Quantitative measurement of horizontal strabismus with digital photography

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PURPOSE To develop a method to calculate the gaze angle in photographs and to determine its validity and reliability in real strabismus patients.

METHODS Photographs of eyes from 15 orthophoric subjects (n = 1,022) with known gaze angle and imaging distance were investigated with the help of a smartphone application developed by the authors. The application provided measurements of the distance from the geometrical center of the cornea to the light reflex (RD) and corneal diameter (CD). The RD/CD ratio of each gaze angle was recorded. To estimate the eyes' gaze angle, an equation to determine the best-fit line for the gaze angle data according to each RD/CD ratio was created. In a second clinical analysis, this equation was applied to photographs of real strabismus patients (n = 72), and the results were compared with measurements taken by a double-masked strabismus specialist. Separately, an equation was created to calculate the imaging distance using the given interpupillary distance.

RESULTS There was a high correlation between the real and estimated gaze angles ($r = 0.990$, $P < 0.001$). The mean error of the estimated gaze angle was found to be $0.03^{\Delta} \pm 4.60^{\Delta}$. There was a high correlation between the real and estimated imaging distance ($r = 0.997$, $P < 0.001$) and a high correlation between the measurements of the application and the specialist ($r = 0.966$, $P < 0.001$). The average error was $-0.68^{\Delta} \pm 6.1^{\Delta}$, and the reliability was high (Cronbach's $\alpha = 0.983$).

CONCLUSIONS The application measured horizontal strabismus in photographs with high reliability. (J AAPOS 2019;23:18.e1-6)

The prism cover and Hirschberg and Krimsky tests are used for quantitative measurement of strabismus, accuracy of which is critical in surgical planning.[1] Of these tests, the gold standard is the prism cover test, which, however, it cannot be used in younger children, who are more susceptible to amblyopia, because the test requires cooperation. The Hirschberg and Krimsky tests have a higher error margin and should only be applied by experienced pediatric ophthalmologists.[1] Therefore, investigators have attempted to develop new and reliable methods, based on photographs and computation, that can be used in younger children.[2-6] However, most of these methods have not been used practically since they are costly and difficult to use. The purpose of the present study was to develop an equation that can reliably estimate the degree of strabismus based on a photograph taken with a smartphone, without being significantly affected by the imaging distance, and to evaluate the reliability of the method.

Materials and Methods

Model Validation

Because of programing limitations, the application (EyeStrab) was initially coded only for the Android platform (https://play.google.com/store/apps/details?id=com.erencerman.eyestrab&hl). Recently it has also been published in IOS App Store (https://itunes.apple.com/us/app/eyestrab/id1447441676). However, the horizontal flash alignment of Android phones was found to interfere with calculations. Thus, an iPhone 6 came to be preferred for photography, because it had vertical flash alignment and high resolution. Photographs were then imported to the application. The resolution of the photograph was 3264 × 2448 pixels (8 megapixels), and the camera imaging angle was 60°. The interface of the application was designed so that the user could manually mark the limbus with a resizable circle and mark the corneal light reflex with a plus sign (Figure 1). The center of the circle was defined as the "geometrical center of the cornea," as previously described.[7] The application was then able to measure the following distances in pixels: (1) geometric center of the cornea to light reflex distance (RD), (2) corneal diameter (CD), and (3) interpupillary distance (IPD). See Figure 1.

Fifteen healthy orthotropic individuals were photographed at different known imaging distances (20, 30, 40, 50 cm). At each imaging distance, the subject was asked to look at specific distances

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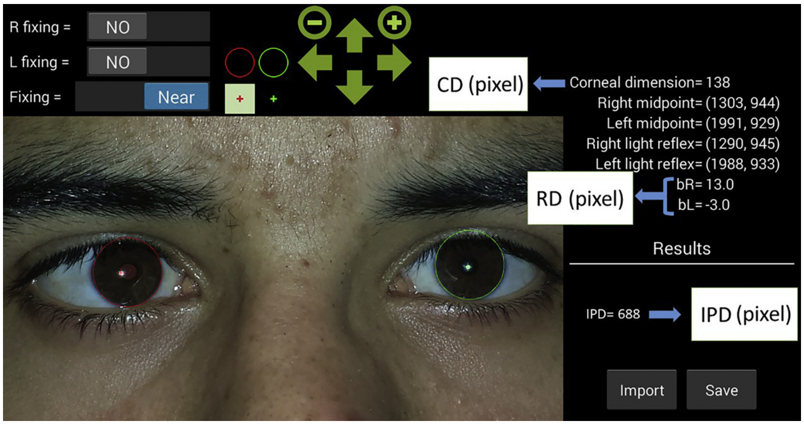

FIG 1. The following distances were calculated in pixels: corneal diameter (CD), geometric center to reflex distance (RD), and interpupillary distance (IPD). These distances were calculated by the application.

on a ruler, with "0" placed at the center of the camera. The midline of the photograph and the face was aligned with the help of a guideline in the application's camera interface. For each eye, the real gaze angle (z_0, z_1) was calculated using a formula created with the help of Geometry Expression (Saltire Software, Tigard, OR) in accordance with the definition of a prism diopter (Figure 2). A total of 511 photos were taken, and a total of 1,022 photographs of eyes with gaze angles ranging from -83^{Δ} to 83^{Δ} were obtained.

It was assumed that the gaze angle was a function of the ratio of RD to CD. This ratio could be easily calculated by the application, because both distances were measured in pixels in the photograph. The best-fit line for the data was determined using the real gaze angle and RD/CD ratio. TableCurve 2D (Systat Software, San Jose, CA) software was used to find the best equation (Figure 3).

$$\textit{Estimated gaze angle} = (c_1) + \frac{c_2}{\left[1+e^{-\left(\frac{RD/CD\ ratio - c_4 * \ln\left(2^{(1/c_5)}-1\right) - c_3}{c_4}\right)}\right]^{c5}}$$

c_1 = −77,9379013054072
c_2 = 139,319650676782
c_3 = − 0,0556254162703235
c_4 = 0,106283020279428
c_5 = 0,411551255814536

The reliability of this function was then analyzed by comparing the real gaze angle to estimated gaze angle.

The application was able to calculate the imaging distance given the IPD in millimeters. The IPD of the 15 subjects was measured in millimeters using an autorefractometer (Nidek, ARK-530A, Japan). Because the application could calculate the IPD in pixels, given millimeters, it was possible to calculate a factor to convert pixels to millimeters on a vertical plane passing through the pupils. The angle of the camera was 60°; thus, one could assume an equilateral triangle with one side lying on that imaginary plane and

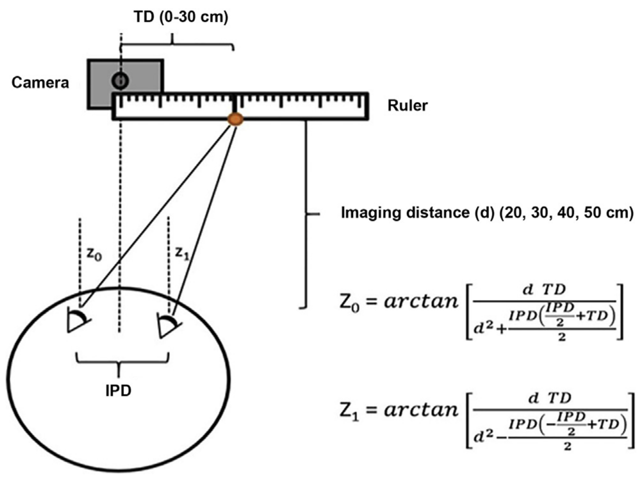

FIG 2. Imaging setup as a diagram. The gaze angles for both eyes (z_0 and z_1) were calculated as indicated in the equation. *TD*, target distance.

passing through interpupillary axis, with the length of this side assumed to be equal to the width of the photograph in pixels. The imaging distance was assumed to be equal to the height of this equilateral triangle and could be calculated in pixels. Therefore, converting pixels to mm with IPD measured in millimeters enabled calculation of imaging distance. This equation was created with Geometry Express software (Figure 4). The estimated imaging distance was compared with the real imaging distance. The effect of imaging distance was analyzed separately.

Clinical Evaluation

The second part of the study was a double-masked clinical investigation of the model's reliability. This study was approved by Marmara University School of Medicine Ethics Committee, and informed consent was obtained from all patients or their parents. The estimated deviation angle obtained by the equation was compared with the measurements obtained by the Krimsky or prism cover testing performed by a strabismus expert. Patients

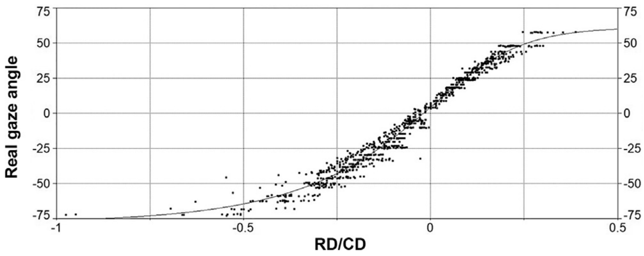

FIG 3. Surface compatibility and equation calculation of data entered using TableCurve 2D software. The surface compatibility equation that best predicts the real gaze angle (y-axis) using RD/CD (x-axis) was obtained via Table2D software; the equation labeled *Rank 54 Eqn 8090 AsymSig (a,b,c,d,e)* was preferred.

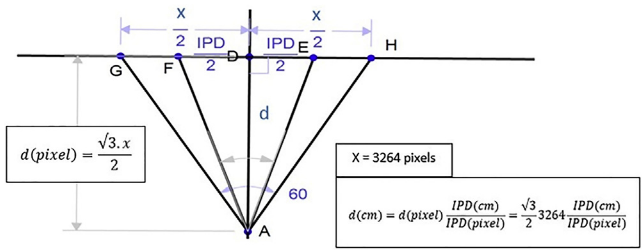

FIG 4. Geometry expression software was used to perform trigonometric calculations.

who applied to Marmara University Department of Ophthalmology for the first time or whose strabismus was followed by the Pediatric Ophthalmology and Strabismus Department were included. Patients with latent strabismus who could not fix to the camera or had corneal surface problems were excluded. Those with manifest strabismus were first assessed by a strabismus specialist using either the Krimsky or prism cover test according to the suitability of the patient. In a separate room, flash photography was performed by the first author (VD) while the patient fixed their gaze to the camera at least with one eye. CD was determined for the fixing eye and then applied to the other eye (Figure 1).

Deviation angles were calculated separately for both eyes using the equation. The deviation angle of the fixing eye was assumed to be the angle κ and was subtracted from the deviation angle of the nonfixing eye. Because it would not be possible to calculate angle κ otherwise, photographs in which the patient was not fixing with at least with one eye were disregarded. The obtained results were compared with the measurements obtained by the strabismus specialist. No particular attention was paid to imaging distance while eyes were photographed.

For reliability testing (Cronbach's α), Bland-Altman analysis, and t tests, IBM SPSS Statistics for Windows Version 23.0 (IBM, Armonk, NY) was used.

Results

Model Validation

In total, 511 photographs of 15 individuals were taken, and measurements were obtained for 1,022 gaze angles. There was a high correlation between the estimated gaze angle found by the equation and the real gaze angle ($r = 0.990$, $P < 0.001$; Figure 5A). Reliability analysis yielded a Cronbach's α value of 0.995. The graph of the Bland-Altman analysis is shown in Figure 5B. According to this analysis, no significant difference was observed between the estimated gaze angle and the real gaze angle using the t test ($P < 0.05$). The average total error was $0.03^\Delta \pm 4.60^\Delta$ (n = 1,022); the average error between -25^Δ and $+25^\Delta$ was found to be $-0.30^\Delta \pm 4.13^\Delta$ (n = 460); and the average error in gaze angles between -25^Δ and $+25^\Delta$ was found to be $0.25^\Delta \pm 4.94^\Delta$ (n = 562).

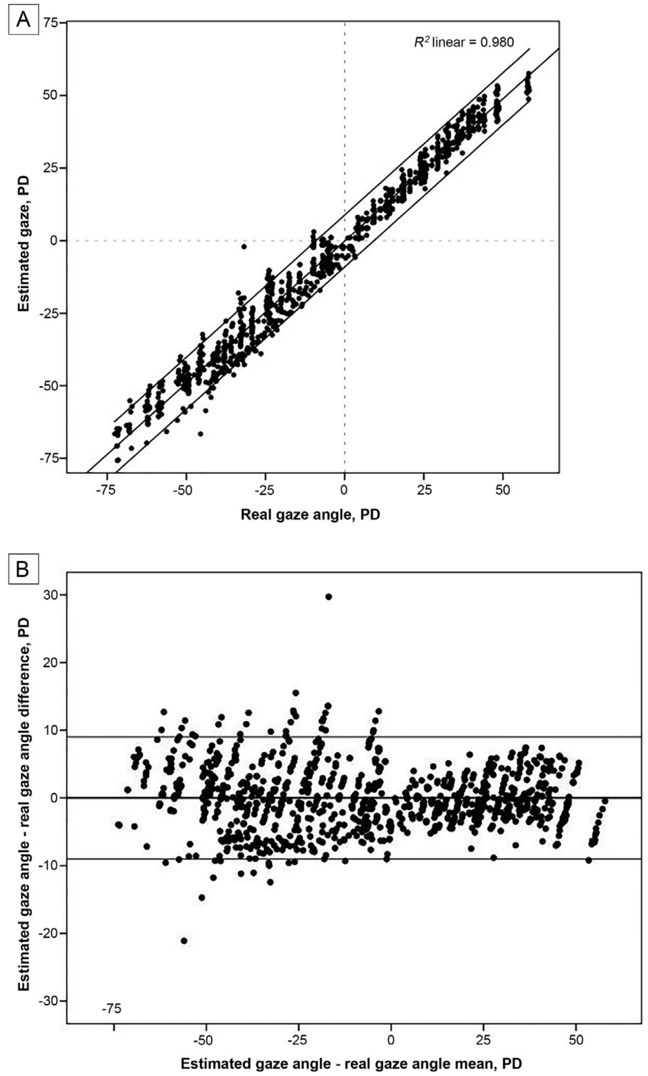

FIG 5. Relationship between the estimated gaze angle and real gaze angle A, Correlation between the estimated gaze angle and real gaze angle, 95% confidence interval lines. B, Bland-Altman analysis of the estimated gaze angle and real gaze angle.

The results of the application's distance estimation, performed according to the method described above at 20, 30, 40, and 50 cm, are presented in Figure 6. There was a high correlation between imaging distance and estimated distance ($r = 0.0997$, $P < 0.001$). On examining the reliability of the photographs taken using the actual imaging distance,

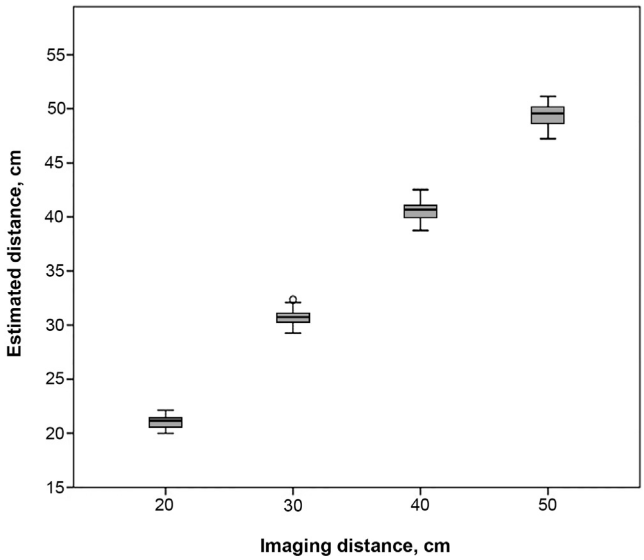

FIG 6. Reliability results of imaging distance calculated in the photographs taken at an imaging distance of 20, 30, 40, and 50 cm with Cronbach's α.

the total reliability coefficient was calculated as the Cronbach's α (0.998). The obtained data, including distances and the average calculated distance and standard deviation, are presented in Table 1. There was no correlation between the gaze angle estimation error and imaging distance ($P > 0.05$).

Clinical Evaluation

A total of 72 patients were photographed. The average age of patients was 8.6 ± 8.4 (range, 1-34) years. While 24 of the patients were diagnosed with exotropia, 48 were diagnosed with esotropia.

Comparison of the estimated deviation angle with the results of the specialist's deviation assessment revealed a high correlation ($r = 0.966$, $P < 0.001$; Figure 7A). The Cronbach's α coefficient was 0.983. The estimated deviation angle and specialist's measurement were compared using Bland-Altman analysis, and there was no statistically significant difference between the two tests ($P > 0.05$) (Figure 7B). The average difference between the estimated deviation and the specialist's measurement was $-0.68^{\Delta} \pm 6.1^{\Delta}$. This error rate was not correlated with patient age or the angle of deviation ($P > 0.05$).

Discussion

Despite technological advances, the prism cover test remains the gold standard for quantifying strabismus. The test is practical and measures deviation after adjustment for κ angle; however, few studies have investigated its reliability and precision. The test is open to interpretation and depends on operator skill. Interexaminer variation has been reported to be about 10^{Δ}.[8] In another study, interexaminer reliability was shown to be about 12^{Δ} for deviations $>20^{\Delta}$

Table 1. Number of photographs obtained per eye by distance and the average calculated distance

Imaging distance, cm	No. photos per eye	Average calculated distance, cm, mean ± SD (range)
20	154	22.46 ± 0.55 (21.33-23.60)
30	222	30.69 ± 0.60 (29.26-32.36)
40	222	40.51 ± 0.79 (38.74-42.53)
50	424	49.38 ± 0.91 (47.24-51.16)

SD, standard deviation.

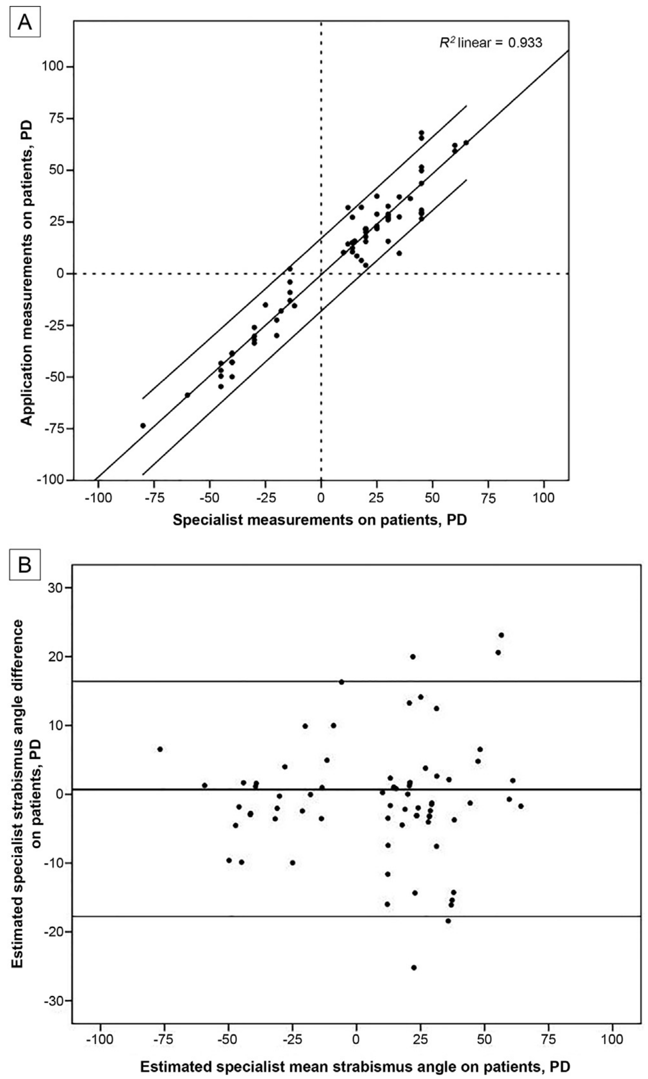

FIG 7. Relationship between the specialist's measurements and the measurement of the deviation angles calculated with the application. A, Correlation between the estimated deviation angles and specialist's deviation angle, 95% confidence interval lines. B, Bland-Altman analysis of the estimated deviation angles and specialist's deviation angle.

and about 6^{Δ} for deviations $<20^{\Delta}$.[9] The same study[9] also states that smaller deviations (10^{Δ}-20^{Δ}) measured using smaller increments (2^{Δ}) had less measurement error than larger deviations ($>20^{\Delta}$) measured in 2.5^{Δ} increments. Since prism bars usually have increments of 2^{Δ} between

0^{Δ} and 25^{Δ} and increments of 5^{Δ} between 25^{Δ} and 45^{Δ}, measurement errors may be affected. Furthermore, the prism cover test is difficult to perform for uncooperative or young children, but the Hirschberg and conventional Krimsky methods are substantially less accurate than the alternate prism and cover tests.[1] Strictly objective documentation is not possible for the prism cover test.

Strabismologists typically document patients with the aid of imaging and photography. However, there is no established method for quantifying photographic evidence. This study presents an approximation of the gaze angle of an eye from a photograph. If the angle κ for each eye is known, the deviation of a patient can be best approximated.

Applying the deviation angle to an automated and computerized system has been investigated for years.[2-5,10-12] Usually the Hirschberg ratio (HR) is used, but high errors have been reported, especially with increased strabismus angles.[4,11,13,14,17] Scholarly work has reported substantial variation in Hirschberg ratio values.[4,5,15-18] This variation is often attributed to individual differences in corneal shape. However, an essential question—whether this variation really exists—has been ignored. Assumption of the existence of a Hirschberg ratio can only exist in a linear function between gaze angle and reflex distance from the corneal center, for example, a = HR*b. Yet why should gaze angle correlate with reflex distance linearly? This study demonstrates that the best-fit function of the relation between them is in fact not linear, but sigmoid, as shown in Figure 3. Brodie[2,19] and DeRespinis and colleagues[10] have also discussed the nonlinearity of that function. We therefore suggest using the term *Hirschberg function* in this context.

To our knowledge, this study is the first to develop a method for calculating photograph-imaging distance. The presented method calculates the imaging distance in pixels, and if the IPD is known in mm, imaging distance can be calculated with good reliability, at least at imaging distances of 20–50 cm. The effect of imaging distance on gaze angle estimation within this range is minimal.

There are several limitations to the study. First, to be able to calculate the deviation of a strabismus patient in a photograph, the angle κ must be known. In this study, information about the angle κ is obtained from the fixating eye, and the same amount of angle κ is assumed for the opposite eye; however, it is known that the angle κ in each eye might differ.[20] This problem could be partially solved by taking two different photos in which each eye was fixated, but there could still be errors in estimation of the real angle κ. This could lead one to miss small-angle strabismus.

Second, photography can be used to assess only manifest strabismus. To assess latent strabismus, the fusion must be disrupted for an adequate period of time and the operator has to take the image of the eye behind the cover or while the fusion is disrupted. To overcome this problem, Yang and colleagues[6] designed a special eye cover that only permits light with a wavelength of 720 nm to permeate; imaging uses a special infrared camera. They measured the deviation angles using the 3D Strabismus Photo Analyzer, which they introduced in previous studies, and took photographs of 30 exotropic, 30 esotropic, and 30 orthophoric subjects. The method was compared with the prism cover test, and the results showed high positive correlation between the two techniques ($r = 0.900$, $P < 0.001$). However, it is not cost-effective, because it requires an infrared camera and a specially designed cover. In our clinical experience, a simple photograph can be taken quickly after removing the cover, but the efficiency of this method is questionable and should be analyzed in future studies.

Third, imaging was performed while the patient was fixating on the camera, and thus only strabismus at near fixation was assessed. However, a second round of imaging or a video imaging with a different fixation distance could be performed.

A recent study showed that binocular optical coherence tomography may also have promising results in quantification of strabismus.[21] However, similar problems can occur, such as misdiagnosing abnormal retinal correspondence, not taking into consideration of the asymmetric angle κ latent strabismus, and deviation with near and far fixation.[22] We believe that future work should aim to analyze video imaging rather than still images and machine learning must be applied for developing software algorithms, so that software might begin to simulate examination by an experienced strabismologist.

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