Automated Analysis of Angle Closure From Anterior Chamber Angle Images

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Purpose. To evaluate a novel software capable of automatically grading angle closure on EyeCam angle images in comparison with manual grading of images, with gonioscopy as the reference standard.

Methods. In this hospital-based, prospective study, subjects underwent gonioscopy by a single observer, and EyeCam imaging by a different operator. The anterior chamber angle in a quadrant was classified as closed if the posterior trabecular meshwork could not be seen. An eye was classified as having angle closure if there were two or more quadrants of closure. Automated grading of the angle images was performed using customized software. Agreement between the methods was ascertained by κ statistic and comparison of area under receiver operating characteristic curves (AUC).

Results. One hundred forty subjects (140 eyes) were included, most of whom were Chinese (102/140, 72.9%) and women (72/140, 51.5%). Angle closure was detected in 61 eyes (43.6%) with gonioscopy in comparison with 59 eyes (42.1%, P = 0.73) using manual grading, and 67 eyes (47.9%, P = 0.24) with automated grading of EyeCam images. The agreement for angle closure diagnosis between gonioscopy and both manual (κ = 0.88; 95% confidence interval [CI], 0.81–0.96) and automated grading of EyeCam images was good (κ = 0.74; 95% CI, 0.63–0.85). The AUC for detecting eyes with gonioscopic angle closure was comparable for manual and automated grading (AUC 0.974 vs. 0.954, P = 0.31) of EyeCam images.

Conclusions. Customized software for automated grading of EyeCam angle images was found to have good agreement with gonioscopy. Human observation of the EyeCam images may still be needed to avoid gross misclassification, especially in eyes with extensive angle closure.

Keywords: anterior chamber angle, gonioscopy, EyeCam, angle closure, automated grading

Gonioscopy is the established reference standard clinical method for angle evaluation.1 Objective capture of gonioscopic views can be obtained with standard goniophotography or EyeCam (Clarity Medical Systems, Pleasanton, CA, USA) goniography.2 Currently, grading of the documented images can be done only manually, but automated solutions are needed to enable clinician independent grading of the angle images.2–4 In the absence of routine gonioscopy in clinical practice,1 such automated angle image analysis potentially may serve as a surrogate for gonioscopy by a clinician.

EyeCam is the anterior segment module of Retcam (Clarity Medical Systems), a pediatric wide-angle fundus photography system.5,6 We have previously evaluated the EyeCam in grading angle status2 and in detecting the extent of angle opening after laser peripheral iridotomy (LPI).3 Building on this, we have developed an automated software algorithm to classify open and closed angles in Eye Cam angle images.7 Further, the algorithm can identify the specific quadrant from its orientation and provide a summary of the number of quadrants that are closed. This article aimed to test this software by comparing automated grading of EyeCam angle images with manual grading of images, with gonioscopy as the reference standard.

Methods

This prospective hospital-based study was approved by the ethics committee of Singapore Eye Research Institute. Written informed consent was obtained from every participant and the study was performed in accordance with the tenets of the Declaration of Helsinki.

Consecutive eligible subjects older than 40 years were recruited from a single glaucoma clinic at a Singapore hospital. After obtaining a detailed ophthalmic history, each subject underwent a standardized examination that included visual acuity assessment, slit-lamp biomicroscopy, Goldmann applanation tonometry, gonioscopy, and imaging with the EyeCam. Subjects with prior intraocular surgery or penetrating eye injury, or corneal disorders, such as corneal endothelial dystrophy, pterygium, or corneal scars that may preclude satisfactory imaging, were excluded from the study. Poor-quality images from EyeCam, with blurred angle details (even in
one quadrant) were excluded from the study. Patients who had previously undergone LPI were not excluded.

**Gonioscopy**

Gonioscopy was performed in the dark in all cases by a single examiner with previous glaucoma fellowship training (SAP), who was masked to imaging findings. A 1-mm light beam was reduced to a narrow slit and the vertical beam was used for assessing superior and inferior angles and offset horizontally for nasal and temporal angles. Static gonioscopy was performed using a Goldmann 2-mirror lens (Ocular Instruments Inc., Bellevue, WA, USA) at high magnification (×16), with the eye in the primary position of gaze. The gonioscopy lens was tilted minimally to permit a view of the angle over the convexity of the iris, avoiding distortion of angle. Care was taken to avoid light falling on the pupil and to avoid inadvertent indentation during examination. The angle in each quadrant was graded as per the Scheie grading system according to the anatomical structures observed during gonioscopy. The anterior chamber angle (ACA) was considered “closed” in that quadrant if the posterior pigmented trabecular meshwork (TM) could not be seen in the primary position without indentation (Scheie grade 3 or 4). The eye was classified as having angle closure if there were two or more quadrants of closure. Indentation gonioscopy was performed to ascertain angle structures in the presence of a pigmented Schwalbe’s line.

**EyeCam Angle Imaging**

Image capture by EyeCam has been described in detail elsewhere. This instrument is identical to the Retcam device used for retinal imaging. In brief, EyeCam imaging was performed on participants in the supine position on a couch, in a darkened room. Images were captured by a single trained technician (TAT) in all four quadrants of the eye at least 20 minutes after the gonioscopy was performed, to avoid any distortion of angle status. After applying topical anesthetic eye drops (proparacaine hydrochloride 0.5% ophthalmic solution; Alcon Laboratories, Inc., Fort Worth, TX, USA), coupling gel was applied to the anesthetized eye before imaging proceeded with a 130° lens held next to the limbus. The illumination light was pointed at the angle rather than the pupil to minimize any pupillary dilatation. If the angle was not visible due to pronounced convexity of iris, the probe was moved anteriorly with angle closure, using gonioscopy as the reference standard. A P value less than 0.05 was considered statistically significant. The sample size calculation was based on comparison of sensitivities for matched groups in a diagnostic study, as reported by Beam et al. With an estimated sensitivity of 82%, the number of subjects required was 78 in this study. Statistical analysis was performed using MedCalc version 12.3.0.0 (Mariakerke, Belgium). Venn diagrams to scale were generated for either two or three quadrants of angle closure to show overlap among the three methods.

**RESULTS**

Out of the 145 consecutive eligible subjects, five were excluded due to missing/poor-quality images. One hundred forty eyes were included for analysis using the automated software. The mean age of included subjects was 60.5 (SD 12.9) years with most being Chinese (102/140, 72.9%) and women (72/140, 51.5%). Five subjects had previously undergone LPI. Gonioscopic angle closure was noted in two
quadrants or more among 61 eyes (43.6%) in comparison to 59 (42.1%, \( p = 0.73 \)) using manual grading of angle images. Automated grading of angle images graded more angle closure eyes but was statistically insignificant in comparison to gonioscopy (67/140, 47.9%, \( p = 0.24 \)).

Table 1 shows the agreement for various definitions of angle closure among the three methods. Generally, two- or three-quadrant closure definitions showed good agreement among methods. The temporal quadrant showed the least agreement with automated grading in comparison with gonioscopy. Manual versus automated grading comparison showed moderate to good agreement. Figure 1a shows a Venn diagram depicting eyes identified by each method for two-quadrant angle closure definition, with automated grading overestimating angle closure. Figure 1b shows a similar diagram for three-quadrant angle closure definition, suggesting slight overestimation by manual grading. However, this difference in agreement was not statistically significant for two (Cochran’s \( Q \) test, manual versus automated, 0.88 vs. 0.74, \( p = 0.12 \)) or three quadrants (0.76 vs. 0.78, \( p = 0.28 \)) of angle closure among the methods. The agreement statistics did not change when subjects with previous LPI were removed from the analysis (data not shown). Table 2 shows that the AUC ROC is indistinguishable and very high for both methods in particular for the predominant two-quadrant definition of angle closure by gonioscopy. The AUC for two-quadrant closure (manual versus automated = 0.974 versus 0.954, \( p = 0.31 \)) was slightly better than three-quadrant closure definition (manual versus automated = 0.927 vs. 0.94, \( p = 0.67 \)), but this was not statistically significant.

Figures 2 and 3 depict EyeCam images showing discrepancy with gonioscopic diagnosis of open and closed angles respectively. The Figure 2A image was graded as closed on both manual and automated grading possibly due to a convex

### Table 1. Kappa Agreement of Manual and Automated Grading of EyeCam Angle Images Compared With Gonioscopy

<table>
<thead>
<tr>
<th>Definition of Closure</th>
<th>Manual vs. Gonioscopy, ( n = 140 )</th>
<th>Automated vs. Gonioscopy, ( n = 140 )</th>
<th>Manual vs. Automated, ( n = 140 )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \kappa ) (95% CI)</td>
<td>AC1</td>
<td>( \kappa ) (95% CI)</td>
</tr>
<tr>
<td>One or more quadrants closed</td>
<td>0.87 (0.79–0.95)</td>
<td>0.87</td>
<td>0.50 (0.36–0.64)</td>
</tr>
<tr>
<td>Two or more quadrants closed*</td>
<td>0.88 (0.81–0.96)</td>
<td>0.89</td>
<td>0.74 (0.63–0.85)</td>
</tr>
<tr>
<td>Three or more quadrants closed†</td>
<td>0.76 (0.64–0.87)</td>
<td>0.79</td>
<td>0.78 (0.67–0.89)</td>
</tr>
<tr>
<td>Four quadrants closed</td>
<td>0.60 (0.44–0.76)</td>
<td>0.76</td>
<td>0.46 (0.28–0.65)</td>
</tr>
<tr>
<td>Superior quadrant closed</td>
<td>0.81 (0.71–0.91)</td>
<td>0.82</td>
<td>0.69 (0.57–0.81)</td>
</tr>
<tr>
<td>Inferior quadrant closed</td>
<td>0.88 (0.81–0.96)</td>
<td>0.89</td>
<td>0.65 (0.52–0.78)</td>
</tr>
<tr>
<td>Nasal quadrant closed</td>
<td>0.65 (0.51–0.79)</td>
<td>0.74</td>
<td>0.64 (0.50–0.78)</td>
</tr>
<tr>
<td>Temporal quadrant closed</td>
<td>0.67 (0.54–0.80)</td>
<td>0.73</td>
<td>0.37 (0.21–0.53)</td>
</tr>
</tbody>
</table>

\( \kappa \), kappa statistic; AC1, first-order agreement coefficient statistic; Cochran’s \( Q \) test: *\( p = 0.12 \), †\( p = 0.28 \).
DISCUSSION

We report the clinical utility of the first automated software for goniophotographic angle assessment. The agreement of this software in comparison with gonioscopy was found to be very good for the two- and three-quadrant definitions of angle closure.

Several anterior segment imaging methods have been developed to address reproducibility and contact issues inherent in gonioscopic angle assessment. Although such techniques can quantitatively assess the anterior chamber angle, none can claim to completely replace gonioscopy for several reasons. 

Assessing the distribution and degree of pigmentation in the TM, 360° circumferential angle view and detection of peripheral anterior synchiae are a few of the advantages with gonioscopy. Furthermore, the low specificity of these devices may limit their usefulness in screening for angle closure. 

Figure 2A was graded as open on both gradings due to partial angle closure, whereas Figure 3B was graded as open with automated grading owing to the presence of pigmented Schwalbe's line. Overall misclassification rate with automated grading for angle assessment was 12.1% (17/140 eyes) with 7.9% false positives (i.e., 11 closed-angle eyes), whereas it was 5.7% (8/140 eyes) and 2.1% (3/140 eyes) with manual grading, respectively. Most open angles on gonioscopy had very light TM pigmentation (6/11) or dense pigmentation (4/11), leading to erroneous marking by automated grading as closed angles, whereas closed angles were marked as open if it was partial angle closure (3/6) or if the angle had a pigmented Schwalbe's line (3/6) in that quadrant. Another reason for error in automated grading was the presence of a convex iris, obscuring angle details and masquerading as closed angle.

Table 2. Receiver Operating Characteristic Curve Analysis to Compare Manual and Automated Grading of EyeCam angle images.

<table>
<thead>
<tr>
<th>Definition of Closure</th>
<th>Manual vs. Gonioscopy, n = 140</th>
<th>Automated vs. Gonioscopy, n = 140</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AUC (95% CI)</td>
<td>Sensitivity</td>
</tr>
<tr>
<td>One or more quadrants closed</td>
<td>0.955 (0.906–0.983)</td>
<td>0.92</td>
</tr>
<tr>
<td>Two or more quadrants closed</td>
<td>0.974 (0.935–0.994)</td>
<td>0.92</td>
</tr>
<tr>
<td>Three or more quadrants closed</td>
<td>0.927 (0.87–0.964)</td>
<td>0.88</td>
</tr>
<tr>
<td>Four quadrants closed</td>
<td>0.891 (0.828–0.938)</td>
<td>0.75</td>
</tr>
</tbody>
</table>

* Comparison of independent ROC curves between manual and automated grading of EyeCam angle images.

Figure 2. EyeCam images: misclassification into closed angles by automated grading method due to (A) convex iris, (B) lightly pigmented TM, and (C) heavy TM pigmentation.
study of 291 subjects, including African American, “Far East” Asian, and Caucasian individuals, Oh et al.\textsuperscript{15} suggested that refractive error and racial origin may influence iris insertion, leading to variation in gonioscopic angle assessment. These limitations may have less bearing on EyeCam grading. Partial angle closure in a quadrant (which was misclassified by the software as open angles) in this study could be due to inclusion of subjects who have undergone LPI. Thus, the actual performance of the software may be better than reported, for as yet untreated angle closure subjects.

Our study had a few limitations. Gonioscopy was performed by a single observer and used the Scheie grading system. Misclassification error rates due to lightly pigmented angles or heavily pigmented TM may need to be addressed using better engineering methods, such as feature extraction techniques. These methods may identify angle structures irrespective of TM pigmentation and may improve the software algorithm in detecting angle closure. Until then, human observation of the images still may be needed to avoid gross misclassification, especially in eyes with extensive angle closure. Although inclusion of subjects who had previously undergone LPI in this study did not affect the overall results, it may be possible that the pigmentation released after LPI may have influenced the automated grading.

In summary, we evaluated a novel automated angle assessment software tool and reported very good diagnostic performance in comparison with gonioscopy. We believe that EyeCam imaging with automated angle assessment has potential to be a useful adjunct in clinical evaluation and documentation of the irido-corneal angle.

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References