Anterior Chamber Angle Imaging with Swept-Source Optical Coherence Tomography: Measuring Peripheral Anterior Synechia in Glaucoma

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Objective: To investigate the use of swept-source optical coherence tomography (OCT) for measuring the area and degree of peripheral anterior synechia (PAS) involvement in patients with angle-closure glaucoma.

Design: Cross-sectional study.

Participants: Twenty-three eyes with PAS (detected by indentation gonioscopy) from 20 patients with angle-closure glaucoma (20 eyes had primary angle-closure glaucoma and 3 eyes had angle-closure glaucoma secondary to chronic anterior uveitis [n = 2] and Axenfeld–Rieger syndrome [n = 1]).

Methods: The anterior chamber angles were evaluated with indentation gonioscopy and imaged by swept-source OCT (Casia OCT, Tomey, Nagoya, Japan) in room light and in the dark using the "angle analysis" protocol, which was composed of 128 radial B-scans each with 512 A-scans (16-mm scan length). The area and degree of PAS involvement were measured in each eye after manual detection of the scleral spur and the anterior irido-angle adhesion by 2 masked observers. The interobserver variability of the PAS measurements was calculated.

Main Outcome Measures: The agreement of PAS assessment by gonioscopy and OCT, the area and the degree of PAS involvement, and the intraclass correlation coefficient (ICC) of interobserver PAS measurements.

Results: The area of PAS (mean $\pm$ standard deviation) was 20.8 ± 16.9 mm^2 (range, 3.9–74.9 mm^2), and the degree of PAS involvement was 186.5 ± 79.9 degrees (range, 42–314 degrees). There was no difference in the area of PAS ($P = 0.90$) and the degree of PAS involvement ($P = 0.95$) between images obtained in room light and in the dark. The interobserver ICCs were 0.99 (95% confidence interval [CI], 0.98–1.00) for the area of PAS and 0.99 (95% CI, 0.97–1.00) for the degree of PAS involvement. There was good agreement of PAS assessment between gonioscopy and OCT images (kappa = 0.79; 95% CI, 0.67–0.91).

Conclusions: Swept-source OCT allows visualization and reproducible measurements of the area and degree of PAS involvement, providing a new paradigm for evaluation of PAS progression and risk assessment for development of angle-closure glaucoma.

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Peripheral anterior synechia (PAS) represents adhesional contact between the peripheral iris and the anterior chamber angle, which can be found in primary and secondary angle closure, acute angle closure, and chronic angle-closure glaucoma. The extent of PAS correlates with the level of intraocular pressure (IOP).[1,2] Measuring the degree of PAS and following its progression would be of relevance and importance for risk assessment of angle-closure glaucoma. Nevertheless, the examination of PAS has depended on indentation gonioscopy,[3] which largely provides qualitative or semiquantitative evaluation of PAS involvement. The advent of anterior segment optical coherence tomography (OCT) technology, including the Visante OCT (Carl Zeiss Meditec, Dublin, CA) and the slit-lamp OCT (SL-OCT, Heidelberg Engineering, GmbH, Dossenheim, Germany), allows noncontact, cross-sectional imaging of the anterior chamber angle.[4] However, the relatively slow scan speed of these instruments (2000 A-scan/s and 200 A-scan/s, respectively) has limited circumferential assessment of the angle and the extent of PAS involvement.

The Casia OCT (Tomey, Nagoya, Japan) is a commercially available swept-source OCT (swept-source laser wavelength of 1310 nm) recently introduced for anterior segment and anterior chamber angle imaging.[5,6] With a scan speed of 30 000 A-scans/s and an axial resolution of <10 μm, multiple high-resolution, cross-sectional images of the angle can be captured within seconds, facilitating examination and measurement of PAS. The objectives of this study

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were to demonstrate the application of the swept-source OCT for imaging PAS and quantify the extent of PAS in terms of the area and the degree of involvement.

Materials and Methods

Subjects

A total of 23 eyes of 20 patients with chronic angle-closure glaucoma with PAS detected by indentation gonioscopy were consecutively recruited for OCT imaging of the anterior chamber angle in the University Eye Center, Hong Kong Eye Hospital. Eyes receiving topical medication(s) affecting the pupil size were not included, but a history of laser iridotomy or trabeculectomy was not an exclusion criterion. Indentation gonioscopy was performed with a 4-mirror gonioprism at the lowest level of ambient illumination that permitted a view of the angle at 16× to 25× magnification. Gonioscopy images showing all quadrants of an eye were taken with a slit-lamp camera. The study was conducted in accordance with the ethical standards stated in the 1964 Declaration of Helsinki and approved by the local clinical research ethics committee with informed consent obtained.

Anterior Segment Optical Coherence Tomography Imaging

The swept-source OCT (Casia SS-1000 OCT) is a form of Fourier-domain OCT that uses a monochromatic tunable fast scanning laser source and a photodetector to detect wavelength-resolved interference signal.[5] All eyes were imaged in the dark (light intensity, 0.3 lux) and then in room light (light intensity, 368 lux) by a trained technician using the "angle analysis" protocol, which was composed of 128 radial B-scans each with 512 A-scans (16-mm scan length). This allowed 360-degree imaging of the whole anterior segment in 2.4 seconds. The subject fixated at an internal fixation target during the imaging. To avoid lid artifact, participants were instructed to pull down the lower lid against the lower orbital rim to expose the lower limbus while the technician elevated the upper lid against the upper orbital rim to expose the upper limbus. All images obtained had no lid artifacts.

Measurement of the Area and Extent of Peripheral Anterior Synechia Involvement

The anterior chamber angle was analyzed every 2.8 degrees from 0 to 359 degrees (i.e., 128 angle meridians were measured in each eye). The extent of PAS in each meridian was measured by the built-in software after manual detection of the scleral spur and the anterior irido-angle adhesion (the iris end point) (Fig 1). The software automatically aligned the scleral spur (visualized in red in the polar plot) and the iris end point (visualized in green in the polar plot) of individual cross-sectional OCT images and then computed the PAS area, which was defined as the area bound below the iris end point and above the scleral spur, and the degree of PAS involvement (Figs 2D and 3D). Although the area of PAS can assume different shapes, the high spatial analysis of the PAS (the anterior chamber angles were analyzed every 2.8 degrees) would provide a close capture of the size and the shape (in 2 dimensions) of the PAS. On average, it took approximately 15 to 20 minutes for measurement of the area and degree of PAS in each eye. The area and the degree of PAS involvement in each eye were measured by 2 masked observers (I.L., H.M.).

Statistics

Statistical analysis was performed using MATLAB R2010a (The MathWorks, Inc., Natick, MA). A single observer (I.L.) evaluated the presence (indicated by 1) and absence (indicated by 0) of PAS at individual clock hours in the gonioscopic and OCT images. The agreement of PAS assessment between gonioscopy and OCT was then evaluated with kappa statistics. A value between 0.0 and 0.2 indicates slight agreement, between 0.21 and 0.40 indicates fair agreement, between 0.41 and 0.60 indicates moderate agreement, between 0.61 and 0.80 indicates substantial agreement, and between 0.81 and 1 indicates almost perfect agreement.[7] The area of PAS and the degree of PAS involvement measured in room light and in the dark were compared with the Wilcoxon signed-rank test. The interobserver variability was calculated with intraclass correlation coefficient (ICC) (2, 1 [2-way random effects, absolute agreement]), and the interobserver agreement was examined with Bland–Altman plots. The ICC is a ratio of between-subject variance over total variance (within-subject variance + between-subject variance). $P<0.05$ was considered statistically significant.

Results

Table 1 shows the demographics of the study participants. All eyes had chronic angle-closure glaucoma, 20 eyes had primary angle-closure glaucoma, and 3 eyes had angle-closure glaucoma secondary to chronic anterior uveitis (n = 2) and Axenfeld–Rieger syndrome (n = 1). By taking all eyes into consideration, the area of PAS ranged from 3.9 to 74.9 mm^2 (mean ± standard deviation

Table 1. Peripheral Anterior Synechia (PAS) Measurements of 23 Eyes from 20 Patients with Chronic Angle-Closure Glaucoma (Peripheral Anterior Synechia Measurements Represent the Average Measurements by Two Observers)

Case	Age (yrs)	Sex	Diagnosis	Degree of PAS Involvement (°)	Area of PAS (mm^2)
A	83	F	PACG	77	8.5
B	83	M	PACG	203	10.9
C1	43	M	Uveitic glaucoma	309	14.6
C2	43	M	Uveitic glaucoma	259	35.6
D	63	M	PACG	221	34.7
E	81	F	PACG	113	20.2
F1	89	F	PACG	137	9.3
F2	89	F	PACG	149	10.2
G	62	M	PACG	280	27.8
H	83	F	PACG	185	39.3
I	50	M	PACG	92	6.8
J	75	F	PACG	224	9.9
K	70	M	PACG	220	27.6
L	67	F	PACG	165	12.6
M1	81	F	PACG	151	19.5
M2	81	F	PACG	42	4.0
N	83	M	PACG	130	6.9
O	66	M	PACG	314	74.9
P	49	M	PACG	84	8.3
Q	55	M	Axenfeld–Rieger syndrome	135	3.9
R	63	F	PACG	260	32.7
S	35	M	PACG	250	44.1
T	51	F	PACG	296	16.4

PACG = primary angle-closure glaucoma.

[SD], 20.8±16.9 mm^2), and the degree of PAS involvement ranged from 42 to 314 degrees (mean ± SD, 186.5±79.9 degrees). There was good agreement between gonioscopy and OCT assessment of the location of PAS with a kappa value of 0.79 (95% confidence interval [CI], 0.67–0.91). The areas of PAS measured in light and dark were 20.9±17.6 and 21.6±17.8 mm^2, respectively. For the degree of PAS involvement, the respective measurements were 187.8±87.5 and 189.4±83.7 degrees. There were no significant differences in the area ($P = 0.90$) and the degree of PAS involvement ($P = 0.95$) measured in light and dark. The interobserver ICCs were 0.99 (95% CI, 0.98−1.00) for the area of PAS and 0.99 (95% CI, 0.97−1.00) for the degree of PAS involvement. The average ± SD (range) differences in area of PAS and degree of PAS involvement between the 2 graders were 1.6±1.7 mm^2 (0.1−6.3 mm^2) and 9.8±6.8 degrees (1−22 degrees), respectively. Figure 4 shows the Bland−Altman plots of the PAS measurements by the 2 graders. The 95% limits of agreement for area of PAS and degree of PAS involvement were −4.5 to 4.6 mm^2 and −25.3 to 21.7 degrees, respectively. There was a proportional bias in the measurement of PAS area ($r = 0.586$; $P = 0.003$), but not for the degree of PAS involvement. The agreement between the graders increased with decreasing area of PAS.

Figure 2 shows an example (case C2, Table 1) with extensive PAS from 10 to 7 o'clock. The polar plot of PAS reveals the circumferential distribution of the PAS, involving 259 degrees, or 72% (259/360) of the angle, with an area of 35.6 mm^2 extending up to 2.7 mm beyond the scleral spur. Figure 3 demonstrates another example with chronic angle-closure glaucoma with trabeculectomy performed (case G, Table 1). The PAS was located from 10 to 6 o'clock, involving 280 degrees of the angle with an area of 27.8 mm^2 and extending up to 3.0 mm beyond the scleral spur around the sclerotomy. Although it is difficult to determine the patency of the sclerotomy with gonioscopy (Fig 3E), the anterior segment OCT image reveals no iris adhesion at the center of the sclerotomy, and the sclerotomy was patent (Fig 3F). Three-dimensional, 360-degree visualization of the PAS of cases C2 and G is shown in Videos 1 and 2 (available at http://aaojournal.org).

It is feasible to differentiate synechial angle closure from appositional angle closure with dynamic dark-light OCT imaging. For appositional closure, the angle was closed in the dark, whereas it was open in the light (Fig 5A). This is in contrast to eyes with synechial closure in which the angle remained closed independently of the lighting condition and pupil size (Fig 5B).

Discussion

This study demonstrated the feasibility of quantifying the area and the degree of PAS involvement for 360 degrees with swept-source OCT in patients with chronic angle-closure glaucoma. We showed that it is feasible to discriminate synechial angle closure from appositional angle closure by varying the lighting condition during the OCT imaging and that the measurements of the area and the degree of PAS involvement were reproducible. Anterior chamber angle imaging with swept-source OCT can become a new paradigm to assess PAS and monitor its progression once the short- and long-term variabilities of the technique are defined.

Documentation of PAS has been primarily based on gonioscopy assessment, most often quantified in terms of number of clock hour involvement. In a population-based survey, Foster and colleagues[8] showed that the proportion of eyes with PAS was positively associated with the angle width. By using a time-domain anterior segment OCT to measure the angle width, Su and colleagues[9] reported smaller angle-opening distance, trabecular iris space area, and angle recess area in eyes with PAS compared with those without. In patients with chronic angle-closure glaucoma, Aung and colleagues[1] showed that for each unit increase in clock hour of PAS, there was a 0.39-mmHg increase in the baseline untreated IOP and a significant correlation between vertical cup-to-disc ratio and clock hours of PAS ($r = 0.28$; $P<0.001$). The close association between the extent of PAS and the angle width and the level of IOP and the severity of optic disc damage in glaucoma signifies the importance of PAS measurement in primary angle closure and angle-closure glaucoma.

Optical coherence tomography outperforms gonioscopy in being a noncontact technique and able to measure the extent of PAS involvement to the precision of degree.

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Figure 1. Measurement of peripheral anterior synechia (PAS). An optical coherence tomography image at the 115-degree meridian was selected for measurement of PAS **(A)**. The scleral spur (*red dot*) and the anterior tip of the irido-angle adhesion (*green dot*) were detected manually **(B)**. A polar plot showing the distribution of PAS can then be constructed with reference to the locations of the scleral spur and the anterior irido-angle adhesion **(C)**. At the meridian of 115 degrees, the anterior irido-angle adhesion is located 2 mm beyond the scleral spur.

Figure 2. An example showing the imaging and measurement of peripheral anterior synechia (PAS) with swept-source optical coherence tomography (OCT) in an eye with angle-closure glaucoma secondary to chronic uveitis (case C2, Table 1). A total of 128 angle meridians were imaged, and the horizontal (0–180 degrees) **(A)** and vertical (90–270 degrees) **(B)** OCT images are shown. Three-dimensional reconstruction **(C)** of the OCT images reveals the morphology of the PAS in the superotemporal segment. A polar plot of the PAS is shown in **(D)**, with the *red line* representing the location of the scleral spur and the *green line* representing the location of the anterior tip of the irido-angle adhesion. I = inferior; N = nasal; S = superior; T = temporal.

Figure 3. An example showing the imaging and measurement of peripheral anterior synechia (PAS) with the swept-source optical coherence tomography (OCT) in an eye with primary angle-closure glaucoma with trabeculectomy performed (case G, Table 1). A total of 128 angle meridians were imaged, and the horizontal (0–180 degrees) **(A)** and vertical (90–270 degrees) **(B)** OCT images are shown. Three-dimensional reconstruction **(C)** of the OCT images reveals an iridectomy and the PAS in the superonasal segment. A polar plot of the PAS is shown in **(D)**, with the *red line* representing the location of the scleral spur and the *green line* representing the location of the anterior tip of the irido-angle adhesion. Note the patency of the sclerotomy cannot be determined with certainty with gonioscopy because of the presence of the iris adhesion **(E),** but a patent sclerotomy adjacent to and beneath the scleral flap (*) is evident in the OCT image (captured at the center of the sclerotomy) **(F)**. I = inferior; N = nasal; S = superior; T = temporal.

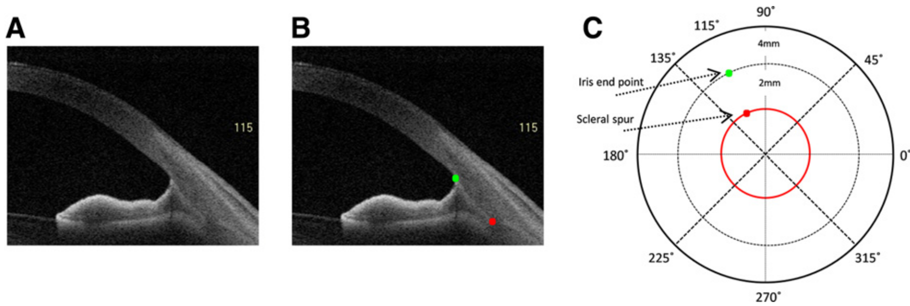
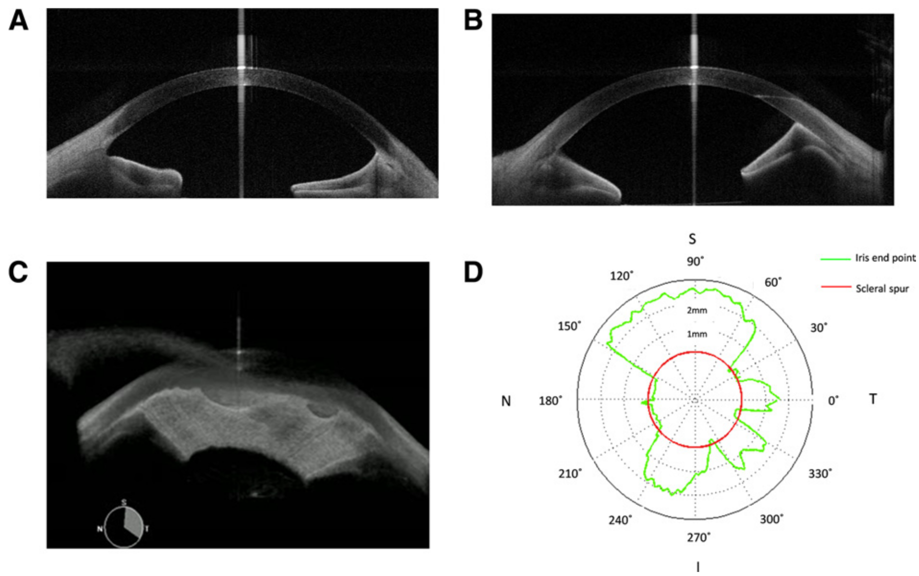


Figure 1.



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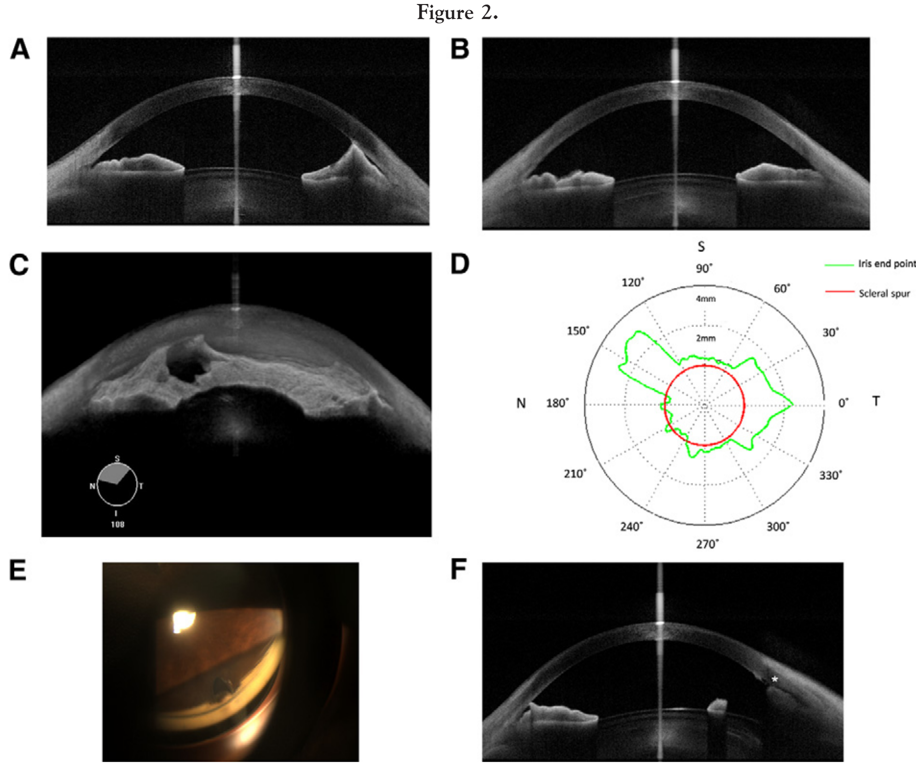

Figure 3.

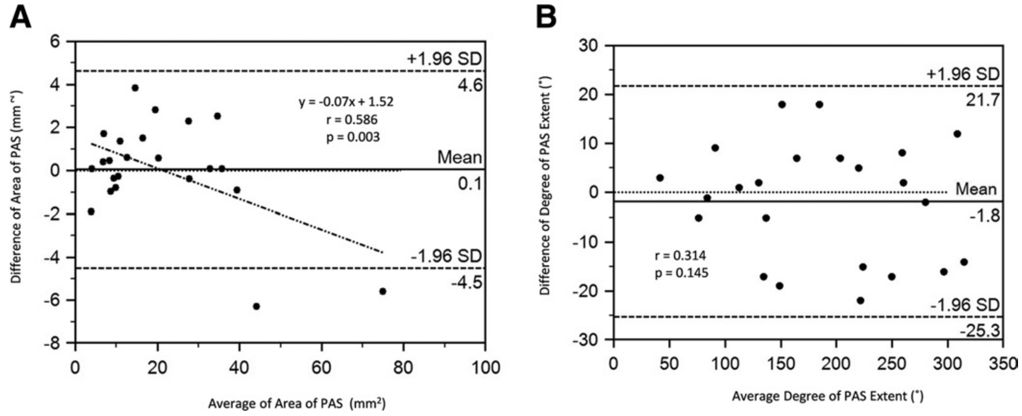

Figure 4. Bland–Altman plots illustrating the agreement of measurement of peripheral anterior synechia (PAS) area **(A)** and degree of PAS involvement **(B)** between 2 observers. SD = standard deviation.

Although it is not feasible to measure the dimensions of iris adhesion at the angle with gonioscopy, swept-source OCT analysis can measure the area of PAS and quantify the involvement in 2 dimensions (Figs 2D and 3D). In this study, the area of PAS ranged from 3.9 to 74.9 mm^2, and the degree of PAS involvement was between 42 and 314 degrees. These measurements are vital for assessment of PAS progression. A prospective study is currently underway to evaluate the role of OCT imaging in assessment of PAS progression and address its relationship with IOP and optic disc measurements in angle-closure glaucoma.

The major obstacles in measuring PAS are differentiating adhesional from appositional angle closure and detecting the scleral spur in regions of adhesional contact. Indentation gonioscopy is the conventional standard to differentiate adhesional from appositional closure. Although the technique of indentation also can be applied to OCT,[10] we showed in this study that synechial closure can be discriminated from appositional closure with dynamic dark-light imaging (Fig 5). Adhesional closure also differs from appositional closure in the angle configuration. Synechial closure often exhibits an obtuse configuration, whereas appositional closure almost always assumes an acute configuration. Although the scleral spur may not always be visible in regions with iris adhesion at the angle, it is possible to trace its location with reference to images at the adjacent meridians that have clear visibility of the scleral spur (with the assumption that the position of the scleral spur does not change in the adjacent angle meridians). The low interobserver measurement variability of the PAS area (ICC, 0.99) and the degree of PAS involvement (ICC, 0.99) indicate that the measurements of PAS were reproducible. It is interesting to note that proportional bias was evident only for measurement of PAS area but not the degree of PAS involvement between the observers (Fig 4). This is probably related to the fact that the former is a 2-dimensional measure, whereas the latter is a 1-dimensional measure. Measurement variability may affect PAS area more than the degree of PAS involvement when the PAS is extensive.

An advantage of using swept-source OCT for PAS assessment is its short scan time. Fewer than 3 seconds are required to image the angle morphology in high resolution circumferentially in 360 degrees. Another advantage of OCT imaging is its ability to discern the patency of scle-

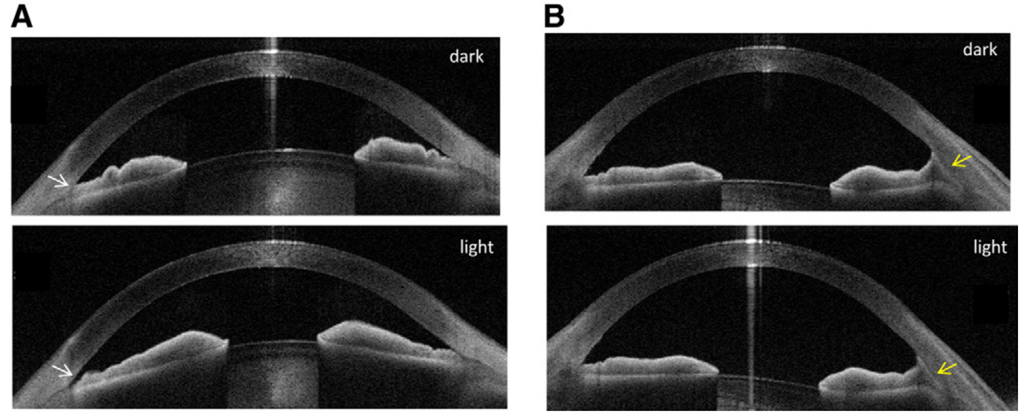

Figure 5. Discrimination of synechial angle closure from appositional angle closure with optical coherence tomography (OCT) imaging in light and dark. In appositional angle closure **(A)**, the angle assumes an acute configuration and the closed angle observed in the dark (*white arrow, top*) is open when it is imaged in the light (*white arrow, bottom*). In synechial angle closure **(B)**, the angle assumes an obtuse configuration and the angle remains closed (*yellow arrows*) independent of the lighting condition.

rotomy, which sometimes is difficult to visualize with gonioscopy when an iris adhesion is present (Fig 3E). However, OCT imaging is not without limitations. It cannot be used to visualize the pigmentation of the trabecular meshwork and the ciliary body; evaluation of these structures would require gonioscopy and ultrasound biomicroscopy, respectively. One shortcoming in the analysis of PAS is that the detection of the scleral spur and the anterior irido-angle adhesion was subjective. Analyzing multiple images for an eye could thus be time-consuming. For this reason, we analyzed only 128 angle meridians for each eye at a spatial resolution of 2.8 degrees. Although we believe this resolution would be sufficient for the detection and measurement of PAS, the resolution of the PAS analysis can be increased by including more OCT images in the scan. Developing software for automatic detection of the scleral spur and iris adhesion would be relevant to shorten the duration of analysis.

In conclusion, imaging the anterior chamber angle with swept-source OCT provides an efficient approach to visualize and quantify PAS. With a low measurement variability, measuring the area and degree of PAS involvement longitudinally would be useful to detect PAS progression in relation to IOP increase and glaucoma progression.

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Footnotes and Financial Disclosures

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