Detection of Primary Angle Closure Using Anterior Segment Optical Coherence Tomography in Asian Eyes

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Objective: To evaluate noncontact anterior segment optical coherence technology (AS-OCT) as a qualitative method of imaging the anterior chamber angle and to determine its ability to detect primary angle closure when compared with gonioscopy in Asian subjects.

Design: Prospective observational case series.

Participants: Two hundred three subjects were recruited from glaucoma clinics in Singapore with diagnoses of primary angle closure, primary open-angle glaucoma, ocular hypertension, or cataract. Both eyes (if eligible) of each patient were included in the study. Exclusion criteria were pseudophakia or previous glaucoma surgery.

Methods: Images of the nasal, temporal, and inferior angles were obtained with AS-OCT in dark and then light conditions. Gonioscopic angle width was graded using the Spaeth classification for each quadrant in low lighting conditions.

Main Outcome Measures: Angle closure was defined by AS-OCT as contact between the peripheral iris and angle wall anterior to the scleral spur and by gonioscopy as a Spaeth grade of 0° (posterior trabecular meshwork not visible). Comparison of the 2 methods in detecting angle closure was done by eye and by individual. Sensitivities and specificities of AS-OCT were calculated using gonioscopy as the reference standard.

Results: Complete data were available for 342 eyes of 200 patients. Of the patients, 70.9% had a clinical diagnosis of treated or untreated primary angle closure. Angle closure in ≥1 quadrants was detected by AS-OCT in 142 (71%) patients (228 [66.7%] eyes) and by gonioscopy in 99 (49.5%) patients (152 [44.4%] eyes). The inferior angle was closed more frequently than the nasal or temporal quadrants using both AS-OCT and gonioscopy. When performed under dark conditions, AS-OCT identified 98% of those subjects found to have angle closure on gonioscopy (95% confidence interval [CI], 92.2–99.6) and led to the characterization of 44.6% of those found to have open angles on gonioscopy to have angle closure as well. With gonioscopy as the reference standard, specificity of AS-OCT in the dark was 55.4% (95% CI, 45.2–65.2) for detecting individuals with angle closure.

Conclusion: Anterior segment OCT is a rapid noncontact method of imaging angle structures. It is highly sensitive in detecting angle closure when compared with gonioscopy. More persons are found to have closed angles with AS-OCT than with gonioscopy. *Ophthalmology 2007;114:33–39 © 2007 by the American Academy of Ophthalmology.*

Primary angle-closure glaucoma (PACG) is a significant cause of blindness in East Asia and South Asia.[1–4] Due to its high prevalence in the populous countries of China and India, PACG may be as common as or more common than POAG on a global scale. It is an aggressive and visually destructive type of glaucoma, and it is estimated that PACG may blind 10 times more people in China than primary open-angle glaucoma (POAG).[5]

Assessment of angle width and configuration is an essential part of making the diagnosis and determining the management of individuals with angle closure. Currently, the traditional method and reference standard for diagnostic

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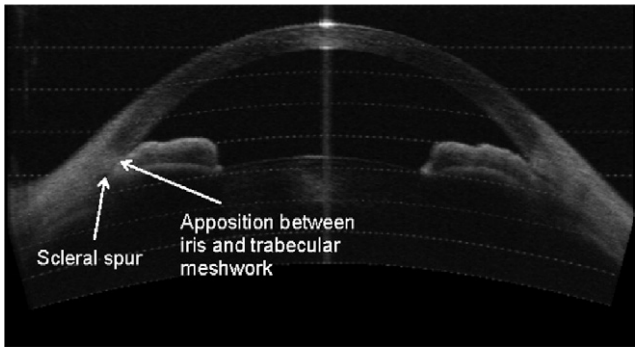

Figure 1. Anterior segment optical coherence tomography image of nasal and temporal angles showing apposition between the peripheral iris and angle wall anterior to the scleral spur.

angle assessment is visualization of angle structures by indirect gonioscopy. However, it is limited by its dependency on single-observer interpretation and is subject to variability even in the hands of experienced practitioners. Ultrasound biomicroscopy (UBM) generates high-resolution images of the angle, which can be used in quantitative analysis, and it adds useful information regarding causal mechanisms of angle closure. However, this method requires trained and experienced technicians and is time consuming. Both gonioscopy and UBM require contact with the globe, and as a result, they can be unpleasant for the patient and can induce artifacts.

Optical coherence tomography (OCT) technology, which originally was used in ophthalmology to image the posterior segment, has also been used to image anterior segment structures such as the cornea. However, the wavelength of this technology (0.8 μm) is insufficient to allow penetration of the sclera and, therefore, imaging of the anterior chamber angle (ACA). In addition, image acquisition at this wavelength is slow. A new anterior segment OCT (AS-OCT) system has been introduced recently that uses a longer wavelength (1.3 μm), allowing deeper penetration and cross-sectional imaging of the anterior chamber (AC) and visualization of the angle.[6] The scanning speed of this new system is 40 times faster than previous anterior segment OCT systems, enabling real-time imaging. This new AS-OCT system has the benefits of being a rapid noncontact method that may be performed by a technician. An early application of AS-OCT technology was the evaluation of the cornea before and after refractive surgery.[7] If AS-OCT were to provide an accurate assessment of angle anatomy, it could provide a rapid diagnostic and screening tool for the detection of angle closure. The aim of this study is to determine the ability of AS-OCT to detect angle closure when compared with gonioscopy in an Asian population.

Table 1. Diagnoses of Subjects Recruited to the Study

Diagnosis	No. of Subjects (%)
Normal (including patients before cataract surgery)	34 (16.7)
Suspected and confirmed narrow angles	68 (33.5)
Primary angle closure with or without glaucomatous optic neuropathy	76 (37.4)
Primary open-angle glaucoma	14 (6.9)
Other	11 (5.4)
Total	203 (100)

Materials and Methods

Study Participants

Ethical approval was obtained from the ethical review board of the National University Hospital Singapore, and written informed consent was obtained from all subjects. The work was carried out in accordance with the World Medical Association's Declaration of Helsinki. Subjects ≥40 years old were recruited from the glaucoma clinics at National University Hospital. We attempted to recruit as many patients as possible with suspected (e.g., with a shallow central or peripheral AC) or confirmed primary angle closure (some of whom had been treated with iridotomy). Patients with a diagnosis of POAG, ocular hypertension, and cataracts also were recruited. Eyes of patients with pseudophakia or previous glaucoma surgery were excluded from the study.

Anterior Segment Optical Coherence Tomography Imaging

All subjects underwent imaging of the angle with a prototype of anterior segment OCT (Carl Zeiss Meditec, Dublin, CA) before any procedures that involved contact with the eye. The details of AS-OCT imaging technology and methods used here have been described[8]; the prototype used in our study provided a larger image (scan length of up to 16 mm and scan depth of up to 8 mm) than the previous prototype. In brief, with the patient in the sitting position images were captured of the inferior (6-o'clock meridian),

Table 2. Detection of Eyes with Appositional Angle Closure by Gonioscopy and Anterior Segment Optical Coherence Tomography (AS-OCT)

	AS-OCT, Closed* (≥1 Quadrants)	AS-OCT, Open	Total	Sensitivity (95% CI)	Specificity (95% CI)
Gonioscopy, Spaeth = 0°, ≥1 quadrants	143	9	152 (44.4%)		
Gonioscopy, open	85	105	190 (55.6%)		
Total	228 (66.7%)	114 (33.3%)	342		
AS-OCT, ≥1 quadrants closed vs. Spaeth = 0° (≥1 quadrants)				94.1% (88.7%–97.1%)	55.3% (47.9%–62.4%)

CI = confidence interval.
*Apposition between the peripheral iris and structures anterior to the scleral spur.

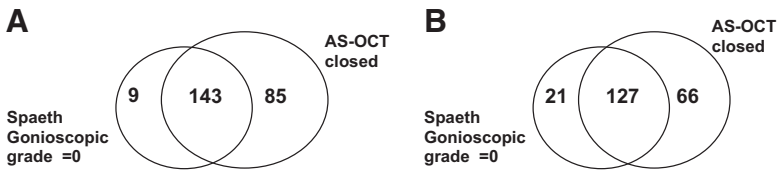

Figure 2. Venn diagrams showing agreement between gonioscopy and anterior segment optical coherence tomography (AS-OCT) in detecting eyes with angle closure. **A**, Number of eyes detected with angle closure by gonioscopy performed in dim lighting and AS-OCT images taken in the dark. **B**, Number of eyes detected with angle closure when the AS-OCT images were obtained from the same eyes with the room lights on.

nasal, and temporal angle quadrants (3-o'clock and 9-o'clock meridians). Due to the design of the prototype, it was not possible to obtain images of the superior angle. Imaging was performed first in dark conditions and then under bright conditions using a measured standardized light source. Three images were taken for each quadrant in dark and light conditions. A single observer (JLS) did imaging of all subjects before gonioscopic examination. The OCT images were processed later using custom software (Mathworks Inc., Natick, MA) that corrected for image distortions arising from the refractive effect of the cornea and aqueous. One of the 3 images per quadrant was selected for analysis based on quality and visibility of the angle structures. The images of the temporal, inferior, and nasal quadrants were analyzed qualitatively by 2 glaucoma specialists (JLS, TA) who were masked to the gonioscopy findings.

Gonioscopy

Subjects underwent gonioscopy by a second, independent observer (WPN) with extensive experience in performing gonioscopy in a research setting, who was masked to the AS-OCT findings. The examination of all subjects was carried out at a low level of ambient illumination with a Goldmann 2-mirror lens. A 1-mm beam of light was reduced to a very narrow slit. The vertical beam was offset horizontally for assessing superior and inferior angles, and a vertically offset horizontal beam was used for nasal and temporal angles. Care was taken to avoid light falling on the pupil during gonioscopy. The assessment was carried out at ×16 magnification. All 4 quadrants were assessed with the eye in the primary position of gaze for measurement of angle width. Minimum adjustment of the lens or eye was allowed to enable a view over the hill of a steep iris while avoiding excessive eye movement and manipulation so as to gain an undistorted view of the angle. Angle widths for all 4 quadrants were graded by 2 methods. The width in degrees was estimated between the posterior pigmented trabecular meshwork and the peripheral one third of the iris (Spaeth grading system).[9] Manipulative and/or indentation gonioscopy with the Goldmann 2-mirror lens or Sussman 4-mirror lens, respectively, was used (except when the angle was wide open) to establish presence or absence of peripheral anterior synechiae (PAS).

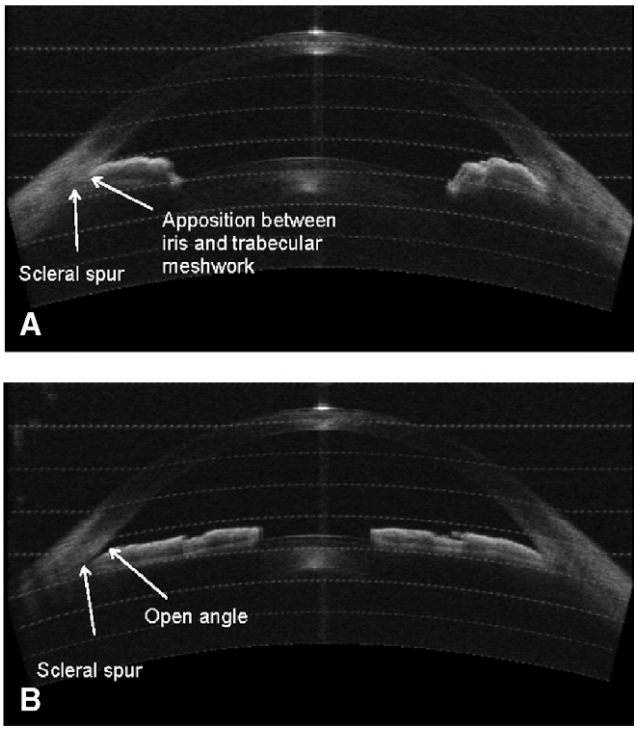

Figure 3. Anterior segment optical coherence tomography images of the nasal and temporal angles. **A**, Both angles are closed when the imaging is performed in dark conditions. **B**, The angle has widened when imaging is repeated with the room lights on.

Definitions/Diagnostic Criteria

An angle quadrant was classified as closed on gonioscopy if the iris was in contact with the posterior (usually pigmented) trabecular meshwork (Spaeth grade, 0°). The angle was defined as closed on an AS-OCT image if contact was visible between the peripheral iris and any part of the angle wall anterior to the scleral spur (Fig 1). For the purposes of this study, only a qualitative analysis was done. An eye was defined as having angle closure on gonioscopy or AS-OCT if one or more of the temporal, inferior, and nasal quadrants were found to be closed. An individual was classified with angle closure if one or more quadrants of the angle were closed in either eye.

Table 3. Detection of Eyes with Synechial Angle Closure by Anterior Segment Optical Coherence Tomography (AS-OCT)

	AS-OCT, Closed* (≥1 Quadrants)	AS-OCT, Open	Total
PAS present, ≥1 quadrants	75	5	80 (23.7%)
PAS absent	149	109	258 (76.3%)
Total	224 (66.3%)	114 (33.7%)	338

PAS = peripheral anterior synechiae.
Peripheral anterior synechiae data not available for 4 eyes.
*Apposition between the peripheral iris and structures anterior to the scleral spur.

Table 4. Detection of Individuals with Angle Closure by Gonioscopy and Anterior Segment Optical Coherence Tomography (AS-OCT)

	AS-OCT, Closed* (≥1 Quadrants), One or Both Eyes	AS-OCT, Open	Total	Sensitivity (95% CI)	Specificity (95% CI)
Gonioscopy, Spaeth = 0°, ≥1 quadrants, one or both eyes	97	2	99 (49.5%)		
Gonioscopy, open	45	56	101 (50.5%)		
Total	142 (71%)	58 (29%)	200		
AS-OCT, ≥1 quadrants closed vs. Spaeth = 0° (≥1 quadrants)				98% (92.2%–99.6%)	55.4% (45.2%–65.2%)

CI = confidence interval.
*Apposition between the peripheral iris and structures anterior to the scleral spur.

Data Analysis

A comparison of AS-OCT and gonioscopy in detecting eyes with angle closure was made using cross-tabulation of the data and presented as Venn diagrams. For the purposes of this study, gonioscopy was defined as the reference standard of angle assessment. Sensitivities and specificities of AS-OCT in detecting individuals with angle closure (see above) of Spaeth grade 0° were calculated. Statistical analyses were performed using SPSS (version 11, SPSS Inc., Chicago, IL).

Results

Characteristics of Study Population

A total of 203 subjects were recruited, of whom 123 (60.6%) were female. The majority of subjects were Chinese (174 [85.7%]), Malay (9 [4.4]), and Indian (12 [5.9%]), and a small number of subjects were of other ethnic origins (8 [3.9%]). The median age of the sample was 62.5 years (range, 40–86). Diagnosis of all recruited subjects is shown in Table 1. A diagnosis of narrow angles or primary angle closure with or without glaucoma was present for 144 (70.9%) patients, some of whom had been treated with laser iridotomy and others in whom the examination was performed before iridotomy. Data were available for 342 eyes of 200 individuals. Mean AC depth (ACD) of subjects' right eyes (measured using IOLmaster, Carl Zeiss Meditec) was 2.68 mm (standard deviation [SD], 0.38), and mean axial length was 23.07 mm (SD, 1.41).

Comparison of Anterior Segment Optical Coherence Tomography and Gonioscopy in Detecting Angle Closure

Analysis by Eye. A closed angle in one or more of the inferior, nasal, and temporal quadrants was found in 152 eyes (44.4%) on gonioscopy (posterior trabecular meshwork not visible; Spaeth, 0°) and in 228 eyes (66.7%) on AS-OCT examination (Table 2). Figure 2A shows that in 143 eyes there is agreement between the 2 methods in detecting angle closure. When the comparison of AS-OCT and gonioscopy was repeated using AS-OCT images obtained under light conditions (but using the gonioscopy gradings obtained in dim lighting), the number of eyes defined as having angle closure with AS-OCT dropped to 193 (57.6%). This is illustrated in Figure 2B. Figure 3 shows how the difference in lighting conditions alters the configuration of the angle on AS-OCT.

Of 338 eyes with available data, 80 (23.7%) had PAS present in one or more quadrants on gonioscopic examination. Seventy-five (93.8%) of these eyes with PAS were categorized as closed with AS-OCT (Table 3).

Analysis by Individual. In 3 subjects, it was not possible to obtain either gonioscopic gradings or AS-OCT images of the relevant eyes. Of the remaining 200 subjects, 142 (71%) were found to have angle closure in one or both eyes with AS-OCT examination and 99 with gonioscopy (49.5%) (Table 4). Anterior segment OCT identified 98% of the subjects found to have closed angles on gonioscopy. In addition, AS-OCT found an additional 45 subjects to have closure who were felt to have open angles on gonioscopy. If gonioscopy is considered the reference standard, this yields a specificity of 55.4% by AS-OCT for detecting angle closure.

Analysis by Angle Quadrant. The highest proportion of closed angles was found in the inferior quadrant on both gonioscopy (130/319 [40.7%] eyes) and AS-OCT (218/319 [68.3%] eyes) (Table 5). In 26 eyes, the inferior angle image was too poor to grade, and in 3 eyes, the angle was not gradable by gonioscopy. Of the 218 eyes in which the inferior angle was categorized as closed using AS-OCT, 205 (94%) were graded as 0° to 20° on gonioscopy. The inferior angle quadrants in the remaining 13 eyes

Table 5. Detection of Angle Closure in Each Angle Quadrant by

	Inferior Quadrant		
	AS-OCT, Closed	*AS-OCT, Open*	*Total*
Gonioscopy, closed (Spaeth, 0°)	122	8	130 (40.7%)
Gonioscopy, open	96	93	189 (59.2%)
Total	218 (68.3%)	101 (31.7%)	319
	Sensitivity, 93.5% (88.2%–97.3%) (95% CI)	Specificity, 49.2% (41.9%–56.6%) (95% CI)	

CI = confidence interval.
Sensitivity and specificity of AS-OCT for detecting a gonioscopically closed (Spaeth, 0°) angle. Good AS-OCT images were not available for the inferior

were graded as >20°. Similar results were seen in the other quadrants.

Discussion

Anterior segment OCT technology enables examiners to obtain detailed cross-sectional images of the ACA while avoiding contact with the globe. These images can be analyzed qualitatively. As a result, it is a quick and easily tolerated procedure for the patient. It also is likely that there is less distortion of angle morphology due to lack of globe manipulation.

In this study, AS-OCT identified almost all eyes as having closed angles that were found by gonioscopy to be closed. Using gonioscopy as a reference standard results in AS-OCT having a sensitivity of 98%. However, many eyes in which gonioscopy suggested open angles were found by AS-OCT to have visible contact between the iris and the structures anterior to the scleral spur in low light conditions. This disparity resulted in low specificity for AS-OCT when using gonioscopy as a gold standard. As can be seen from Figure 2A, AS-OCT identified ≥1 quadrants as closed in 85 eyes that were apparently open in all 4 quadrants on gonioscopy. The majority of eyes in which AS-OCT identifies angle closure have a Spaeth gonioscopy grading of 0° to 20°. However, when analyzed by quadrant, a small number of cases of angle width >20° on gonioscopy are closed on AS-OCT images.

There are several possible explanations for this finding:

- *Differences in lighting conditions.* Although both gonioscopy and AS-OCT examinations were undertaken under dim lighting conditions, complete darkness was possible for the AS-OCT examination because no visible light is required to obtain the image. Despite efforts to use as little light as possible for gonioscopy and to minimize the length of the slit beam, the anterior segment and pupil are exposed to light during gonioscopy. This small amount of light may be sufficient to open up an angle that would be closed in the dark. This is in part confirmed by our finding that fewer eyes were classified as having closed angles when imaged using AS-OCT in the light (Fig 2B).
- *Distortion of the anterior segment by gonioscopy.* It is possible that the Goldmann gonioscopy lens, when placed on the globe, causes some displacement of anterior segment structures, resulting in opening of the angle in some quadrants. The act of placing a gonioscope on the eye inevitably will cause some distortion of the angle configuration if the lens is ill fitting or if there is inadvertent pressure. This distortion may be caused by either the observer or the upper lid of the subject (especially if the palpebral fissure is small). Excessive tilting of the lens, in an attempt to see over the apex of a very convex iris, also may cause indentation of the cornea, leading to widening of the angle, and the mistaken impression that the angle is wider than it is. Pressure from the upper lid on the edge of the gonioscope may result in inadvertent mechanical distortion of the cornea, making the drainage angle appear artificially narrower.[10]
- *Landmarks are not the same using the 2 methods.* Whereas with gonioscopy it is possible to visualize landmarks such as Schwalbe's line and the posterior (usually pigmented) area of the trabecular meshwork, the anterior limitations of the trabecular meshwork are less easy to identify with AS-OCT. Because the position of the scleral spur is easier to determine and the trabecular meshwork lies anterior to this structure, we defined angle closure as the presence of any contact between the iris and angle structures anterior to the scleral spur. Angle closure on gonioscopy was defined as Spaeth grade 0° and, therefore, required apposition between the iris and entire extent of the posterior trabecular meshwork. In short, this difference in definitions could have resulted in AS-OCT detecting more eyes with angle closure than gonioscopy.

Ultrasound biomicroscopy studies demonstrate the dramatic changes in angle width that take place when going from dark to light conditions.[11] We also have found that the angle opens on AS-OCT imaging when room lights are switched on. This suggests that it is the difference in illumination that may be the most important factor in the discrepancy between gonioscopy and AS-OCT findings.

A study comparing UBM and gonioscopy performed under standard room illumination found that (similar to this study) there was a tendency for gonioscopy to overestimate angle width in eyes with narrow angles.[12] A recent article evaluating slit lamp–mounted noncontact goniometry (which utilizes AS-OCT technology similar to that used in this study

Gonioscopy and Anterior Segment Optical Coherence Tomography (AS-OCT)

Nasal Quadrant			Temporal Quadrant		
AS-OCT, Closed	*AS-OCT, Open*	*Total*	*AS-OCT, Closed*	*AS-OCT, Open*	*Total*
44	10	54 (16.4%)	39	20	59 (18.5%)
87	189	276 (83.6%)	59	200	259 (81.4%)
131 (39.7%)	199 (60.3%)	330	98 (30.8%)	220 (69.2%)	318
Sensitivity, 81.5% (68.6%–90.8%) (95% CI)	Specificity, 68.5% (62.6%–73.9%) (95% CI)		Sensitivity, 66.1% (52.6%–77.9%) (95% CI)	Specificity, 77.2% (71.6%–82.2%) (95% CI)	

quadrant of 23 eyes, nasal quadrant of 12 eyes, and temporal quadrant of 24 eyes.

to obtain quantitative measurements of the angle width) and gonioscopy in grading angle width reported 85% sensitivity and 90% specificity for detecting occludable angles using the UBM-derived parameter of angle opening distance at a cutoff value of <290 μm.[13] The authors of both these articles defined an occludable angle as having a Shaffer grade of ≤ 2. We employed more stringent criteria in this study by requiring apposition between the peripheral iris and trabecular meshwork (angle closure). These criteria were used to simplify the analysis and minimize the variability that could arise from the subjective nature of grading angle width on both gonioscopy and AS-OCT imaging. It will be possible to perform quantitative measurements of angle width on AS-OCT using the same parameters as have been developed for UBM. Defining cutoff measurements for narrow angles on AS-OCT will be the subject of further data analyses.

The use of a single observer could result in a systematic bias of the gonioscopy findings and is a weakness of the study. In addition, the knowledge that there were a large number of subjects with angle closure potentially could have biased the observers (of both gonioscopy and AS-OCT) towards grading an angle as closed.

Much research has been published over the last decade investigating early diagnosis and treatment of PACG in Asian populations. Potential screening tests for people with angle closure include some measure of central or peripheral ACD.[14–16] In this initial assessment of a prototype device, AS-OCT appears to be a promising screening tool for angle closure. It is rapid, does not require contact with the eye, and is easily tolerated by the patient, and the images can be collected and analyzed objectively by non–medical health care professionals. Although AS-OCT identified more subjects as having closed angles than gonioscopy, it is not clear that gonioscopy is an ideal reference standard. The weaknesses of gonioscopy as a diagnostic technique already have been discussed, and we believe it is likely that cases of closure were missed by gonioscopy. If we turn things around and assess the data using AS-OCT as the reference standard to examine the performance of gonioscopy, we find that gonioscopy has low sensitivity (68.3%) and high specificity (96.6%).

Sensitivity and specificity are likely not to be the best way of measuring the performance of AS-OCT in the absence of a clear reference standard, and for that reason, we have presented the data in multiple ways. An additional limitation to the use of sensitivities and specificities in this study is the fact that the sample is not population based but a selected group of patients with glaucoma and angle closure. Because of the oversampling of people with angle closure, even the subjects with open angles in this study may have narrower angles than a true normal community-based population. This is an important consideration, and additional studies of normal populations are needed.

Longitudinal studies will be required to determine whether eyes classified as closed only by AS-OCT are indeed at risk of developing PACG. A short-term surrogate method for estimating the risk for these persons is to look at the proportion of eyes with AS-OCT–determined angle closure that have coexisting PAS. In this study, AS-OCT detected angle closure in 93.8% of cases with gonioscopic evidence of PAS. Some of the eyes with PAS in this study have a laser iridotomy and, therefore, may have open angles alongside areas of synechial closure. Previous reports have documented that a substantial proportion of eyes with "open" angles on gonioscopy have PAS on close examination, raising the possibility that gonioscopy may be missing cases of angle closure.[17]

Until we get answers to these questions, the conclusions that can be drawn from this study are that AS-OCT provides a simple, user-friendly, objective method of assessing the drainage angle that is well tolerated by the patient. It has advantages over UBM, as it does not require contact with the globe. Furthermore, AS-OCT allows for a dynamic cross-sectional view of the angle, which may be helpful in determining mechanisms and appropriate management of patients with PACG in this Asian population. When compared with gonioscopy, AS-OCT has excellent sensitivity in detecting angle closure.

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