

# Development and Preliminary Evaluation of a Smartphone App for Measuring Eye Alignment

Shrinivas Pundlik<sup>1</sup>, Matteo Tomasi<sup>1</sup>, Rui Liu<sup>2,3</sup>, Kevin Houston<sup>1</sup>, and Gang Luo<sup>1</sup>

<sup>1</sup> Schepens Eye Research Institute of Mass Eye & Ear, Harvard Medical School, Boston, MA, USA

<sup>2</sup> Eye & ENT Hospital, Fudan University, Shanghai, China

<sup>3</sup> NHC Key Laboratory of Myopia (Fudan University), Laboratory of Myopia, Chinese Academy of Medical Sciences, Shanghai, China

**Correspondence:** Rui Liu, Eye & ENT Hospital, 83 Fenyang Road, Shanghai, China 200031. e-mail: rui\_liu@aliyun.com

**Received:** 11 June 2018

**Accepted:** 20 October 2018

**Published:** 8 February 2019

**Keywords:** smartphone app; eye alignment; strabismus

**Citation:** Pundlik S, Tomasi M, Liu R, Houston K, Luo G. Development and preliminary evaluation of a smartphone app for measuring eye alignment. *Trans Vis Sci Tech.* 2019; 8(1):19, <https://doi.org/10.1167/tvst.8.1.19>

Copyright 2019 The Authors

**Purpose:** We evaluate a smartphone application (app) performing an automated photographic Hirschberg test for measurement of eye deviations.

**Methods:** Three evaluation studies were conducted to measure eye deviations in the horizontal direction. First, gaze angles were measured with respect to the ground truth in nonstrabismic subjects ( $n = 25$ ) as they fixated monocularly on targets of known eccentricity covering an angular range of approximately  $\pm 13^\circ$ . Second, phoria measurements with the app at near fixation (distance = 40 cm) were compared with the modified Thorington (MT) test in normally-sighted subjects ( $n = 14$ ). Third, eye deviations using the app were compared to a cover test with prism neutralization (CTPN;  $n = 66$ ) and Synoptophore ( $n = 34$ ) in strabismic subjects. Regression analyses were used to compare the app and clinical measurements of the magnitude and direction of eye deviations (prism diopters,  $\Delta$ ).

**Results:** The gaze angles measured by the app closely followed the ground truth (slope = 1.007,  $R^2 = 0.97$ ,  $P < 0.001$ ), with a root mean squared error (RMSE) of 2.4 $\Delta$ . Phoria measurements with the app were consistent with MT (slope = 0.94,  $R^2 = 0.97$ ,  $P < 0.001$ , RMSE = 1.7 $\Delta$ ). Overall, the strabismus measurements with the app were higher than with Synoptophore (slope = 1.15,  $R^2 = 0.91$ ,  $P < 0.001$ ), but consistent with CTPN (slope = 0.95,  $R^2 = 0.95$ ,  $P < 0.001$ ). After correction of CTPN values for near fixation, the consistency of the app measurements with CTPN was improved further (slope = 1.01).

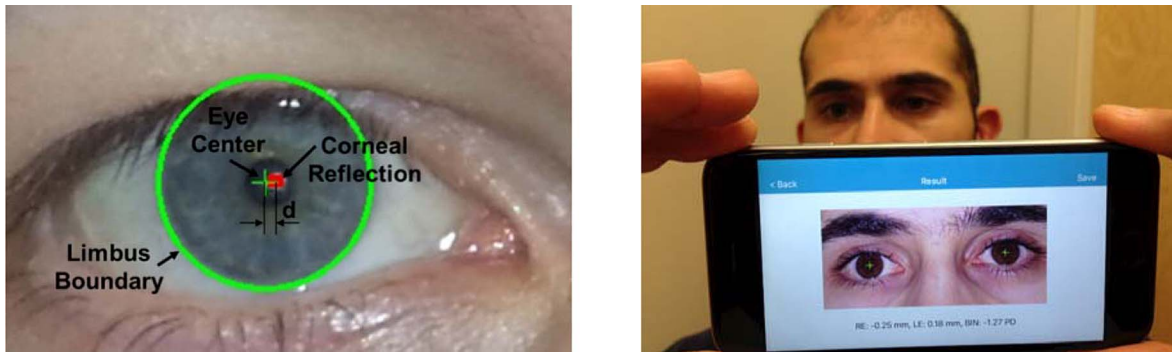
**Conclusions:** The app measurements of manifest and latent eye deviations were consistent with the comparator clinical methods.

**Translational Relevance:** A smartphone app for measurement of eye alignment can be a convenient clinical tool and has potential to be beneficial in telemedicine.

## Introduction

Proper alignment of the eyes is important for normal binocular vision. Strabismus (or tropia) refers to the misalignment of the eyes under binocular viewing. Strabismus is a main cause of amblyopia in children,<sup>1–3</sup> leading to permanently reduced vision in one eye if not identified and treated early.<sup>4–7</sup> Adults with various neurologic conditions as a result of stroke or traumatic brain injuries also can suffer strabismus,<sup>8</sup> and consequently are more likely experience double vision, increased risk of fall with injury,<sup>9</sup> and decreased quality of life.<sup>10</sup>

Measurement of eye alignment is difficult and requires a high degree of training and experience. With present methods, patients must hold precise fixation on a target as the examiner alternately covers an eye while introducing a series of prism lenses (cover test with prism neutralization [CTPN], or also referred to as alternate prism cover test). The examiner watches for elimination of refixation eye movements with gradually increasing prism power, which, even in cooperative patients, requires a high degree of observational skill and experience to determine correctly. Accurate measurement becomes more challenging when patients are unable to fully participate in the exam, such as young children<sup>11</sup> or



**Figure 1.** The EyeTurn app for measurement of eye deviations. (Left) Features detected by the app via automatic image processing: limbus boundary denoted by a green circle, its center denoted by a green cross, and the corneal reflection due to the flash denoted by a red dot. The distance between the eye center and corneal reflection, shown as 'd', is compared between the two eyes to detect eye deviation. (Right) To measure the eye alignment using a single picture, the phone is held 30 cm from the eyes of the subject and a picture is taken as the subject fixates binocularly. This mode of operation is well suited for measuring or screening for manifest eye deviation. Permission to publish photograph was obtained via a signed consent to publish document.

adults with brain injuries. Intermittent strabismus and smaller magnitudes of deviations that are not visually obvious ( $<15$  prism diopters [ $\Delta$ ])<sup>12</sup> may cause cases to remain undiagnosed.

The photographic or automated Hirschberg method, which is based on comparison of the displacement of corneal reflections between the eyes, has been known for strabismus measurement for many decades, but was limited originally by insufficient camera resolution. As camera resolution capability has rapidly improved over the last approximately 10 years, computer-aided approaches for processing digital photographs<sup>13</sup> and stand-alone commercial devices that use the photographic Hirschberg method have emerged (e.g., Volk Eye Check, Spot Vision Screener).<sup>14</sup> Compared to these standalone systems, modern smartphone cameras provide better value, improved accessibility, and better cameras. Based on our calculations using a Hirschberg ratio (HR) of approximately  $22 \Delta/\text{mm}$ ,<sup>15,16</sup> currently available smartphone cameras can theoretically be accurate to  $1.3\Delta$ , slightly better than the current resolution in the clinical gold standard (steps on a typical prism bar used for cover tests in strabismus measurement). Therefore, it should be feasible technically to use images from a smartphone camera for measurement of strabismus.

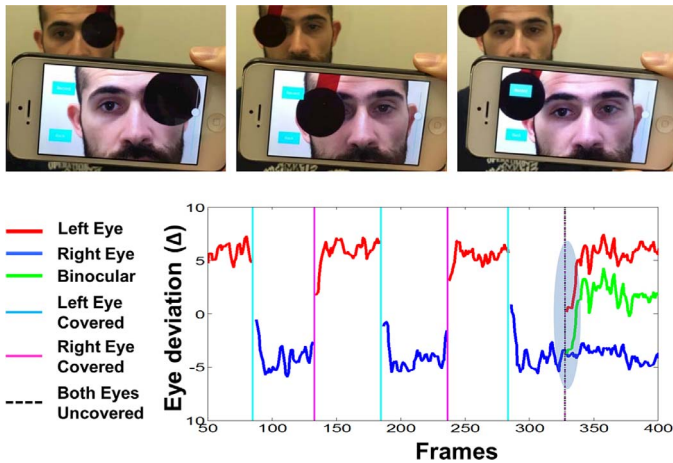
We have developed a smartphone application (app), EyeTurn, which implements the photographic Hirschberg method and also uses a novel video analysis mode that enables automated dissociated measurements (i.e., prism-free cover test) in an attempt to address measurement in intermittent strabismus and phoria. Our goal was to determine

baseline feasibility of the smartphone-based eye alignment measurement approach. This study describes the core functionalities of the app and reports the results of laboratory and preliminary comparison to common clinical measurements of eye misalignment. Our hypotheses were: (1) the app would provide accuracy consistent with our resolution-predictions of  $\pm 2\Delta$ , and (2) that the app measurements would be correlated significantly with clinical methods. We also aimed to evaluate individual measurement of the HR (calibration) compared to use of the population norm.

## Methods

### Core Functionalities of the EyeTurn App

Using a conventional smartphone with a high resolution rear camera and flash (for example, Samsung Galaxy S4 and above; Samsung, Seoul, South Korea, and iPhone 5 and above; Apple, Cupertino, CA), the EyeTurn app automatically detects the difference in corneal reflection position relative to the eye center (based on fitting a curve to the limbus boundary) to calculate ocular misalignment, and provide an objective measure of eye deviation from the captured image of the patient's eyes (Fig. 1). The captured images are processed entirely within the smartphone using custom image processing algorithms, and the eye deviation measurements are displayed on the screen usually within a couple of seconds. We use iris center (center of the eye, or the center defined by the limbus curve) instead of pupil center as the reference for computing the corneal reflection decentration, as it has been reported



**Figure 2.** Cover testing mode for dissociated measurements using the app. (Top row) Alternating cover–uncover test using the video-based cover test mode. This novel operational mode can be used for dissociated measurements. The examiner alternately covers the eyes (first two images on top row). The frame with both eyes uncovered (third image on the top row) is selected for automatic processing by the app for measurement of the eye deviation. (Bottom row) Eye movement trace after offline processing of the video of the alternate cover test shows the movements of the eyes after the cover is removed. Negative values show temporal deviation (outward), whereas positive values show nasal deviation (inward). There is a brief duration after removing the cover during which the deviation can be measured (highlighted by the oval gray zone). It should be noted that the eye movement trace in this figure was generated by processing the video recorded by the smartphone on a desktop computer using the same image processing software used in the app, but may be included as part of the app in the future. Permission to publish photograph was obtained via a signed consent to publish document.

to be a more robust reference for measuring ocular alignment, especially when computing binocular differences.<sup>17</sup> Also, for darker iris colors, the limbus boundary is better-delineated than the pupil boundary in visible spectrum images captured by a typical smartphone camera. The corneal reflection decentration distance is converted to prism diopters ( $\Delta$ ) using an HR in the range of previously reported values.<sup>15,16</sup>

The app offers various operating modes through which the eye deviation can either be measured monocularly or binocularly. Additionally, the app also allows dissociated measurement, for example to measure intermittent strabismus condition or phoria, where the deviation between the eyes is not manifest. In clinic, measurement under dissociated conditions is done by performing either cover–uncover or alternate-cover tests with prisms (CTPN). One key feature of the app is the ability to measure eye deviations

under dissociated conditions without the need for prism neutralization. In this operational mode, the examiner presses a button to record a video, while the patient fixates on a target binocularly. The patient's binocular fusion is broken in the traditional manner by either cover–uncover (of one eye) or alternate cover (involving both eyes). The examiner ultimately uncovers one eye and the app records this entire event as a video sequence (Fig. 2). The user is prompted with audio tones to assist in the timing of the cover–uncover. The video frame just after uncovering an eye can be selected for processing the maximum dissociated eye deviation. Due to the high frame-rate of video capture (30 Hz), we can measure the deviation before a recovery vergence eye movement can be initiated. Figure 2b shows an example of the eye movement trace obtained when performing the alternate cover test, with a smartphone recording the video of this event.

## EyeTurn App Evaluation

The EyeTurn app was evaluated in three separate studies to test different aspects and operational modes of the app as described below. The study was conducted in accordance with the tenets of the Declaration of Helsinki at three different sites: Schepens Eye Research Institute (Boston, MA), Spaulding Rehabilitation Hospital (Boston, MA) and Eye & ENT Hospital of Fudan University (Shanghai, China). Informed consent was obtained from all the participants or their proxies (parents or guardians) in case of underage subjects. Selection was affected neither by sex nor age. The study was approved by the local institutional review boards of the study sites.

### Study 1: Monocular Eye Deviation Measurement

The accuracy and reliability of the app related to the measurement of the angle of deviation was determined by inducing eye gaze shift in nonstrabismic subjects. The subjects sequentially fixated on targets of known eccentricity placed on the rear surface of the smartphone along the horizontal direction with their head stabilized in a chin–forehead rest (Fig. 3). The app does not need to be used in this manner in actual practice; however, for the purpose of establishing the true deviation values for the fixation targets, such a controlled setup was necessary. The test setup covered an angular range of  $\pm 13^\circ$  (approximately  $\pm 23\Delta$  with respect to a central fixation corresponding to camera lens). Two trials were performed per subject to determine test–retest



**Figure 3.** Experimental setup to measure the accuracy of the app in Study 1. Subjects without strabismus fixated on 13 targets on the rear side of a smartphone placed at a distance of 30 cm with their head resting on a chin-head rest. Twelve of the 13 fixation targets were a black cross on a white background. The center target was the smartphone camera. With the known distances, true eye deviation magnitudes with respect to the central fixation point were computed (angular range covered by the fixation targets was  $\pm 13^\circ$  or  $\pm 23\Delta$ ) and compared to measurements with the app.

repeatability. A total of 25 nonstrabismic normally-sighted subjects between 20 and 40 years old, of various different iris colors participated in the study. All subjects were able to resolve the 1 cm separation of the fixation targets at 30 cm without refraction correction.

The HR for each subject was determined using data from all 13 fixation points by plotting the app measurement against the known angular deviation for each fixation point, and determining best fit of this scatter plot using linear regression. The slope of this function represents the individual's HR and the  $y$ -intercept is the individual's angle  $\kappa$  (the angle between the visual and optical axes, represented as  $\kappa$ ).<sup>18,19</sup> We measured the within-subject test-retest repeatability of the app in estimating the HR and  $\kappa$  using a Bland-Altman<sup>20</sup> plot to compute 95% confidence interval (CI) of the difference between two trials. Furthermore, we tested the accuracy of using a population average value of the HR by comparing the absolute gaze angles estimated by the app measurements and the true deviation of the fixation targets (via regression analysis using MATLAB; Mathworks, Natick, MA). The HR used for a subject was the average HR of the rest of the subjects to ensure statistical robustness.

## Study 2: Laboratory Evaluation of App Cover Test Mode

In a second study, dissociated phoria measurements with the app were compared to the Modified Thorington (MT) test. Inclusion criteria were uncorrected near visual acuity of 20/30 or better in each eye, no suppression, and no other visual impairments. Fourteen normally-sighted subjects participated in the study (age  $\leq 40$  years), including one subject with intermittent exotropia, but with equal acuity in each eye. Subjects rested their head in a chin-head rest and the phone was mounted 40 cm from the eyes. A 20/30 size letter attached below the phone camera lens served as a fixation point and controlled accommodation. The eyes were alternately covered and then uncovered by an examiner with an occluder while the subject maintained fixation.<sup>21</sup> The app generated auditory tones to guide the examiner when to change the cover from one eye to the other. A higher-pitched tone was a cue to stop alternate cover and to uncover both eyes. The app recorded for 2 seconds after the final higher-pitched tone, resulting in 30 recorded frames. The app displayed the recorded frames and the user swiped through the frames to find and select the first frame after uncovering the eyes, which then was processed by the app to output the measurement value. Each subject was tested three times with the app in quick succession. Phoria also was measured using an MT near card (at 40 cm). The order of MT and the app testing was balanced. Linear regression analysis was used to compare the app and MT measurements.

## Study 3: Comparison of the App to CTPN in Patients With Strabismus

A diverse population of strabismic patients were recruited from Spaulding Rehabilitation Hospital and Eye & ENT Hospital of Fudan University. Inclusion criteria were prior diagnosis of horizontal strabismus (constant or intermittent exotropia or esotropia) and no other visual impairments. A total of 74 subjects were enrolled, and valid data for 66 subjects were collected (subject details in the Table). Use of picture mode or cover test (dissociated) mode in the EyeTurn app was left to the discretion of the examiners, which included a pediatric ophthalmologist specialized in strabismus (RL) and an optometrist specialized in vision rehabilitation who routinely performs CTPN in clinic (KH). The clinical staff tested the patients first with CTPN and then with the EyeTurn app to prevent bias of the cover test results by the objective app measurement (there is a subjective component to the

**Table.** Strabismus Measurement Study Participant Characteristics

Total patients	
Recruited	$n = 74$
Excluded	$n = 8$ (6 app error <sup>a</sup> , 1 operator error, 1 statistical outlier <sup>b</sup> )
Valid data	$n = 66$
Age (years)	
Overall	Median = 13, IQR = 19, Min = 4, Max = 63
Children	$n = 36$ (Median = 10, IQR = 4)
Adults <sup>c</sup>	$n = 26$ (Median = 31.5, IQR = 29.75)
Sex	
Male	$n = 36$
Female	$n = 30$
Measurement mode	
Picture	$n = 32$ (11 children, 21 adults)
Video	$n = 34$ (25 children, 9 adults)
Eye deviation ( $\Delta$ ) in horizontal direction <sup>d</sup>	
Exo-deviation	$n = 47$ (Median = 23.5, IQR = 16.62, Min = 5.6, Max = 58.2)
Eso-deviation	$n = 19$ (Median = 24, IQR = 16, Min = 9.25, Max = 58.2)

IQR, interquartile range.

<sup>a</sup> App failed to provide a result due to captured image (software errors, such as inability to detect eyes or errors in fitting the limbus curve).

<sup>b</sup> Points lying outside the 99% observational bounds for the data involving clinical test measurements versus app measurements.

<sup>c</sup> Exact age was not available for four adult subjects.

<sup>d</sup> Summary statistics using corrected prism values are reported.

cover test in deciding when there is reversal of movement). The CTPN testing was performed as is typically done clinically using prism bars.<sup>21</sup> For deviations larger than  $45\Delta$ , two prisms were separately put on each eye. Measurements with Synoptophore (Model: SBISA Synoptophore, Florence, Italy) were available for a subset of the strabismic subject population ( $n = 34$ ) at the Eye & ENT Hospital of Fudan University site and are reported as well (Supplementary Table S1).

Linear regression analysis was used to compare the app measurements of strabismus angle with CTPN and Synoptophore measurements. Since the CTPN measurements were done at near fixation to facilitate

direct comparison with the app measurements, corrections were made to the recorded CTPN values during data processing to account for the finite distance between the prism and center of rotation of the eye.<sup>22</sup> We arrived at a value of the distance between prism and center of rotation of eye by assuming a population average value of 24 mm for axial length<sup>23</sup> and a back vertex distance of 10 mm.

## Results

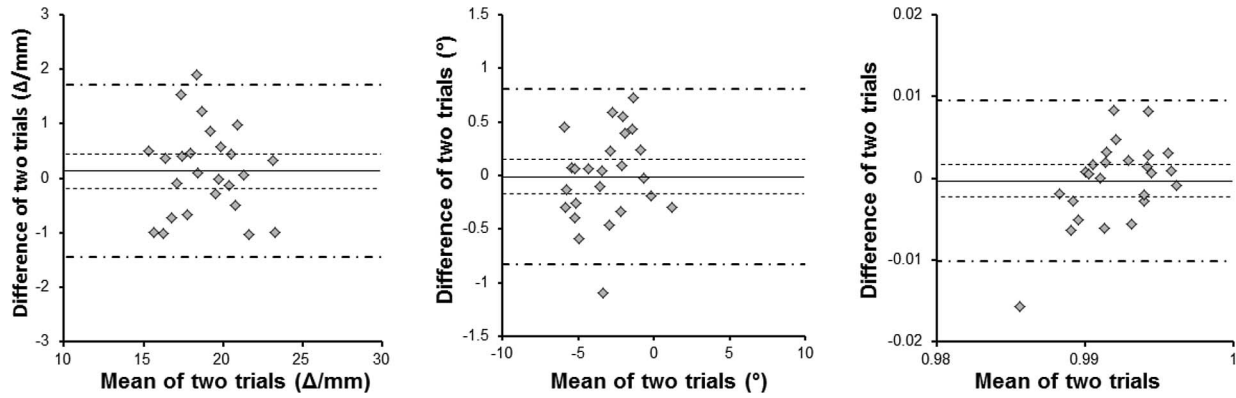
### Study 1: Monocular Eye Deviation Measurement

Bland-Altman plots in Figure 4 show the within subject test–retest repeatability of the app-measured values for the HR (slope),  $\kappa$  (intercept), and the  $R^2$  values for the lines fitting the scatter of the app-measured deviation and the known eccentricity of fixation targets. The mean  $\pm$  standard deviation (SD) HR measured for our sample was  $19.26 \pm 1.78 \Delta/\text{mm}$ ,  $\kappa$  was  $3.13 \pm 1.98^\circ$  (nasal), and  $R^2$  over the study population was  $0.99 \pm 0.003$ . The mean  $\pm$  95% CI of the difference between the test–retest values of HR,  $\kappa$ , and  $R^2$  values was  $0.13 \pm 1.57\Delta$ ,  $-0.01 \pm 0.82^\circ$ , and  $-0.0 \pm 0.01$ , respectively.

The app-measured deviation angles were consistent with the true deviation for different angles of fixation (slope = 1.007, intercept =  $-0.19$ ,  $R^2 = 0.97$ ,  $P < 0.001$ ; Fig. 5, Left). Population average value of the HR was used to convert the app linear displacement measurement (mm) to angular deviations. The data showed that the root mean squared error (RMSE) of the measured deviation (in  $\Delta$ ) increases with the true deviation magnitude (Fig. 5, Right) across all subjects for two cases: when using the population average value for HR (min, 1.3; max, 3.6; average, 2.5) and using individual HR values (min, 1.4; max, 2.5; average, 1.9).

### Study 2: Dissociated Phoria Measurements

Based on MT measurements, more people had exophoria ( $n = 12$ ) than esophoria ( $n = 2$ ) in our study population, with an overall range between  $-24\Delta$  and  $15\Delta$  (esodeviations, positive sign; exodeviations, negative sign). The mean and 95% CI of within-subject differences for MT measurements were  $-1\Delta$  and  $\pm 2.8\Delta$ , respectively. In the case of the app, there was no significant difference between measurement trials (repeated measures ANOVA,  $F(2,41) = 0.198$ ,  $P = 0.98$ ), and the mean and 95% CI of the within-subject measurement difference was  $0.4\Delta$  and  $\pm 2.3\Delta$ , respectively. The app measurements closely matched the MT measurements (Fig. 6; linear regression: slope



**Figure 4.** Test-retest repeatability of within-subject measurements with the app using the Bland-Altman plots. (Left) slope or the HR of the subjects between two trials, (Center) intercept or the angle kappa ( $\kappa$ ), and (Right) the  $R^2$  values of line fitted to ground truth versus app deviation data for each subject are shown. Each point represents one subject ( $n = 25$ ). The dash and dot lines represent the 95% CI of the difference between two measurements. The solid line represents the mean difference between two measurements over the entire population and the dashed lines are its 95% CI limits.

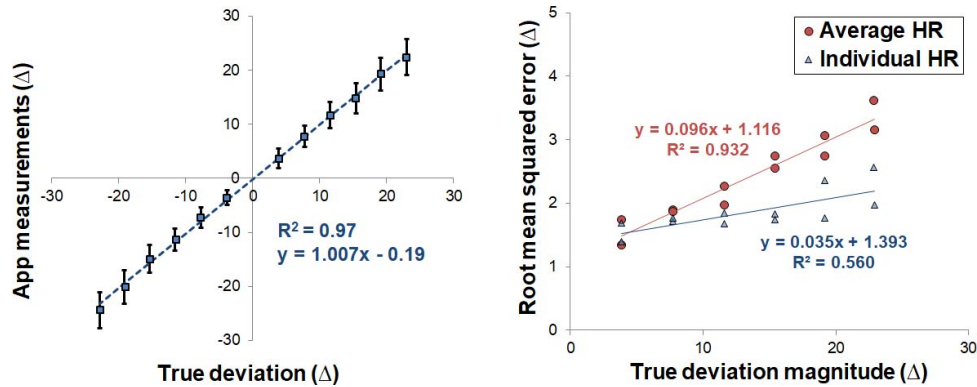
= 0.94; intercept =  $-1.12$ ;  $R^2 = 0.97$ ,  $P < 0.001$ ). The root mean squared difference between app and MT was  $1.7\Delta$ .

### Study 3: Strabismus Measurement

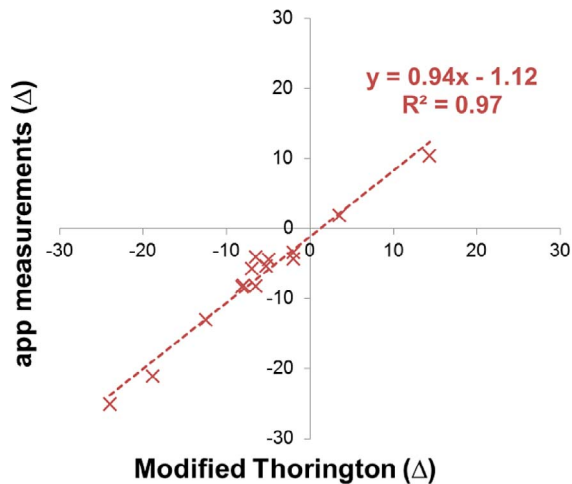
Based on the CTPN measurements, the range of strabismus angle was between approximately  $\pm 60\Delta$  (negative values denoting exotropia), with the smallest magnitude of strabismus angle being  $6\Delta$ . There were twice as many subjects with exotropia ( $n = 49$ ) than esotropia ( $n = 18$ ) within the study population (Table). The app measurements of strabismus angles were consistent with CTPN measurements (linear

regression: slope = 0.95, intercept =  $-0.86$ ,  $R^2 = 0.95$ ,  $P < 0.001$ ; Fig. 7, Left). The strabismus measurements with the app also were strongly correlated with the Synoptophore measurements, but unlike the CTPN comparison, the angular estimates of deviation with the app were higher than Synoptophore measurements (linear regression: slope = 1.15, intercept =  $-3.19$ ,  $R^2 = 0.91$ ,  $P < 0.001$ ).

After correction of CTPN values to account for the distance between the center of rotation of the eye and the prism surface when using near fixation, the slope of the regression line between app and CTPN

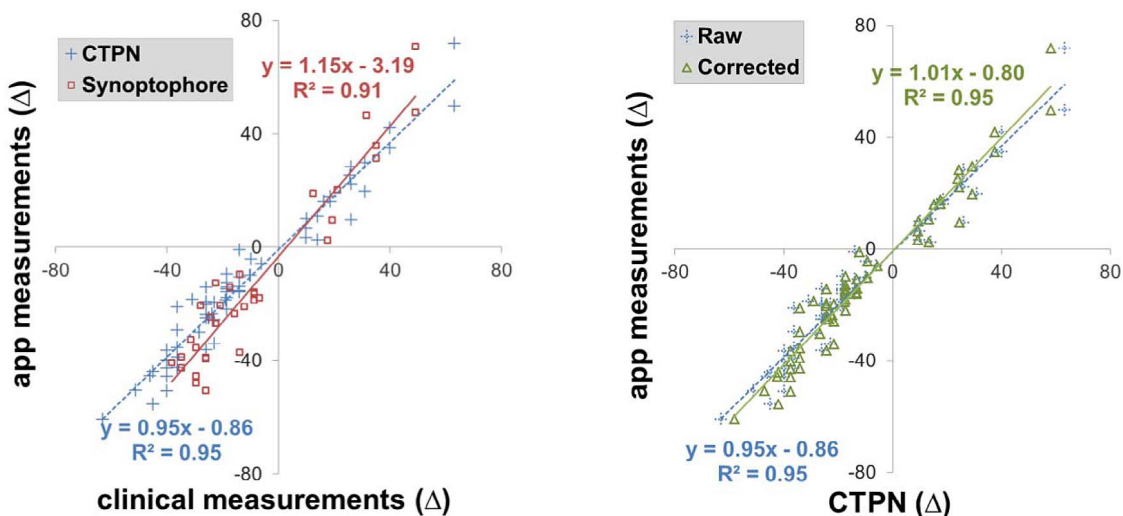


**Figure 5.** Comparison of app-measured eye deviation angles to the true deviation angles for the fixation targets in Study 1. (Left) The app measurements were normalized and scaled using population average HR across subjects. For each fixation point of known eccentricity, the sample mean of the app measurement is shown. Error bars: standard deviation. The dashed line represents the regression line fitted to the overall data and indicates good agreement between the app values and the ground truth. (Right) RMSE in the app measurements is shown for different magnitudes of ground truth deviations across all subjects for two cases: when using population average HR and when using individual HR values. At smaller magnitudes, RMS error when using population average HR is comparable to using individual HR value and the difference is approximately  $1\Delta$  for the highest magnitude tested ( $23\Delta$ ). This implies that using population average HR for measurements will not lead to large inaccuracies at small angle deviations, while being reasonably accurate for larger deviation magnitudes.



**Figure 6.** Results of app cover test mode evaluation in Study 2. Dissociated phoria measurement ( $n = 14$ ) were consistent between the app and MT (slope = 0.94,  $R^2 = 0.97$ ,  $P < 0.001$ ). The root mean squared difference between app and MT was  $1.7\Delta$ .

measurements increased to 1.01 (Fig. 7, Right). The mean  $\pm$  SD absolute difference between the app and CTPN measurements was  $5.4 \pm 4.2\Delta$ . The difference between the app and corrected CTPN measurements were similar ( $5.4 \pm 4.1\Delta$ ), with a root mean squared difference of  $6.8\Delta$ . The mean  $\pm$  SD absolute difference between the app and Synoptophore measurements was  $10.1 \pm 11\Delta$ .



**Figure 7.** Comparison of the app and clinical measurements in strabismic subjects. (Left) The overall magnitudes of the strabismus angles measured by the app were consistent with the prism alternating cover test or CTPN ( $N = 66$ , slope = 0.95,  $R^2 = 0.95$ ,  $P < 0.001$ ) and slightly higher with Synoptophore ( $N = 34$ , slope = 1.15,  $R^2 = 0.91$ ,  $P < 0.001$ ). (Right) After correcting the values of prism neutralization for near fixation, the slope of the line fitting between the app and CTPN measurements increased to 1.01. This indicates that app measurements generally agree with CTPN measurements in clinical settings.

## Discussion

The results of the in-lab and clinical evaluation showed that through its various operating modes, the EyeTurn app measurements are repeatable (95% CI of within-subject HR differences =  $\pm 1.57\Delta$ ), accurate with respect to the ground-truth (average RMSE of  $2.5\Delta$  for eye deviation measurements), and generally consistent with the commonly used clinical methods, such as the CTPN test, MT with red Maddox rod, or Synoptophore (slope of regression lines is close to 1). For strabismus measurements, CTPN generally is considered the clinical gold standard. While the app measurements were consistent with it, there are some important underlying issues related to use of prisms and the app for measuring eye deviations that must be considered when comparing the two methods.

The first issue is related to measurements with prisms at near fixation (the app and CTPN measurements were obtained at near fixation). At near fixation, the distance between the prism and the center of rotation of the eye becomes a factor affecting the magnitude of the prism power required for neutralization.<sup>22</sup> The actual prism power required for neutralization is larger than the true deviation as the distance between the prism and center of rotation of the eye increases. It should be noted that no such limitation exists for the use of the app at near fixation.

Since there always is a finite distance between the center of rotation of the eye and the physical location of the prism (approximately back vertex distance + half of axial length), it leads to an overestimation of deviation when neutralizing at near fixation. After this error is corrected, CTPN and app measurements become even more consistent (slope becomes 1.01). It should be noted that precise measurement of the distance between the eye and prism was not possible in actual clinical testing, and the above compensation was based on average prism-to-eye distance for all subjects while assuming that the fixation distance was constant. While there was a good agreement between the overall app and CTPN measurements, individual differences existed (6.8 $\Delta$  root mean squared difference). While CTPN may be the clinical gold standard for eye deviation measurement, it cannot be considered as ground-truth. Hence, the variability comes from the app and the CTPN, especially when measuring a diverse population including cases of intermittent strabismus. Here, we limited the discussion to the probable causes of error within the app that might lead to differences with respect to CTPN.

One possible source of error in the app measurements is the use of a population average HR value for computing the deviation (HR value of 19.26 $\Delta$ /mm corresponding to the mean of 25 normally sighted adult subjects tested in the eye-deviation study in the lab). Normally, we would expect some variance in the HR values in a randomly sampled population, which would lead to noise in the estimates around the mean, but the mean itself should not change considerably (for example, larger error bars around the mean in Fig. 5, Left). Hence, use of population average HR can lead to an error in individual measurements (Fig. 5, Right). However, at lower deviation magnitudes (<15 $\Delta$ ), use of the population average HR has a relatively low impact on accuracy (both curves overlap at lower angles before diverging for larger angles in Fig. 5, Right). Even at the highest measured deviation magnitude (23 $\Delta$ ), the difference between RMSE for the population average HR and individual HR curves is approximately 1 $\Delta$ , indicating that the difference is small compared to the measured magnitude. Thus, the app is more accurate in lower angular ranges where it needs to be more accurate to reliably measure small angle strabismus, and the decrease in the accuracy at higher deviations is still comparable with the resolution of measurement offered by the prism bar, which is currently the clinical gold standard. In the context of providing prism correction for strabismic individuals, the

accuracy of the app at lower angle deviations is important as 10 $\Delta$  power is considered the upper range of feasible prism prescription (weight and aberration are problematic at higher values). Even for higher prism values the app provides a good starting point for trialing prism lenses, which can then be refined.

HR for an individual depends on two factors: the corneal curvature and anterior chamber depth.<sup>16,24,25</sup> It is likely that there are age-, sex-, or ethnicity-related differences in HR values. Ethnicity-related differences in corneal curvature<sup>26–28</sup> and anterior chamber depth,<sup>29</sup> age-related differences in anterior chamber depth,<sup>30</sup> and sex-related differences in the corneal curvature<sup>31</sup> have been reported. While overall our app measurement closely matched CTPN measurements for our study population, the HR value used in the app could be customized for a given individual or population in the future (for example, when using the app for screening children of a particular race), if sound biometric data are available. This is future work as we further tune the app for use in diverse scenarios.

We included comparisons of app measurements with Synoptophore as it also is an accepted clinical method for strabismus measurement in addition to or instead of CTPN. On average, the app measurements were higher than Synoptophore measurements (slope of line fitting = 1.15). A possible reason for this discrepancy could be the differences in the setup of Synoptophore measurements (taken with far fixation targets) compared to the app (near fixation). The measurement setup of Synoptophore may result in an increase in the measured angle in subjects with esotropia and a decrease in the case of exotropia.<sup>32–34</sup> In our study population of strabismic subjects, we had more subjects with exotropia than esotropia, which may result in relatively smaller deviations with Synoptophore compared to the EyeTurn app.

With phoria measurements, our aim was to determine if the alternating cover test method with the video recording mode of the app can detect eye deviations in dissociated conditions. Since some amount of phoria is present even in nonstrabismic individuals, this allowed app evaluation in obtaining clinically meaningful eye deviation measurements. The MT method has been more reliable/repeatable than other phoria measurement methods<sup>35</sup> and the app measurements were consistent with it. The app measurements were slightly more repeatable than MT (95% CI of within subject differences  $\pm$  2.3 $\Delta$  with the app compared to  $\pm$  2.8 $\Delta$  for MT).

The EyeTurn app presented in this study is an early prototype that is undergoing further develop-



ment. Thus, the app and preliminary evaluation studies presented here have some limitations. In this study, we evaluated the ability of the app to measure eye alignment only at near fixation distances, in primary gaze, and only along horizontal direction. We also did not evaluate the effect of glasses on the accuracy of the app. Since the evaluation was limited to assessing the baseline ability of the app with commonly used clinical examinations, this study did not test any special or complicated patient cases. Future studies will involve evaluation of an updated version of the app to address the above issues.

The EyeTurn app has many unique features and differences compared to existing devices for strabismus detection and/or measurement, such as photoscreeners (Spot, Plusoptix, iScreen, Volk Eye Check),<sup>14</sup> vision screeners for detecting amblyogenic factors,<sup>36</sup> and vision screening mobile apps (GoCheckKids<sup>37</sup>). First, it is self-contained within a conventional smartphone and does not require any external accessories or smartphone attachments for measurement. Second, it provides an objective measure of strabismus in terms of prism diopters without requirement of any explicit calibration or tightly controlled measurement conditions. Third, the app uses a semi-automated video analysis mode to enable dissociated measurements in intermittent strabismus and phoria; thus, combining the aspects of traditional cover testing with photographic Hirschberg method. In conclusion, the results showed that the app can reliably measure binocular and dissociated eye deviations in the horizontal direction and the app measurements are consistent with the clinical gold standard.

## Acknowledgments

Supported by the National Eye Institute (Bethesda, MD; NIH SBIR R43EY025902) and by the Mass Eye & Ear Curing Kids Grant.

Disclosure: **S. Pundlik**, EyePhone, LLC (I), Mass Eye & Ear (P); **M. Tomasi**, EyePhone, LLC (I), Mass Eye & Ear (P); **R. Liu**, None; **K. Houston**, EyePhone, LLC (I), Mass Eye & Ear (P); **G. Luo**, EyePhone, LLC (I), Mass Eye & Ear (P)

## References

1. Freeman AW, Nguyen VA, Jolly N. Components of visual acuity loss in strabismus. *Vision Res.* 1996;36(5):765–774.

2. Robaei D, Rose KA, Kifley A, Cosstick M, Ip JM, Mitchell P. Factors associated with childhood strabismus: findings from a population-based study. *Ophthalmology.* 2006;113:1146–1153.
3. Cotter SA, Tarczy-Hornoch K, Song E, et al. Fixation preference and visual acuity testing in a population-based cohort of preschool children with amblyopia risk factors. *Ophthalmology.* 2009;116:145–153.
4. Klaver P, Marcar V, Martin E. Neurodevelopment of the visual system in typically developing children. *Prog Brain Res.* 2011;189:113–136.
5. Williams C, Northstone K, Harrad RA, Sparrow JM, Harvey I. Amblyopia treatment outcomes after screening before or at age 3 years: follow up from randomised trial. *BMJ.* 2002;324:1549.
6. Epelbaum M, Milleret C, Buisseret P, Dufier JL. The sensitive period for strabismic amblyopia in humans. *Ophthalmology.* 1993;100:323–327.
7. Eibschitz-Tsimhoni M, Friedman T, Naor J, Eibschitz N, Friedman Z. Early screening for amblyogenic risk factors lowers the prevalence and severity of amblyopia. *J AAPOS.* 2000;4:194–199.
8. Rowe F. The profile of strabismus in stroke survivors. *Eye (Lond).* 2010;24:682–685.
9. Pineles SL, Repka MX, Yu F, Lum F, Coleman AL. Risk of musculoskeletal injuries, fractures, and falls in medicare beneficiaries with disorders of binocular vision. *JAMA Ophthalmology.* 2015;133:60–65.
10. Chang MY, Velez FG, Demer JL, Isenberg SJ, Coleman AL, Pineles SL. Quality of life in adults with strabismus. *Am J Ophthalmol.* 2015;159:539–544.e532.
11. Kemper AR, Clark SJ. Preschool vision screening in pediatric practices. *Clin Pediatr.* 2006;45:263–266.
12. Loudon SE, Rook CA, Nassif DS, Piskun NV, Hunter DG. Rapid, high-accuracy detection of strabismus and amblyopia using the pediatric vision scanner. *Invest Ophthalmol Vis Sci.* 2011;52:5043–5048.
13. Almeida JDSd, Silva AC, Paiva ACd, Meireles-Teixeira JA. Computational methodology for automatic detection of strabismus in digital images through Hirschberg test. *Comp Biol Med.* 2012;42:135–146.
14. Barnard S, Johnson E. Detecting strabismus. *Optician.* 2013;15.11.13:27–30.
15. Hasebe S, Ohtsuki H, Tadokoro Y, Okano M, Furuse T. The reliability of a video-enhanced

- Hirschberg test under clinical conditions. *Invest Ophthalmol Vis Sci.* 1995;36:2678–2685.
16. Jagini KK, Vaidyanath H, Bharadwaj SR. Utility of theoretical Hirschberg ratio for gaze position calibration. *Optom Vis Sci.* 2014;91:778–785.
  17. Barry JC, Backes A. Limbus versus pupil center for ocular alignment measurement with corneal reflexes. *Invest Ophthalmol Vis Sci.* 1997;38:2597–2607.
  18. Model D, Eizenman M. An automated Hirschberg test for infants. *IEEE Trans Biomed Eng.* 2011;58:103–109.
  19. Model D, Eizenman M, Sturm V. Fixation-free assessment of the Hirschberg ratio. *Invest Ophthalmol Vis Sci.* 2010;51:4035–4039.
  20. Altman DG, Bland, J M. Measurement in medicine: analysis of method comparison studies. *Statistician.* 1983;32:307–317.
  21. Carlson NB, Kurtz BD. *Clinical Procedures for Ocular Examinations.* Norwalk, CT: Appleton & Lange; 1990.
  22. Thompson JT, Guyton DL. Ophthalmic prisms: deviant behavior at near. *Ophthalmology.* 1985; 92:684–690.
  23. Artal P. Optics of the eye and its impact in vision: a tutorial. *Adv Optics Photon.* 2014;6:340–367.
  24. Hasebe S, Ohtsuki H, Kono R, Nakahira Y. Biometric confirmation of the Hirschberg ratio in strabismic children. *Invest Ophthalmol Vis Sci.* 1998;39:2782–2785.
  25. Brodie SE. Photographic calibration of the Hirschberg test. *Invest Ophthalmol Vis Sci.* 1987;28:736–742.
  26. Mashige KP. A review of corneal diameter, curvature and thickness values and influencing factors. *South Afr Optom.* 2013;72:185–194.
  27. Matsuda LM, Woldorff CL, Kame RT, Hayashida JK. Clinical comparison of corneal diameter and curvature in Asian eyes with those of Caucasian eyes. *Optom Vis Sci.* 1992;69:51–54.
  28. Lam CSY, Loran DFC. Designing contact lenses for oriental eyes. *J Br Contact Lens Assoc.* 1991; 14:109–114.
  29. Feng MT, Belin MW, Ambrósio R, et al. Anterior chamber depth in normal subjects by rotating scheinpluf imaging. *Saudi J Ophthalmol.* 2011;25:255–259.
  30. Bhardwaj V, Rajeshbhai GP. Axial Length, Anterior chamber depth-a study in different age groups and refractive errors. *J Clin Diag Res.* 2013;7:2211–2212.
  31. Zhang YY, Jiang WJ, Teng ZE, et al. Corneal curvature radius and associated factors in chinese children: the Shandong Children Eye Study. *PLoS One.* 2015;10:e0117481.
  32. Georgievski Z. Synoptophore versus prism and cover test measurements in strabismus.: a question of instrument convergence? *Strabismus.* 1995;3:71–77.
  33. Giribaldi M, Jolly N. Measurement of the deviation and the effects of dissociation levels: synoptophore versus prism bar cover test. In: *51st Annual Scientific Conference of the Orthoptic Association of Australia.* Wollongong NSW; 1994.
  34. Nowakowska O, Broniarczyk-Loba A. Estimation of squint angle measurements performed with synoptophore and prism cover-test (PCT). *Klin Oczna.* 2005;107:100–102.
  35. Schroeder TL, Rainey BB, Goss DA, Grosvenor TP. Reliability of and comparisons among methods of measuring dissociated phoria. *Optom Vis Sci.* 1996;73:389–397.
  36. Nassif DS, Piskun NV, Hunter DG. The Pediatric Vision Screener III. Detection of strabismus in children. *Arch Ophthalmol.* 2006;124:509–513.
  37. Arnold RW, Silbert DI. Efficacy of a mobile smart phone vision-screening device with automated image-processing analysis in the evaluation of amblyopia risk factors in preschool children. *J AAPOS.* 2015;19:e9–e10.