Reproducibility of Anterior Chamber Angle Measurements with Anterior Segment Optical Coherence Tomography

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PURPOSE. To study the reproducibility and variability of iridocorneal angle (ICA) measurements by using anterior segment optical coherence tomography (AS-OCT) by expert and nonexpert observers.

METHODS. Twenty-three healthy volunteers (nonexperts with a basic knowledge of ophthalmology) acquired five consecutive AS-OCT images in the enhanced anterior segment single mode in the 180° to 0° meridian of the right eyes of their peers. Two experts and the 23 nonexperts analyzed the images. The ICA software tool was used to determine the angle opening distance (AOD) and the trabecular iris surface area (TISA) at 500 and 750 µm. A random intercept model was fitted to evaluate the variability of acquiring an image. For both the experts and the nonexperts, inter- and intraobserver variability of analyzing an AS-OCT image was determined with the coefficient of variation (CV). Reproducibility was qualified by using the intraclass correlation coefficient (ICC).

RESULTS. There was no statistically significant difference in the variability of acquiring an image. The range of intraobserver variability in image analysis was from 9.4% to 12.5% in the experts and from 4.2% to 17.4% in the nonexperts. Interobserver variability was 10.7% in the experts and 10.2% in the nonexperts. The reproducibility was high, 0.875 and 0.942 in the experts and 0.906 in the nonexperts.

CONCLUSIONS. The overall reproducibility of the ICA measurements with the AS-OCT is good in open angles. Inter- and intraobserver variability showed similar mean values of reproducibility between the experts and nonexperts. The wide range of intraobserver variation in the nonexperts suggests that this group should undergo extensive instruction before routinely analyzing AS-OCT images. (Invest Ophthalmol Vis Sci. 2011;52:2095–2099) DOI:10.1167/iovs.10-5872

Although the current gold standard to assess the iridocorneal angle (ICA) measurements is gonioscopy, this procedure is relatively invasive for the patient and the result relies on the physician’s subjective assessment and experience.¹

Recently, anterior segment optical coherence tomography (AS-OCT) has come into use for the assessment of the ICA in a more objective way. AS-OCT enables in vivo measurement and objective assessment of the anterior eye segment through a noncontact technique.²⁻⁵ The AS-OCT is becoming a promising technology for assessing the ICA and has the advantage of enabling scanning through an opaque cornea or examining painful eyes.¹,⁶⁻⁷ The built-in software of the AS-OCT system (Visante; Carl Zeiss Meditec, Inc. Dublin, CA) offers measurable parameters but also requires time-consuming and subjective user input, which may compromise measurement reproducibility.⁸

A reliable measurement of the ICA and its subsequent clinical evaluation may eventually facilitate the choice of an appropriate treatment. ICA parameters, such as the angle-opening distance (AOD) and the trabecular iris surface area (TISA), are used to quantify the ICA and are measured with reference to the location of the scleral spur (Fig. 1).

Since the scleral spur is used as the reference point for the relative position of the trabecular meshwork and is therefore vital for the diagnosis of angle closure, it represents an important anatomic landmark. However, the location of the scleral spur has to be determined by hand, and this necessity introduces an important human factor in the analysis of an AS-OCT image, possibly generating nonnegligible intra- and interobserver variance. Studies investigating the visibility of the scleral spur with AS-OCT showed a visualization between 70% and 78.9%.⁶⁻⁹ Other studies have evaluated the reproducibility of the AOD and TISA with self-designed software and report reliable measurements with increasing variability when more than one observer identifies the scleral spur.⁵,⁸,¹⁰,¹¹

The purpose of the present study was to investigate the variability due to repeated AS-OCT image acquisitions from a single subject by a single operator, together with studying inter- and intraobserver reproducibility of generating ICA data with the standard software offered by Carl Zeiss Meditec, Inc. to determine the feasibility of using ICA assessment in daily practice.

METHODS

The study was conducted in accordance with the World Medical Association Declaration of Helsinki. Twenty-three healthy volunteers were recruited from the University Eye Clinic Maastricht and gave their informed consent. The volunteers, indicated as nonexperts, were medical students with only basic knowledge of ophthalmology. These nonexperts were given detailed instructions (including an instruction manual as well as an oral instruction) by an expert on how to acquire and analyze an AS-OCT image using a protocol that was especially designed for this study (citation protocol in Supplementary Materials,

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http://www.iovs.org/lookup/suppl/doi:10.1167/iovs.10-5872/-/DCSupplemental). Since the location of the scleral spur was of crucial importance for this study, it was highlighted in our protocol by using clarifying illustrations (Figs. 1A, 1B). The protocol was designed to limit human influence on the image analysis to the choice of the positioning of the green dot on the scleral spur. Although small manual adjustments after placing the ICA tool are possible, such adjustments were not allowed in our protocol. If the observer was not satisfied with the placement of the marks of the ICA tool, the ICA tool was deleted, and the software was restarted until the observer was satisfied with the result.

All subjects underwent five consecutive AS-OCT images of the right eye taken by one of their fellow nonexpert observers.

The five images were all acquired in the enhanced anterior segment single (EASS) mode, in the 180° to 0° meridian (from temporal to nasal), and under the same light conditions (>200 lux). The EASS automatically averages four frames per image, to minimize the noise–contrast ratio. All subjects had an undilated pupil and were asked to look at the internal fixation light. The images were analyzed with the AS-OCT software (ver. 2.0.1.88; Visante, Carl Zeiss Meditec, Inc.).

The software included an ICA module. Once an image was acquired, the ICA tool had to be manually placed on the scleral spur, after which the software automatically generated the AOD and the TISA at 500 μm and 750 μm (Fig. 1C).

All data were analyzed using a statistical software package (SPSS ver. 16.0; SPSS Inc., Chicago, IL).

Variability Due to Repeated AS-OCT Image Acquisitions by a Single Operator

For the assessment of variability due to repeated AS-OCT image acquisitions, the 23 nonexperts each acquired five images of the right eye of one of their fellow nonexpert peers. The two experts analyzed all 115 (23 × 5) acquired images in random order. A random intercept model was fitted to account for possible correlation introduced in the data due to repeated image acquisitions within one subject. The subjects (23 in total) were considered a random effect, whereas the expert observers (n = 2) and the repeated image acquisitions (n = 5) were taken as fixed-effect factors.

Variability and Reproducibility of Analyzing an AS-OCT Image

The images were randomly analyzed, with a time interval of 2 minutes between each image. To reduce the influence of observer memory with regard to the assignment of the scleral spur position, the program was shut down during the interval, after which the adjustments were newly set up and the images were randomly offered again.

All (expert as well as nonexpert) observers assessed the nasal and temporal angles according to the protocol. Statistical analyses of the ICA data were subsequently performed for the separate groups of experts and nonexperts, to check for differences in reliability.

**Expert Analysis.** A random intercept model was also used to determine whether the observers were significant sources of variation in the ICA analysis. The subjects (n = 23) were a random effect, whereas the expert observers (n = 2) and the repeated image acquisitions (n = 5) were fixed-effect factors.

In addition, the ICA data of the five repeated image acquisitions per subject (23 in total) were averaged for each expert. The standard deviation (SD) per subject was calculated and also averaged for the 23 subjects in total. The coefficient of variation (CV) was obtained by dividing the SD by the mean. The mean CV was calculated afterward for both the experts, apart and together. These calculations were made for all parameters.

Intraclass correlation coefficients (ICCs) were used as measures of intra- and interobserver reliability. ICCs, based on the available data of the repeated image acquisitions, were computed for each single observer as a measure of intraobserver reproducibility. For the computation of interobserver ICC, the ICA data was averaged over the five repeated image acquisitions. Finally, a Bland-Altman plot was used to facilitate visual interpretation of the interobserver agreement between the two experts.

**Nonexpert versus Expert Analysis.** From the five images that were acquired from each of the 23 subjects, one image was randomly chosen per subject. This procedure was repeated four times,

**TABLE 1. Outcome Parameters as Estimated by the Random Intercept Model**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Expert 1</th>
<th>Expert 2</th>
<th>P Value for the Difference in Means</th>
</tr>
</thead>
<tbody>
<tr>
<td>AOD 500, mm</td>
<td>0.472 ± 0.036</td>
<td>0.486 ± 0.036</td>
<td>0.055</td>
</tr>
<tr>
<td>AOD 750, mm</td>
<td>0.680 ± 0.046</td>
<td>0.689 ± 0.046</td>
<td>0.362</td>
</tr>
<tr>
<td>TISA 500, mm²</td>
<td>0.163 ± 0.014</td>
<td>0.173 ± 0.014</td>
<td>0.0005</td>
</tr>
<tr>
<td>TISA 750, mm²</td>
<td>0.309 ± 0.024</td>
<td>0.321 ± 0.024</td>
<td>0.0095</td>
</tr>
</tbody>
</table>

Data are the mean ± SE for each expert.
Figure 2. Bland-Altman plot of the four parameters, showing a high agreement between the two experts.
to provide a reasonably random sample. Thereafter, all 23 nonexpert observers analyzed the five images in a random order. These images were used to study the inter- and intraobserver reproducibility of the ICA analysis performed by the nonexpert observers.

The CV was calculated for each observer (n = 23) separately and for the whole group of nonexperts together. The ICCs of the image measurement replications were computed for each of the 23 nonexpert observers.

For the comparison between experts and nonexperts, the experts analyzed the same images.

**RESULTS**

The sample consisted of 23 nonexpert subjects, of whom 9 were men and 14 were women with a mean age of 22.96 ± 1.89 years. None of them was known to have ocular disease.

All images were assessed by the same 23 nonexperts and by 2 experts (1 man, 1 woman). In all AS-OCT images the scleral spur was identifiable, so that there was no need to exclude images due to nonvisibility of the scleral spur.

**Variability Due to Repeated AS-OCT Image Acquisitions by a Single Operator**

In the random intercept model that was used to assess the variability due to repeated AS-OCT image acquisitions, the images (n = 5 for each of the 23 subjects) did not significantly (P > 0.8) differ from each other for all outcome parameters. This result shows that repeated acquisitions of the AS-OCT images were not a significant source of variability in the outcome parameters.

**Variability and Reproducibility of Analyzing an AS-OCT Image**

**Expert Analysis.** In analyzing the ICA assessments made by the experts, the same random intercept model was used. The mean values of each of the four outcome parameters, as estimated by the random intercept model are shown in Table 1. For parsimonious reasons, only the P values for estimated differences in the means are displayed. A statistically significant difference between the observers was detected in two of the outcome parameters (TISA 500, TISA 750), with a third one on the verge of significance (AOD 500).

**DISCUSSION**

Apart from a slight statistically significant intraobserver reproducibility difference for TISA 500 and the TISA 750, no significant difference in the variability of acquiring AS-OCT images made by the experts was found in our study. In a previous study, it was stated that when AS-OCT image acquisitions are performed by less-experienced operators, the percentage of variability due to repeated AS-OCT image acquisitions, the CVs were averaged for both sides. The mean CV for the two experts was 10.4% ± 5.7% for the AOD 500, 9.4% ± 4.5% for the AOD 750, 12.5% ± 7.0% for the TISA 500, and 10.5% ± 5.3% for the TISA 750. There were no statistically significant differences between the two experts.

Intraobserver ICCs for expert 1 were 0.881, 0.844, 0.889, and 0.887 for AOD 500, AOD 750, TISA 500, and TISA 750, respectively. For expert 2, the intraobserver ICCs were 0.935, 0.909, 0.987, and 0.936 for these parameters. Given their high values (mean ICC 0.875 ± 0.021 in expert 1 and 0.942 ± 0.033 in expert 2), as well as the fact that the replications did not differ significantly in the modeling approach, one ICA reading per subject was obtained after averaging over the five repeated measurements. Thereafter, the interobserver ICC was computed: 0.988 for AOD 500 and AOD 750, 0.978 for TISA 500, and 0.987 for TISA 750.

**Nonexpert versus Expert Analysis.** There were no statistically significant differences between the nasal and the temporal CVs; therefore, the CVs were averaged. The mean CV for the nonexperts was 9.8% ± 5.6% for AOD 500, 9.6% ± 4.8% for AOD 750, 11.5% ± 5.9% for TISA 500, and 9.9% ± 4.9% for TISA 750.

Intraobserver ICCs ranged from 0.549 to 0.965, with a mean of 0.902 ± 0.09 for AOD 500, and from 0.572 to 0.972, with a mean of 0.897 ± 0.08 for AOD 750. The TISA 500 ICC ranged from 0.670 to 0.963, with a mean of 0.909 ± 0.08, and the TISA 750 from 0.635 to 0.973, with a mean of 0.913 ± 0.07. The box plot, shown in Figure 3 illustrates the intraobserver ICC of the 23 nonexperts for analysis of the four parameters. There were no statistically significant differences between the experts and nonexperts in intraobserver or interobserver CV (P = 0.09 to P = 0.3).

Table 2 shows the absolute means of all nasal and temporal parameters for the experts and nonexperts. There were no statistically significant differences between the absolute means of the nasal and temporal parameters for the experts (P = 0.5 to P = 0.8) or the nonexperts (P = 0.4 to P = 0.8).

**FIGURE 3.** Box plot showing the intraobserver ICCs based on five image measurement replications of the nonexpert analysis.
nongradable images could be higher. The varying levels of observer experience would thus affect the performance of AS-OCT as a screening tool. Another study stated that the Visante OCT (Carl Zeiss Meditec, Inc.) can be operated by a technician with minimal expertise. The latter findings correspond to our study. However, the fact that the nonexperts (medical students) received a solid instruction on how to analyze the image may have influenced our results.

The analyses of the ICA assessments showed a mean CV of 10.2% among the nonexperts in our reproducibility study. These results were similar to those of the expert analysis, which showed a mean CV of 10.7%. However, the range was larger in the nonexpert group.

Radhakrishnan et al. indicated an AOD 500 cutoff of 190 μm for detecting occludable angles. The 10% variation that we found in the analysis of our reproducibility study of the ICA will probably be acceptable in most cases in daily practice.

Previous studies have reported low intra- and interobserver variability in ICA measurements acquired by using AS-OCT, lending supporting evidence to their reliability. However, in two of these studies the anterior chamber angle and the opening width were used, but both these parameters are unsuitable for irregular iris profiles. Other studies have evaluated the reproducibility of the ICA with self-designed software.

In previous studies, the anterior chamber was imaged with the anterior segment single protocol, whereas the enhanced mode (EASS) was used in the present study. The EASS mode combines four anterior segment single scans and produces a better visualization of the scleral spur, making a more precise localization of the scleral spur by the observer possible. In our study, the scleral spur was visible in all images, in both the nasal and temporal angles. The use of the EASS mode probably contributed to the good results of the nonexperts.

We are also aware of limitations in the present reproducibility study. The images were taken in only one meridian (temporal to nasal), other meridians (i.e., inferior/superior were not investigated). Recent literature states that the temporal angle is the largest and the inferior angle the smallest. Our data suggest that there is no difference in the absolute values of the nasal and the temporal angles. However, the purpose of our study was not to compare different angles but to investigate the reproducibility of ICA parameters within one angle. Another limitation of our study is that we included only young, healthy volunteers without ocular disease (i.e., narrow angle glaucoma). The analysis of ICA parameters of narrow-angle glaucoma patients may be less reliable due to a poorer visibility of the scleral spur.

Overall, the present results have shown that ICA measurements with the built-in Visante OCT software are useful for clinical practice. A standardized protocol for the analysis of AS-OCT images including a solid instruction for nonexperts should be helpful to further safeguard high reproducibility.

References


