Assessment of Circumferential Angle Closure with Swept-Source Optical Coherence Tomography: a Community Based Study

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• PURPOSE: To evaluate the diagnostic performance of swept-source optical coherence tomography (SS-OCT, CASIA SS-1000; Tomey Corporation, Nagoya, Japan) for angle closure detection, in comparison with gonioscopy, in a community setting.

• DESIGN: Reliability analysis.

• METHODS: A total of 2027 phakic subjects aged ≥50 years, with no previous history of glaucoma, laser (including peripheral iridotomy), intraocular surgery, or ocular trauma, were consecutively recruited from a community polyclinic in Singapore. Gonioscopy was performed by a single trained ophthalmologist. SS-OCT angle scans, which obtain radial scans for the entire circumference of the angle, were analyzed by a single examiner, masked to the subject's clinical details. On SS-OCT images, angle closure was defined as contact between the iris and any part of the angle wall anterior to the scleral spur. Different cutoff values of the degree of circumferential angle closure (≥35%, ≥50%, and ≥75%) were taken for analysis to assess SS-OCT performance in detecting angle closure.

• RESULTS: A total of 1857 subjects (91.6%) were included in the final analysis after excluding poor-quality SS-OCT scans. Almost 90% of the subjects were Chinese, with a mean age of 61.8 ± 6.7 years, and more than half were women (63.5%). The overall AUC of SS-OCT manual grading against gonioscopy was 0.84 (95% confidence interval, 0.81-0.88). The prevalence of angle closure on SS-OCT was 26.1% for the ≥35% definition, with an area under the curve of 0.80 (0.77-0.84), sensitivity of 82.5% (75.3%-88.4%), and specificity of 78.5% (76.5%-80.4%). The first-order agreement coefficient statistics for the 2-quadrant gonioscopic definition of angle-closure with corresponding ≥35%, ≥50%, and ≥75% angle closure definitions for SS-OCT were good at 0.89 (0.83-0.93), 0.88 (0.842-0.93), and 0.88 (0.831-0.99), respectively.

• CONCLUSIONS: In this large community-based study, SS-OCT exhibited moderate performance for angle closure detection compared to gonioscopy as the reference standard. (Am J Ophthalmol 2019;199:133–139. © 2018 Elsevier Inc. All rights reserved.)

PRIMARY ANGLE CLOSURE GLAUCOMA (PACG), A major form of glaucoma especially in Asia, is potentially preventable in early stages by performing laser iridotomy in eyes with a narrow anterior chamber angle (ACA). Identifying eyes with angle closure could allow for earlier treatment of those at risk for PACG.

The current reference clinical standard for angle closure assessment is gonioscopy, which is subjective and requires patient cooperation, anesthesia, and contact with the eye. With the development of the anterior segment devices such as high-frequency ultrasound biomicroscopy (UBM), Scheimpflug imaging, and anterior segment optical coherence tomography (AS-OCT), direct noncontact imaging of the ACA is now widely available. These approaches for evaluating the ACA primarily depend on obtaining a single cross-sectional scan of the anterior segment, which means that the rest of the angle is not visualized.[1]

Swept source optical coherence tomography (SS-OCT, CASIA SS-1000; Tomey Corporation, Nagoya, Japan) has a wide scanning range of 16 mm, which allows an entire cross-section of the anterior chamber to be captured simultaneously. The SS-OCT's low density 3-dimensional angle scan simultaneously obtains 128 meridional radial scans of the anterior chamber for the entire circumference of the angle.[2] We recently evaluated the device for its ability to detect angle closure in a clinic-based study in Singapore using its in-built semiautomated algorithm, termed iridotrabecular contact index (ITC index).[3] The AUC for detecting gonioscopic angle closure using 16 scans per eye was 0.83.

The aim of this study was to examine the agreement and diagnostic accuracy of the SS-OCT using all the 128 meridional angle scans in detecting angle closure compared to gonioscopy in a large community-based sample.

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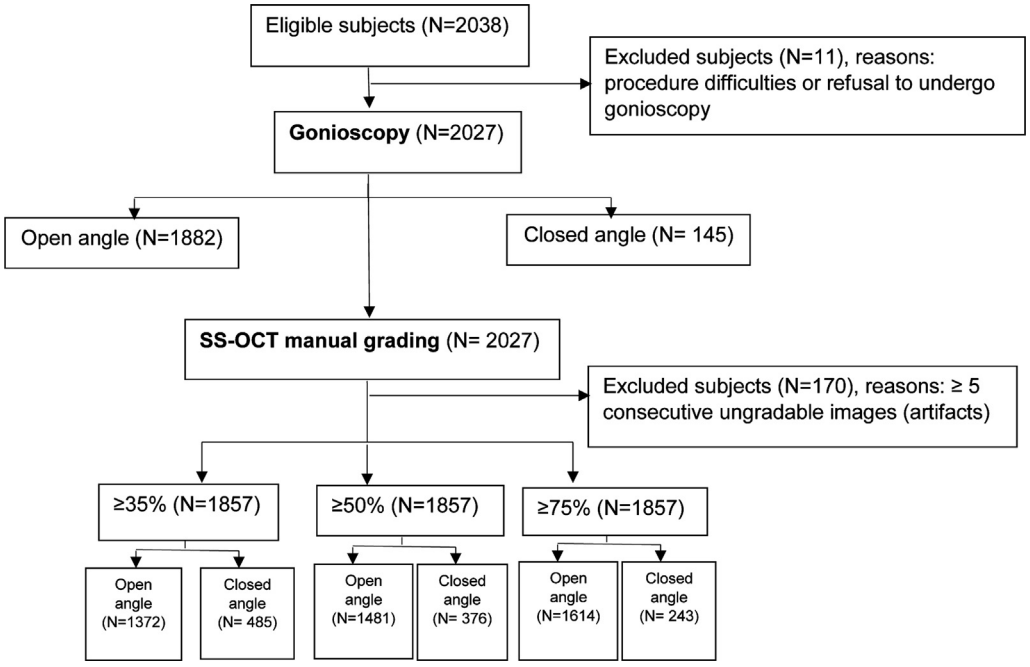

FIGURE 1. Standards for Reporting of Diagnostic Accuracy (STARD) flow chart of participants.

METHODS

• **STUDY POPULATION AND RECRUITMENT:** The study had the approval of the ethics review board of Singhealth and was performed in accordance with the tenets of the Declaration of Helsinki. Data for this reliability analysis were obtained from a prospective cross-sectional study, where subjects aged ≥50 years with no previous history of glaucoma, laser (including peripheral iridotomy), intraocular surgery, or ocular trauma were consecutively recruited from a single government community polyclinic providing primary health care services. This polyclinic serves >10 000 people per month, mainly of lower to middle socioeconomic status, with a high proportion requiring chronic disease management. A total of 2038 consecutive subjects were eligible and screened for this study, after written informed consent was obtained, from June to September 2013.

• **SWEPT-SOURCE OPTICAL COHERENCE TOMOGRAPHY IMAGING:** All subjects underwent SS-OCT (CASIA SS-1000; Tomey Corporation, Nagoya, Japan) imaging before any contact procedure, under dark room conditions (20 lux). The upper eyelid was gently elevated and the lower eyelid was gently pulled down by the operator so that the ACA could be seen in the scan window, taking care to avoid inadvertent pressure on the globe. Patients were asked to focus on an internal fixation target, and once the patient had been optimally positioned, each eye was scanned with the 3-dimensional angle analysis scan (which takes 2.4 seconds) using the auto alignment function. This algorithm takes 128 consecutive meridional scans, each consisting of 512 A-scans across the anterior chamber.

Both angles of each meridional scan were assessed and classified as open or closed by a single trained ophthalmologist (N.P.) who was masked to gonioscopy findings. We have previously reported a good intra- and interobserver agreement for image grading using SS-OCT.[4] A closed angle on an SS-OCT image was defined as contact between the iris and any part of angle wall anterior to the scleral spur.

• **GONIOSCOPY:** Indentation gonioscopy was performed in the dark in all cases by a glaucoma fellowship–trained ophthalmologist (M.T.) using a Sussman 4-mirror goniolens (Ocular Instruments Inc, Bellevue, Washington, USA), who was standardized against another ophthalmologist with subspecialty glaucoma training (T.A.). A weighted kappa of 0.82 was achieved for the assessment of angle grading. This examiner was masked to imaging results. A 1-mm light beam was reduced to a narrow slit, and the vertical beam was offset horizontally for evaluating nasal and temporal angles and maintained vertically for assessing superior and inferior angles. The examination was performed with the subject's eye in the primary position of gaze. Care was taken to avoid light from falling on the pupil and to avoid inadvertent indentation during examination. In some cases, the gonioscopy lens was tilted slightly to allow a view of the angle over the convexity of the iris, avoiding ocular distortion. The angle in each quadrant was graded per the modified Scheie grading

TABLE 1. Baseline Characteristics of Individuals Screened for Angle Closure Using Gonioscopy and Swept-Source Optical Coherence Tomography

Variable	Result (N = 1857)
Age (y), mean ± SD	61.8 ± 6.70
Sex (male:female)	678:1179
Ethnicity (Chinese:non-Chinese)	1621:236
SS-OCT closed angles prevalence %, cutoff	
≥35%	26.12 (485/1857)
≥50%	20.25 (376/1857)
≥75%	13.09 (243/1857)
Gonioscopy closed angles prevalence %	
≥2 quadrants	7.49 (139/1857)
≥3 quadrants	5.17 (96/1857)

SS-OCT = swept-source optical coherence tomography.

system, according to the anatomic structures observed during gonioscopy. The ACA was considered "closed" in a quadrant if the posterior pigmented trabecular meshwork could not be seen in the primary position without indentation. An eye was classified as having angle closure if there were 2 or more closed quadrants.

• **STATISTICAL ANALYSIS:** Right eyes were selected for analysis. Demographic parameters were summarized by mean and standard deviation for continuous variables; median and range were used where appropriate. First-order agreement coefficient (AC1) statistics were used to assess the agreement between categorical variables. Receiver operating characteristic curves, with calculations of area under the curve (AUC) and 95% confidence intervals (CIs), were used to assess the performance of the SS-OCT manual grading for identifying eyes with angle closure, using gonioscopy as the reference standard.

We have chosen the optimal cutoff on the basis of the best sensitivity and specificity values given by the ITC index in-built software, previously reported (≥35%),[5] then a median value (≥50%), and an arbitrary stricter criterion for angle closure (≥75%). The AUC based on any percentage contributing to 2 quadrants gonioscopic angle closure definition was defined as overall AUC. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), and negative likelihood ratio (LR-) for the cutoff values of ≥35%, ≥50%, and ≥75% were reported for ≥2 or ≥3 quadrants of angle closure.[5] We also calculated diagnostic accuracy with corresponding 95% CI. We defined diagnostic accuracy as overall probability that a subject will be correctly classified. In order to perform a sectoral comparison, we took the corresponding gonioscopic superior, inferior, temporal, and nasal degrees in the SS-OCT images and defined an SS-OCT quadrant as closed when half of more of that quadrant was closed (cutoff value of ≥50%). A P value <.05 was considered statistically significant for all comparisons. Statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, North Carolina, USA).

RESULTS

ELEVEN SUBJECTS WERE EXCLUDED OWING TO PROCEDURE difficulties or refusal to undergo gonioscopy. Of the 2027 included, 170 subjects' SS-OCT images (164 with gonioscopic open angles and 6 with gonioscopic closed angles) were discarded owing to poor quality or artifacts (eyelid, movement, and corneal opacities) in more than 5 consecutive scans. Therefore, data from the right eyes of 1857 subjects (91.6%) who completed the protocol were included in the final analysis (Figure 1).[6] Almost 90% were Chinese, with a mean age of 61.8 ± 6.7 years, and more than half were women (63.5%).

The prevalence of closed angles detected with SS-OCT (26.1%, 20.3%, and 13.1% for ≥35%, ≥50%, and ≥75% criteria, respectively) was higher than with gonioscopy (7.49% for 2 quadrants closed, Table 1).

Table 2 shows the agreement (AC1 statistic) for the 3 cutoff values for SS-OCT angle closure definition (≥35%, ≥50%, and ≥75%). The AC1 statistic for a 2-quadrant definition of angle closure at ≥35%, ≥50%, and ≥75% was 0.89, 0.88, and 0.88, respectively. The AC1 for each quadrant was 0.86 (0.80-0.91), 0.82 (0.74-0.90), 0.81 (0.74-0.88), and 0.80 (0.72-0.86) for the superior, inferior, temporal, and nasal quadrant, respectively. The overall AUC of SS-OCT manual grading against gonioscopy was 0.84 (0.81-0.88) (Figure 2). Diagnostic accuracy ranged between 77.5% and 88.7% for various definitions of angle closure. The cutoff criterion of ≥35% was found to be optimal for the best classification for angle closure across various gonioscopic angle closure definitions with a sensitivity of 82.5% (75.3%-88.4%) and a specificity of 78.5% (76.5%-80.4%) for 2-quadrant angle closure (Table 3). In this case, the NPV was 98.23% (97.48%-98.75%) with a moderate LR+ of 3.83 (3.41-4.30). The sensitivity decreased and the specificity increased at higher percentage cutoffs for SS-OCT-defined angle closure, while the PPV, LR+, and LR- increased. The NPV did not show much difference with stricter angle closure definition.

The superior quadrant exhibited the best AUC (0.79, 95% CI 0.75-0.82), the highest sensitivity for angle closure detection (78.2%, 95% CI 71.1%-84.2%), and the highest closed angle rate on both gonioscopy (160/1857) and SS-OCT imaging (484/1857) (Table 4). The nasal quadrant had the highest specificity (84.2, 95% CI 82.5-85.9) and the inferior quadrant had the highest NPV (98.4, 95% CI 97.7-98.8).

TABLE 2. Agreement Between the Various Definitions of Angle Closure by Manual Grading of Swept-Source Optical Coherence Tomography Versus Gonioscopy for Angle Status

	Agreement Between Gonioscopy and SS-OCT, AC1 (95% CI)		
Gonioscopic Angle Closure	≥35%	≥50%	≥75%
≥2 quadrants closed	0.89 (0.84-0.93)	0.88 (0.84-0.93)	0.88 (0.83-0.92)
≥3 quadrants closed	0.90 (0.84-0.95)	0.88 (0.83-0.94)	0.86 (0.80-0.92)

AC1 = first order agreement coefficient statistics; CI = confidence interval; SS-OCT = swept-source optical coherence tomography.

DISCUSSION

USING GONIOSCOPY AS THE REFERENCE STANDARD, MANUally graded SS-OCT images were able to detect angle closure with nearly 80% sensitivity and specificity in this large community-based population of mostly Chinese older individuals attending polyclinics in Singapore. As seen in previous studies, SS-OCT tends to classify more angles as closed angles than gonioscopy.[5,7–9] This reduces its performance against the current reference standard, but it will take additional research to determine which test better predicts patient outcomes.

OCT likely detects higher rates of angle closure for several reasons. Imaging is performed in dark ambient conditions, maximizing pupil size, while the light from the slit lamp used in gonioscopy can induce some pupillary constriction. SS-OCT does not require contact, whereas gonioscopy can inadvertently compress the cornea, opening the angle.[10] Also the consideration of small iridotrabecular contact on SS-OCT scans[1]—possibly overlooked in gonioscopy—may play a role in explaining why SS-OCT detects more closed angles compared to gonioscopy. We observed a discrepancy in the degree of angle closure discovered between SS-OCT and gonioscopy. Based on SS-OCT, 35% or more of the circumference closed is sufficient to predict angle closure of 2 quadrants or more (equivalent to 50% or more) on gonioscopy. The discrepancy is likely to be based on the fact that a quadrant in gonioscopy can be partially closed. If we consider a gonioscopic quadrant as 25% of the circumference, the case of an eye that has, for example, 40% of the circumference closed in SS-OCT may correspond to an eye with 2 quadrants partially closed (20% closed each quadrant) in gonioscopy.

Overall, we found a higher prevalence of angle closure using SS-OCT (using all cutoff definitions) when compared with gonioscopic angle closure. Assuming a 10% population prevalence of narrow angles, the PPV of manually graded SS-OCT would be 23.7% in individuals >50 years of age. This means that approximately 1 in 4 of those with abnormal findings on screening would actually have 2 or more quadrants closed on gonioscopy.

Approximately 8% of the SS-OCT images were discarded owing to poor quality or artifacts that made the identification of the scleral spur not possible. This agrees with previous findings using the same device with semiautomated grading (ITC index)[5] and is slightly higher than the one reported by Rigi and associates in a smaller population (5.6%).[11] However, it is lower than the 30% rate of nongradable images using an earlier OCT device, the Visante (Carl Zeiss Meditec, Dublin, California, USA).[12] Screening programs that relied on SS-OCT would have to consider the need for additional testing for these individuals.

The results of the current study are somewhat better than those previously reported using the Visante AS-OCT. In a similar Singapore polyclinic screening study that evaluated the Visante AS-OCT, Lavanya and associates reported a lower AUC for the Visante (0.76), while the present study had an AUC of 0.84.[7] The slight improvement compared

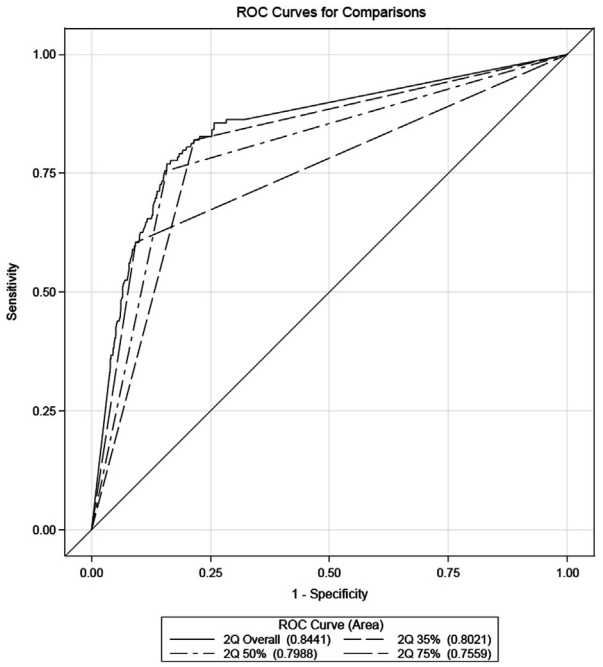

FIGURE 2. Receiver operating characteristic (ROC) curve for swept-source optical coherence tomography (SS-OCT) manual grading against 2 quadrants, closed gonioscopic reference standard. SS-OCT manual grading with ≥35%, ≥50%, and ≥75% as cutoff criteria for angle closure.

TABLE 3. Diagnostic Performance Indicators for Different Cutoff Values of Swept-Source Optical Coherence Tomography Manual Grading With Gonioscopic Angle Closure Definitions

Gonioscopic Angle Closure	Cutoff Criteria	AUC (95% CI)	Sensitivity (95% CI), %	Specificity (95% CI), %	PPV[a] (95% CI), %	NPV[a] (95% CI), %	LR+ (95% CI)	LR-(95% CI)
≥2 quadrants closed	≥35%	0.80 (0.77-0.84)	82.5 (75.3-88.4)	78.5 (76.5-80.4)	23.7 (21.7-25.9)	98.2 (97.5-98.8)	3.83 (3.41-4.30)	0.22 (0.16-0.32)
	≥50%	0.80 (0.76-0.84)	75.5 (67.6-82.3)	84.2 (82.5-85.9)	27.0 (25.2-30.9)	97.7 (96.0-98.3)	4.79 (4.16-5.53)	0.29 (0.22-0.39)
	≥75%	0.76 (0.72-0.80)	60.8 (52.3-68.9)	90.9 (89.5-92.2)	35.2 (30.9-39.9)	96.6 (95.9-97.2)	6.71 (5.50-8.17)	0.43 (0.35-0.53)
≥3 quadrants closed	≥35%	0.81 (0.77-0.85)	84.7 (76.0-91.2)	77.0 (75.0-78.0)	16.7 (15.1-18.4)	98.94 (98.3-99.3)	3.69 (3.28-4.16)	0.20 (0.12-0.32)
	≥50%	0.75 (0.71-0.80)	84.7 (76.0-91.2)	77.06 (75.0-78.0)	16.7 (15.1-18.4)	98.9 (98.3-99.3)	3.69 (3.28-4.16)	0.20 (0.12-0.32)
	≥75%	0.75 (0.71-0.80)	61.2 (50.8-70.7)	89.7 (88.2-91.0)	24.3 (19.2-30.2)	97.7 (96.8-98.4)	5.92 (4.81-7.29)	0.43 (0.34-0.55)

CI = confidence interval; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; NPV = negative predictive value; PPV = positive predictive value.
[a]7. 5% (2 quadrants) and 5.17% (3 quadrants) gonioscopic closed angles prevalence.

TABLE 4. Diagnostic Performance Indicators for Different Cutoff Values of Swept-Source Optical Coherence Tomography Manual Grading With Gonioscopic Angle Closure Definition by Quadrants

Quadrant	Cutoff Criteria	AUC	Sensitivity (95% CI), %	Specificity (95% CI), %	PPV[a] (95% CI), %	NPV[a] (95% CI), %	LR+ (95% CI), %	LR-(95% CI), %
Superior	≥50%	0.79 (0.75-0.82)	78.1 (71.1-84.2)	78.8 (76.8-80.7)	25.9 (23.6-28.2)	97.4 (96.6-98.1)	3.68 (3.26-4.15)	0.28 (0.21-0.37)
Nasal	≥50%	0.76 (0.72-0.80)	61.8 (52.9-70.2)	84.2 (82.5-85.9)	22.4 (19.6-25.6)	96.8 (96.0-97.2)	3.92 (3.30-4.66)	0.45 (0.36-0.56)
Inferior	≥50%	0.76 (0.72-0.81)	72.7 (62.2-81.7)	79.7 (77.8-81.5)	14.8 (12.9-16.9)	98.4 (97.7-98.8)	3.59 (3.06-4.19)	0.34 (0.24-0.48)
Temporal	≥50%	0.75 (0.71-0.79)	70.3 (61.3-78.2)	80.2 (78.3-82.0)	19.4 (17.2-21.8)	97.6 (96.8-98.1)	3.55 (3.06-4.12)	0.37 (0.28-0.49)

AUC = area under the curve; CI = confidence interval; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; NPV = negative predictive value; PPV = positive predictive value.
[a]7.5% (2 quadrants) and 5.17% (3 quadrants) gonioscopic closed angles prevalence.

to the diagnostic performance of 2 single scans by Visante can be explained by the fact that it may not be necessary to assess 128 scans to correlate well with gonioscopic diagnosis. However, assessing only 1 vertical and 1 horizontal scan can lead to more false-positive results if the adjacent scans from the same quadrant are open. The previous work had higher sensitivity (88.4%) but lower specificity (62.9%) than the current study. We obtained a good agreement between SS-OCT and gonioscopy (AC1 0.89, 0.88, and 0.88 at ≥35%, ≥50%, and ≥75%, respectively), while the quadrant agreement reported for the Visante was found to be lower: AC1 of 0.45, 0.51, 0.74, and 0.75 for the superior, inferior, nasal, and temporal quadrants, respectively.[1]

As in previous reports, the superior quadrant had the highest rates of angle closure on both gonioscopy and OCT imaging.[1,13] That said, no dramatic differences in AUC were seen when comparing the AUC using individual quadrants in this or previous studies. This is consistent with a previous study done by Melese and associates using SS-OCT that found that the threshold values were the smallest superiorly, but superior-angle parameters (angle opening distance and trabecular-iris circumference volume) were less accurate for classifying narrow angles, with lower sensitivities than the inferior angle.[14] At different criteria of angle closure using SS-OCT, we observed that PPV and LR+ were relatively low while NPV remained high and LR- was relatively low. This could mean that SS-OCT works better to rule out the diagnosis of angle closure, but detecting angle closure by SS-OCT does not confirm the diagnosis based on gonioscopy. Interestingly, Baskaran and associates recently reported that Visante AS-OCT imaging can "predict" incident gonioscopic angle closure developing after 4 years of follow-up.[15] It is not known if SS-OCT will also be able to detect such incident cases, and we should seek to establish the minimal number of tests and timelines needed to determine incident angle closure developing over time using SS-OCT.

Some limitations of the current study include nearly 8% ungradable images, potential error in manual grading of images, reliance on a single person's gonioscopy, and use of only a Sussman lens as opposed to a Goldmann lens (which may have decreased the rate of identified angle closure). Grading images manually is a laborious process; automation of image grading will be the next step in achieving consistency. As mentioned before, it is probable that it may not be necessary to assess so many scans of the angle circumference to achieve an equivalent gonioscopic diagnosis of angle closure. SS-OCT is also a more expensive technology than gonioscopy and previous versions of AS-OCT devices. Finally, as this was a polyclinic-based study, there exists the potential for some inherent sampling bias, as we included patients in a primary care setting in Singapore.

In summary, manually graded SS-OCT images detected gonioscopy-defined angle closure with about 80% sensitivity and specificity. Further research is needed to determine the outcomes of those who screen positive using SS-OCT in order to inform screening programs for angle closure.[16]

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