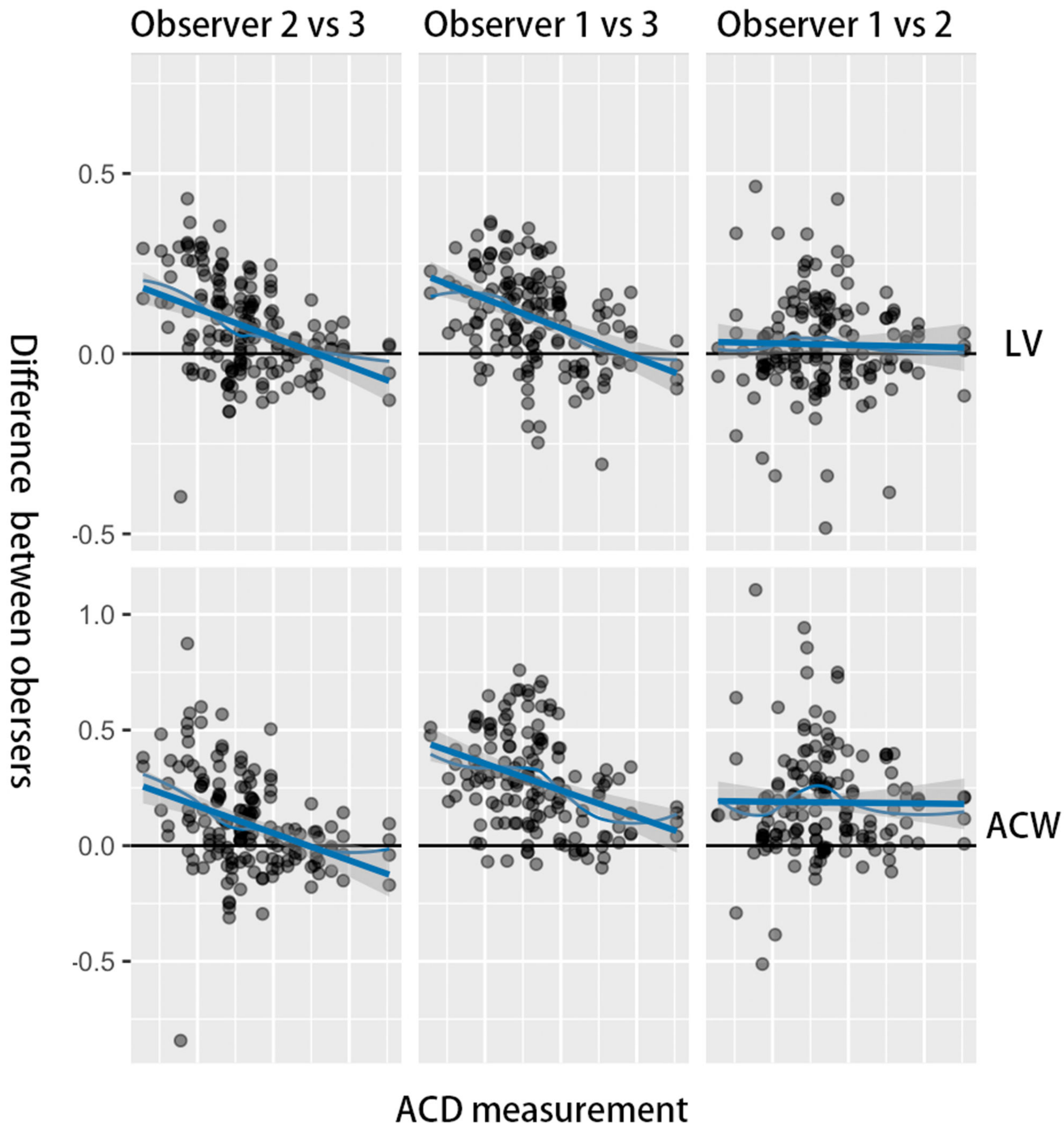

Figure 4.

Descriptive figures of the relationships between anterior chamber depth (ACD) and the difference of anterior chamber measurements between observers. Three columns represent paired comparisons of observers from left to right: Observer 2 vs Observer 3, Observer 1 vs Observer 3 and Observer 1 vs Observer 2. The two rows represent anterior chamber measurements from top to bottom: lens vault (LV) and anterior chamber width (ACW). The heavy line with shaded confidence interval is a linear fit, and the curve is a non-parametric, locally weighted regression smooth to assess the appropriateness of the linear fits. Significant negative associations were noted between ACD and inter-observer differences of LV/ACW in the comparison between Observer 2 and 3 as well as between Observer 1 and 3, but not between Observer 1 and 2.

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Table 1.

Regression of ACD and the inter-observer difference.

	Observers	β	Lower limit of 95% CI	Upper limit of 95% CI	SE	t	P value
ACD	Observer 2 vs 3	0.002	−0.023	0.027	0.013	0.136	0.892
LV		−0.165	−0.253	−0.077	0.045	−3.677	<0.001
ACW		−0.238	−0.389	−0.088	0.077	−3.096	0.002
ACD	Observer 1 vs 3	0.014	−0.031	0.059	0.023	0.606	0.544
LV		−0.171	−0.247	−0.095	0.039	−4.419	<0.001
ACW		−0.252	−0.366	−0.137	0.058	−4.302	<0.001
ACD	Observer 1 vs 2	0.012	−0.029	0.053	0.021	0.582	0.560
LV		−0.017	−0.108	0.075	0.047	−0.356	0.722
ACW		−0.042	−0.213	0.129	0.087	−0.479	0.632