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TITLE:
Using an Automated Hirschberg Test App to Evaluate Ocular Alignment

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KEYWORDS:
strabismus, smartphone app, intermittent strabismus, phoria, tropia, cover test, prism neutralization, Hirschberg test, prism and alternate cover test, simultaneous prism cover test

SUMMARY:
We present a protocol of using a smartphone app to perform Hirschberg test for measuring manifest and intermittent ocular misalignment (strabismus) under near and far fixation conditions.

ABSTRACT:
A smartphone app has been developed to perform the automated photographic Hirschberg test for objective measurement of ocular misalignment. By computing the difference in corneal reflection generated by the phone camera flash relative to the iris center based on high resolution images, the app can measure misalignment with a much higher precision than the naked eye performing the Hirschberg test. It has been validated in a previous clinical evaluation study by comparing to the clinical gold standard—prism and alternate cover test. The goal of this article is to describe the testing techniques regarding how to use the app to measure ocular alignment for different fixation distances, without or with cover to break fusion, as well as angle kappa, so that users can use the app to perform equivalent tests typically done in clinic using prisms.

INTRODUCTION:
Measurement of eye alignment is frequently performed in vision care clinics. Cover test with prism neutralization is the commonly used clinical method for quantifying the degree of eye misalignment (strabismus). This method requires a high degree of training and experience. Accurate measurement becomes more challenging when patients cannot fully engage in the exam such as young children[1], individuals with brain injuries or stroke[2], or developmental

disabilities[3]. Furthermore, there is a need for ocular alignment testing in school screening, because strabismus develops during childhood in an estimated 5−8% of the US population[4], and is a substantial risk factor for amblyopia with about 30−40% of cases of amblyopia attributed to strabismus[5-7]. However, school nurses are normally not trained to conduct the standard cover test with prism neutralization for such screening. For non-eye care professionals, an additional challenge in strabismus screening is that intermittent strabismus (misalignment is not always manifested) and smaller magnitudes of misalignment are not visually obvious (<15 prism diopters [Δ])[8].

In an attempt to address the challenges in the detection and measurement of strabismus, we have developed a smartphone app (EyeTurn) that implements and automates the photographic Hirschberg method[9] by comparing the displacement of corneal reflections between the eyes. While conventional photographic Hirschberg method has been shown to have good reproducibility in clinics[10,11], the cost for dedicated, standalone devices is a barrier for wide adoption. By providing an easy-to-use tool to measure eye alignment with standard smartphones, we hypothesize it will be widely adopted in school vision screening and used by non-eye care professionals. Our previous evaluation studies have shown that the app measurement is consistent with the current clinical standard of prism and alternate cover test[12], for strabismus magnitudes of esotropia and exotropia up to 60Δ. In a pilot school screening study, we also showed that the app can help the school nurse detect children with intermittent exotropia who were missed by standard school vision screening protocols[13].

The iOS version of the app is currently available to researchers and clinicians upon request for research purposes. The requesters have thus far included school nurses, pediatric ophthalmologists, optometrists, neuro-ophthalmologists, and strabismus specialists. The purpose of this article is to share the detailed app protocols for using the app to evaluate ocular alignment under different viewing conditions, namely, near and far fixation distance; with and without eye covering to break binocular fusion.

PROTOCOL:

This study was conducted in accordance with the tenets of the Declaration of Helsinki, at Schepens Eye Research Institute (Boston, MA) and Spaulding Rehabilitation Hospital (Boston, MA). Informed consent was obtained from all the participants. The study was approved by the local institutional review boards of Mass Eye and Ear (Boston, MA).

NOTE: Subject inclusion criteria were prior diagnosis of horizontal strabismus (constant or intermittent exotropia or esotropia) and no other visual impairments. This study was a part of a larger one reported previously[12]. Data for 14 subjects recruited in the US in the larger study[12] are reported here with permission. An optometrist specialized in vision rehabilitation who routinely evaluate strabismus in clinic performed prism and alternate cover test, following by measurement with the app to prevent bias of the cover test results by the objective app measurement.

1. Prepare the test

NOTE: Testing can be performed in any environment; however, the following controls are likely to aid in successful testing.

1.1. Conduct the test in a well-lit environment. Let the patients face in a direction such that corneal reflections from windows and ceiling lights are not located in the center of the eyes. Try to avoid strong background light, such as windows.

NOTE: Usually it helps to have a ceiling light right above the head, or a window on one side of the patient. Sometimes, asking the patient to hold their hand above their brow or using a visor can help shield the eyes from strong light sources which create additional reflections on the cornea, as needed. Turning off point light sources such as canister lights or gooseneck lamps will decrease the intensity of extra corneal reflections, making it easier for the software to detect the reflection from the camera flash as intended. If point light source is needed it may be diffused by pointing it at the wall or using a diffuser (i.e., lamp shade).

2. Measure tropia (manifest strabismus) with single snapshot—near fixation

2.1. Launch the app and set the mode to snapshot (button at upper right corner).

2.2. Select near fixation (button at lower right corner).

2.3. Hold the phone in landscape orientation about 40 cm from the patient at eye level with the rear-camera facing the patient to be measured.

NOTE: The distance does not have to be accurately controlled. The app can automatically compensate for different distances.

2.4. Instruct the patient to fixate on the flash light, which is off at this point. For tests requiring precise accommodation such as when screening for accommodative esotropia, paste a fixation target (such as a letter) on the back of the phone, directly below or above the flashlight.

2.5. While the patient confirms he/she is fixating, press the round button to take a snapshot, which will be analyzed by the app.

2.6. When the analysis is completed, the app will show detected eye features: limbus (iris outer) boundary indicated by a large circle (green), the center of the eye indicated by a cross (green), and the location of the corneal reflection indicated by a small circle (red). Verify these features are detected without obvious errors (such as incorrect limbus fitting, or incorrect location or missing corneal reflection).

2.7. On the same screen, under the captured picture, the app will show the measurements related to the eye alignment. If satisfied with the results, press the save button to save the current test in the phone. Otherwise, press the back-arrow button to retest.

3. Measure tropia (manifest strabismus) with snapshot—far fixation

NOTE: To measure tropia for far fixation, the angle kappa for each eye needs to be measured at least once. The app will automatically choose the latest measurement of angle kappa in the history. If it is not available for either eye, the app will give a reminder to first obtain this measurement (see section 6 for details of angle kappa measurement).

3.1. Launch the app and set the mode to snapshot (button at upper right corner).

3.2. Select far fixation mode (button at lower right corner).

3.3. Hold the phone in landscape orientation about 40 cm from the patient at eye level with the rear face of the phone facing the patient.

NOTE: The distance does not have to be accurately controlled. The app can automatically compensate for different distances.

3.4. Place the phone slightly below two eyes so that the patient can look above the phone and fixate a target in the distance (typically 5 m away). Make sure the camera is in approximately between the two eyes, not too far to the side of either eye.

3.5. While making sure the patient is fixating properly, press the round button to take a snapshot.

3.6. When the analysis is completed, the app will show detected eye features: limbus boundary indicated by a large circle (green), the center of the eye indicated by a cross (green), and the location of the corneal reflection indicated by a small circle (red). Verify these features are detected without obvious errors (such as incorrect limbus fitting, or incorrect location or missing corneal reflection).

3.7. Under the picture there are measurement outcomes for eye alignment including prism diopters. If satisfied with the results, press the save button to save the test in the phone. Otherwise, press the back-arrow button to retest.

4. Measure intermittent strabismus or phoria with cover test—near fixation

4.1. Launch the app and toggle on the cover test mode (button at upper right corner), and select near fixation (button at lower right corner).

4.2. Hold the phone in landscape orientation about 40 cm from the patient.

NOTE: The distance does not have to be accurately controlled. The app can automatically compensate for different distances.

4.3. Instruct the patient to fixate the flash light, which is turned off at this point. For tests requiring precise accommodation, paste a fixation target on the back of the phone, directly below or above the flashlight.

4.4. Use an occluder to cover one of the eyes.

4.5. Press the round button. The app will start to monitor the status of the two eyes (whether one eye is covered).

4.6. While making sure the patient is fixating properly, remove the occluder quickly (i.e., cover-uncover test), or first move the occluder between the two eyes to perform alternate covering a few times and then take the occluder away quickly. The app will automatically take a picture as soon as the occlude is taken away from eyes.

4.7. When the analysis is completed, the app will show detected eye features: iris indicated by a large green circle, the center of the eye indicated by a green cross, and corneal reflection from flash indicated by a small red circle. Verify these features are detected without obvious errors.

4.8. Under the picture there are measurement outcomes for eye alignment in prism diopters. If satisfied with the results, press the save button to save the test in the phone. Otherwise, press the back-arrow button to retest.

5. Measure intermittent strabismus or phoria with cover test—far fixation

NOTE: To measure intermittent ocular misalignment for far fixation, the angle kappa for each eye needs to be measured at least once. The app will automatically choose the latest angle kappa measure. If it is not available for either eye, the app will give a reminder to first obtain this measurement (see section 6 for details of angle kappa measurement).

5.1. Launch the app and set the mode to cover test (button at upper right corner).

5.2. Select far fixation (button at lower right corner).

5.3. Hold the phone in landscape orientation about 40 cm from the patient at eye level.

NOTE: The distance does not have to be accurately controlled. The app can automatically compensate for different distances. It is best if the flash light/camera is between the eyes. Since the camera and flash are off to one corner in most phone models, this means the phone display itself will be slightly off-center.

5.4. Instruct the patient to look just above the phone and to fixate the target in distance (typically 6 m away).

5.5. Use an occluder to cover an eye.

5.6. Press the round button. The app will start to detect the uncovering of the eye.

5.7. While making sure the patient is fixating properly, remove the occluder quickly (i.e., cover-uncover test), or first move the occluder between the two eyes to perform alternate covering a few times and then take the occluder away quickly. The app will automatically take a picture as soon as the occluder is taken away from eyes.

5.8. When the analysis is completed, the app will show detected eye features: limbus boundary indicated by a large circle (green), the center of the eye indicated by a cross (green), and the location of the corneal reflection indicated by a small circle (red). Verify these features are detected without obvious errors (such as incorrect limbus fitting, or incorrect location or missing corneal reflection).

5.9. Under the picture there are measurement outcomes for eye alignment in prism diopters. If satisfied with the results, press the save button to save the test in the phone. Otherwise, press the back-arrow button to retest.

6. Measure angle kappa

6.1. Launch the app and set the mode to snapshot.

6.2. Select near fixation.

6.3. Hold the phone in landscape orientation about 40 cm from the patient at eye level.

NOTE: The distance does not have to be accurately controlled. The app can automatically compensate for different distances.

6.4. Instruct the patient to use the eye to be tested (either eye) to fixate on the flash light, which is off at this point. Have the other covered by hand or an occluder.

6.5. While making sure the patient is fixating properly, tap the round button to take a snapshot, which will be analyzed by the app.

6.6. When the analysis is completed, the app will show the detected eye features: limbus boundary indicated by a large circle (green), the center of the eye indicated by a cross (green), and the location of the corneal reflection indicated by a small circle (red). Verify these features are detected without obvious errors (such as incorrect limbus fitting, or incorrect location or missing corneal reflection). Under the picture there are measurement outcomes for angle kappa (in degrees).

REPRESENTATIVE RESULTS:

In this work, we describe the protocols to evaluate ocular alignment using a smartphone app that performs the photographic Hirschberg test. The interface of the app is shown in Error! Reference source not found.. The users can choose to perform cover test or measure a patient with both eyes fixating at a target simultaneously, either at near or far fixation distances. Once the viewing conditions are determined depending on the test purposes, the users can follow the protocols and take a photo of the patient. After image processing, the app will show the analysis results to the users. As an example shown in Error! Reference source not found., the limbus boundaries (green circles) of the two eyes as well as the corneal reflection of the flash light (red dots) were detected correctly. This suggests that the ocular alignment measure (18.5Δ) shown below the image is not subject to image analysis error. In this particular case, the patient had left exotropia, which is obvious from the image as the corneal reflection offset was much larger in the left eye. However, the app does not report which eye is deviated, because in cases of small strabismus angle and unknown angle kappa, it would be unreliable for the app to determine the deviated eye. For comparison, an example without strabismus is shown in Error! Reference source not found.. **Figure 4** shows an example of erroneous limbus detection. While the detection of corneal reflection (small red circle) is correct, the green circle apparently does not match the limbus boundary. The test should be redone.

According to cover test on those subjects, the range of strabismus angle was between 25Δ esotropia to 50Δ exotropia, with the smallest magnitude of strabismus angle being 6Δ. There were 10 subjects with exotropia and 4 subjects with esotropia. As the linear regression analysis showed (slope = 1.02, R^2 = 0.94, $p < 0.001$), the app measurements of strabismus angles were consistent with clinical cover test measurements (**Figure 5**).

FIGURE LEGENDS:

Figure 1: User interface of the strabismus testing app. Users can toggle on cover test and fixation distance. Under different conditions, the instructions given to the patient may be different, as described in the protocol.

Figure 2: A case of left exptropia. This is the results shown to the users, who should verify the detection of limbus boundary and corneal reflection before reading the strabismus angle. If those image features are not detected correctly, the users should redo the test.

Figure 3: An example under near fixation without cover test. The corneal reflection and eye center were aligned well in both eyes. Therefore the horizontal (HOR) ocular misalignment was almost zero, as the app reported.

Figure 4: An example of erroneous limbus detection.

Figure 5: Comparison of strabismus angle measurement using the app with clinical measurements done with covert testing (n = 14). Negative values indicate exotropic deviations, positive values indicate esotropic deviations. Overall, measurements with the app were consistent with the clinical measurements of strabismus. This figure has been modified

from our previous publication[12].

DISCUSSION:

A person without professional training can use the EyeTurn app to capture pictures of the eyes and obtain ocular alignment measurements, which might be interpreted by an eye care specialist onsite or remotely. The app only provides magnitude of the misalignment, rather than any interpretation or diagnosis. Eye care professionals such as optometrists or ophthalmologists should determine if the misalignment is significant or not, and make a diagnosis after considering other factors including the conditions under which the measurement was taken.

Taking good quality pictures is essential for the measurement. The camera should be placed at a position between two eyes. Being too far away from the midline can cause a difference in the image size between two eyes, and consequently result in measurement inaccuracy.

The limbus boundary is one of the key features that the app uses for locating eye position. Verifying the limbus boundary fitting (the green circle in results) is a crucial step. If the fitting appears to be inaccurate, the measurement will be subject to errors and the eye care professional will not be able to correctly interpret the test. Usually for patients with larger eye fissures, i.e., iris area being more revealed, the fitting will be robust and accurate. On the other hand, for patients with smaller eye fissures, which have only a small portion of the left and right boundaries revealed, the fitting may be prone to inaccuracies. In this situation, operators can ask the patients to open their eyes widely, or gently lift the eyelid wide open. The current version does not provide measurement of vertical misalignment, which will be implemented in future versions.

In addition to the promise for use in strabismus clinics, another potential application of the app is in vision screening. For prevention of amblyopia, the American Academy of Pediatrics strongly endorsed the development of cost-effective image-based screening as a means to extend screening to all children[14]. Red reflex method, which compares the brightness of the "red eye" flash artifact with the strabismus eye being a lighter or brighter red color, can detect both refractive error and strabismus, but cannot quantify the magnitude of the strabismus. Devices implementing the red flex method include Photoscreener and Vision Screener[15,16]. These photoscreeners have not been widely adopted by school districts, likely due to cost. Compared to standalone systems, modern smartphone cameras provide better value, improved accessibility, and rapidly improved and higher resolution cameras. Recently, there is an app that implements the red reflex method, GCK app[17]. The GCK app has some limitations in that it does not give a quantitative measurement of strabismus and requires more control of ambient lighting than the Hirschberg methods. The app presented in this article can be potentially an alternative or complementary solution for vision screening, because of its ease of use and equivalent accuracy with standard clinical measurement using prisms.

ACKNOWLEDGMENTS:

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Kids Grant.

DISCLOSURES:

All authors have a pending patent application on a method of measuring strabismus using a smartphone camera. The technology is being commercialized by EyeNexo LLC, which was founded by authors GL, PS, MT and KH, under a license from Mass Eye and Ear.

REFERENCES:

1. Kemper, A. R., Clark, S. J. Preschool vision screening in pediatric practices. *Clinical Pediatrics.* **45** (3), 263-266 (2006).

2. Rowe, F., VIS group UK. The profile of strabismus in stroke survivors. *Eye.* **24** (4), 682-685 (2010).

3. Black, K., McCarus, C., Collins, M. L. Z., Jensen, A. Ocular Manifestations of Autism in Ophthalmology. *Strabismus.* **21** (2), 98-102 (2013).

4. Taylor, K., Elliott, S. Interventions for strabismic amblyopia. *Cochrane Database of Systematic Reviews.* **10** (8), Cd006461 (2011).

5. Cotter, S. A. et al. Fixation preference and visual acuity testing in a population-based cohort of preschool children with amblyopia risk factors. *Ophthalmology.* **116** (1), 145-153 (2009).

6. Robaei, D. et al. Factors Associated with Childhood Strabismus: Findings from a Population-Based Study. *Ophthalmology.* **113** (7), 1146-1153 (2006).

7. Tarczy-Hornoch, K. et al. Risk factors for decreased visual acuity in preschool children: the multi-ethnic pediatric eye disease and Baltimore pediatric eye disease studies. *Ophthalmology.* **118** (11), 2262-2273 (2011).

8. Chan, K. W., Deng, L., Weissberg, E. M. Detection of Strabismus by Non-Health Care Professionals in an Ethnically Diverse Set of Images. *JAMA Ophthalmology.* **134** (1), 30-36 (2016).

9. Hunter, D. G., Guyton, D. L. Vertical location of the corneal light reflex in strabismus photography. *Archives of Ophthalmology.* **116** (6), 767-771 (1998).

10. Eskridge, J. B., Wick, B., Perrigin, D. The Hirschberg test: a double-masked clinical evaluation. *American Journal of Optometry and Physiological Optics.* **65** (9), 745-750 (1988).

11. Hasebe, S., Ohtsuki, H., Tadokoro, Y., Okano, M., Furuse, T. The reliability of a video-enhanced Hirschberg test under clinical conditions. *Investigative Ophthalmology & Visual Science.* **36** (13), 2678-2685 (1995).

12. Pundlik, S., Tomasi, M., Liu, R., Houston, K., Luo, G. Development and Preliminary Evaluation of a Smartphone App for Measuring Eye Alignment. *Translational Vision Science & Technology.* **8** (1), 19-19 (2019).

13. Cheng, W. et al. The EyeTurn App for School Vision Screening. *American Academy of Optometry Annual Meeting.* San Antonio, TX (2018).

14. Committee on Practice and Ambulatory Medicine and Section on Ophthalmology. Use of Photoscreening for Children's Vision Screening. *Pediatrics.* **109** (3), 524-525 (2002).

15. Simons, B. D., Siatkowski, R. M., Schiffman, J. C., Berry, B. E., Flynn, J. T. Pediatric photoscreening for strabismus and refractive errors in a high-risk population. *Ophthalmology.* **106** (6), 1073-1080 (1999).

16. Kerr, N. C., Somes, G., Enzenauer, R. W. The effect of developmentally-at-risk status on the

reliability of the iScreen(R) photorefractive device in young children. *The American Journal of Orthopedics.* **61**, 117-123 (2011).

17. Arnold, R. W., O'Neil, J. W., Cooper, K. L., Silbert, D. I., Donahue, S. P. Evaluation of a smartphone photoscreening app to detect refractive amblyopia risk factors in children aged 1-6 years. *Clinical Ophthalmology.* **12**, 1533-1537 (2018).

Figure 1

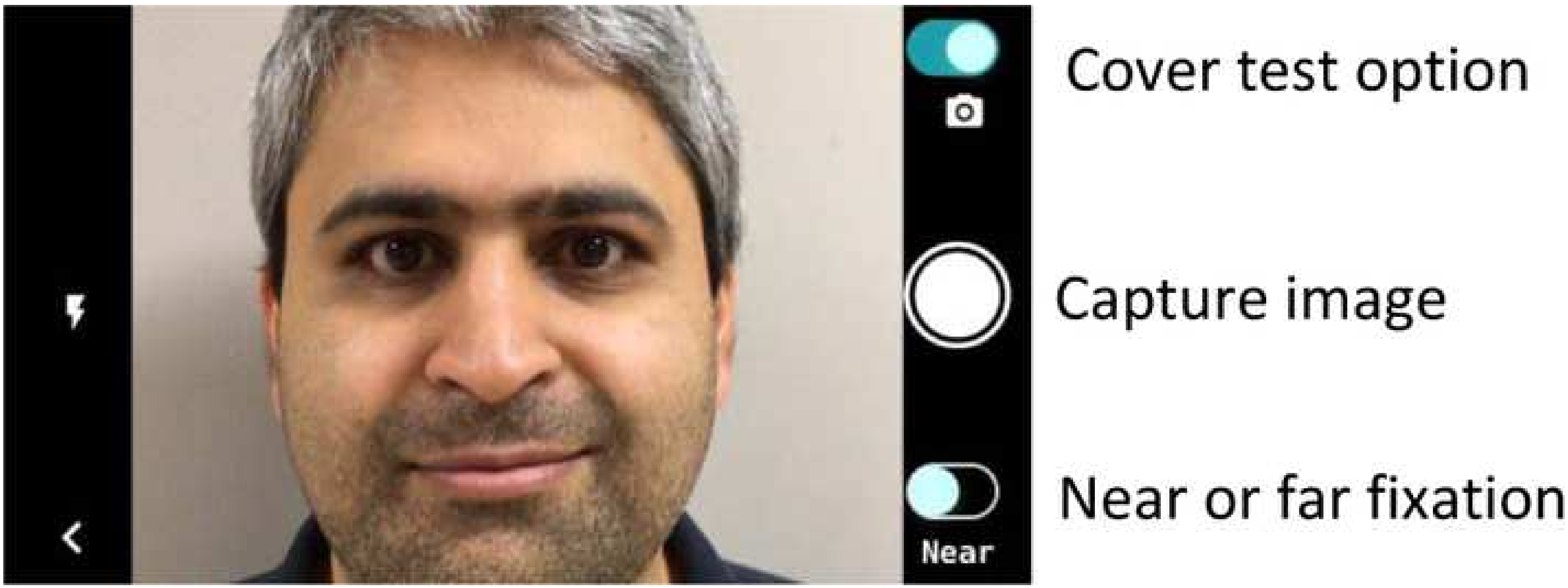
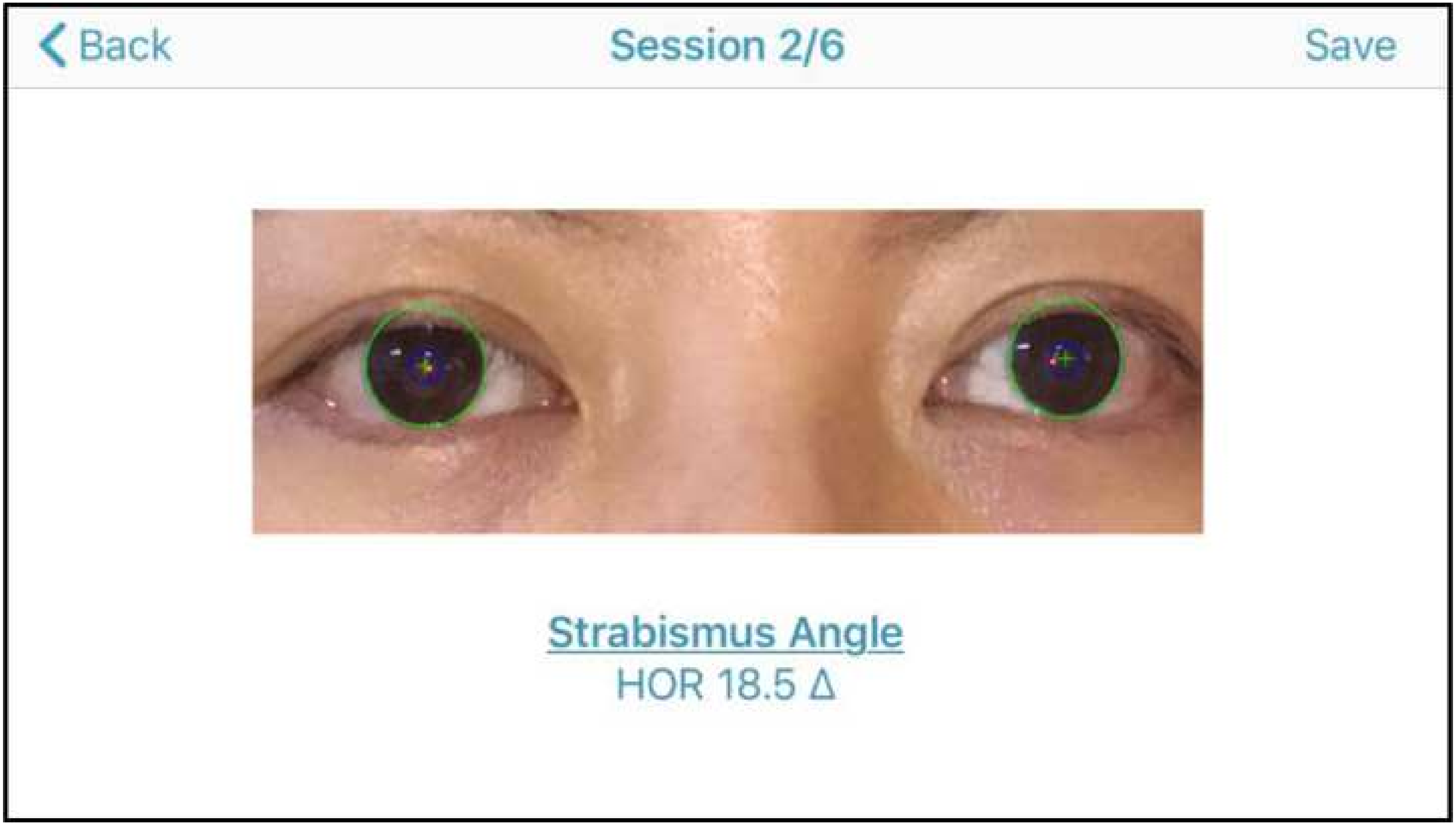


Figure 2



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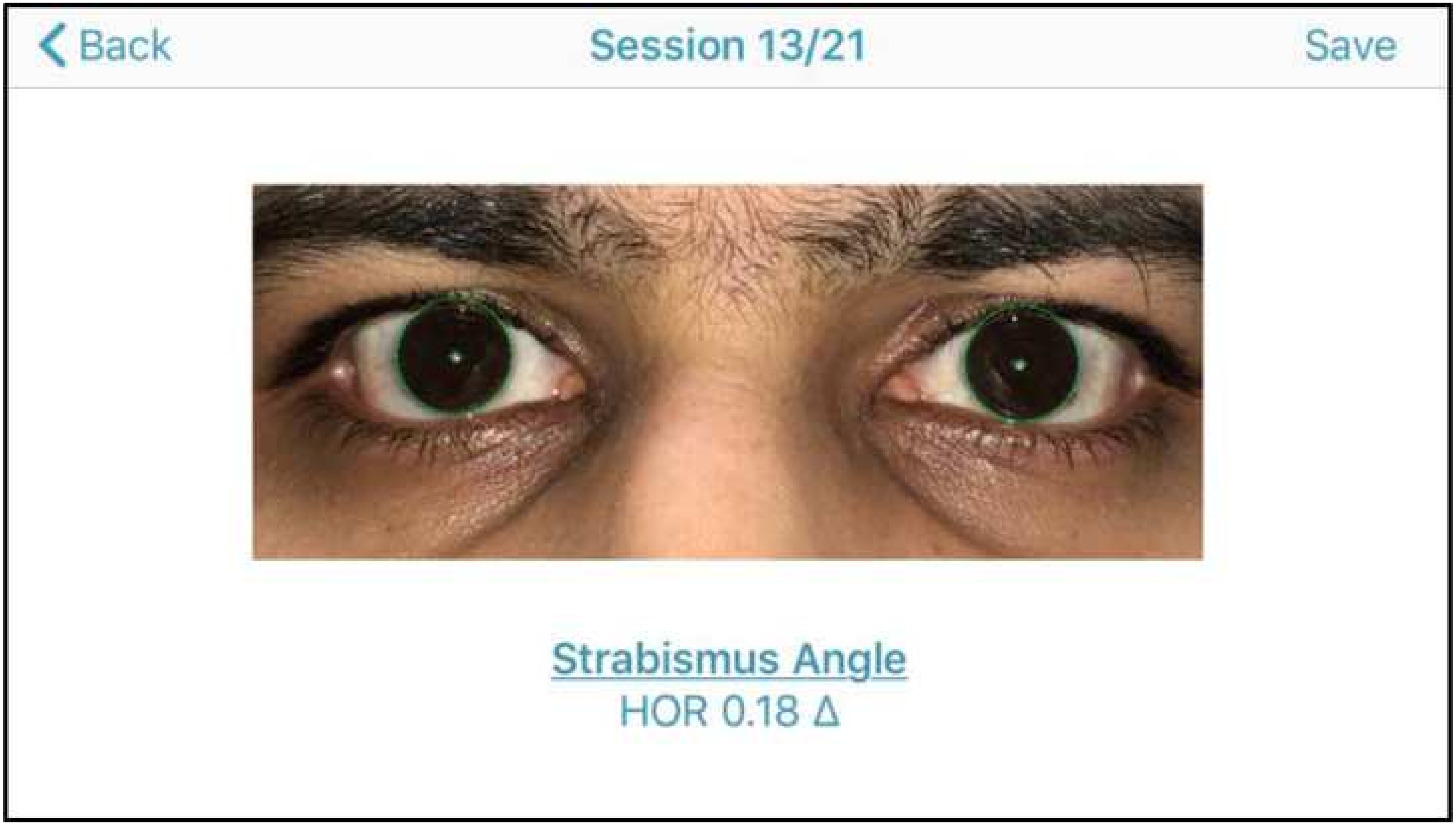

Figure 4

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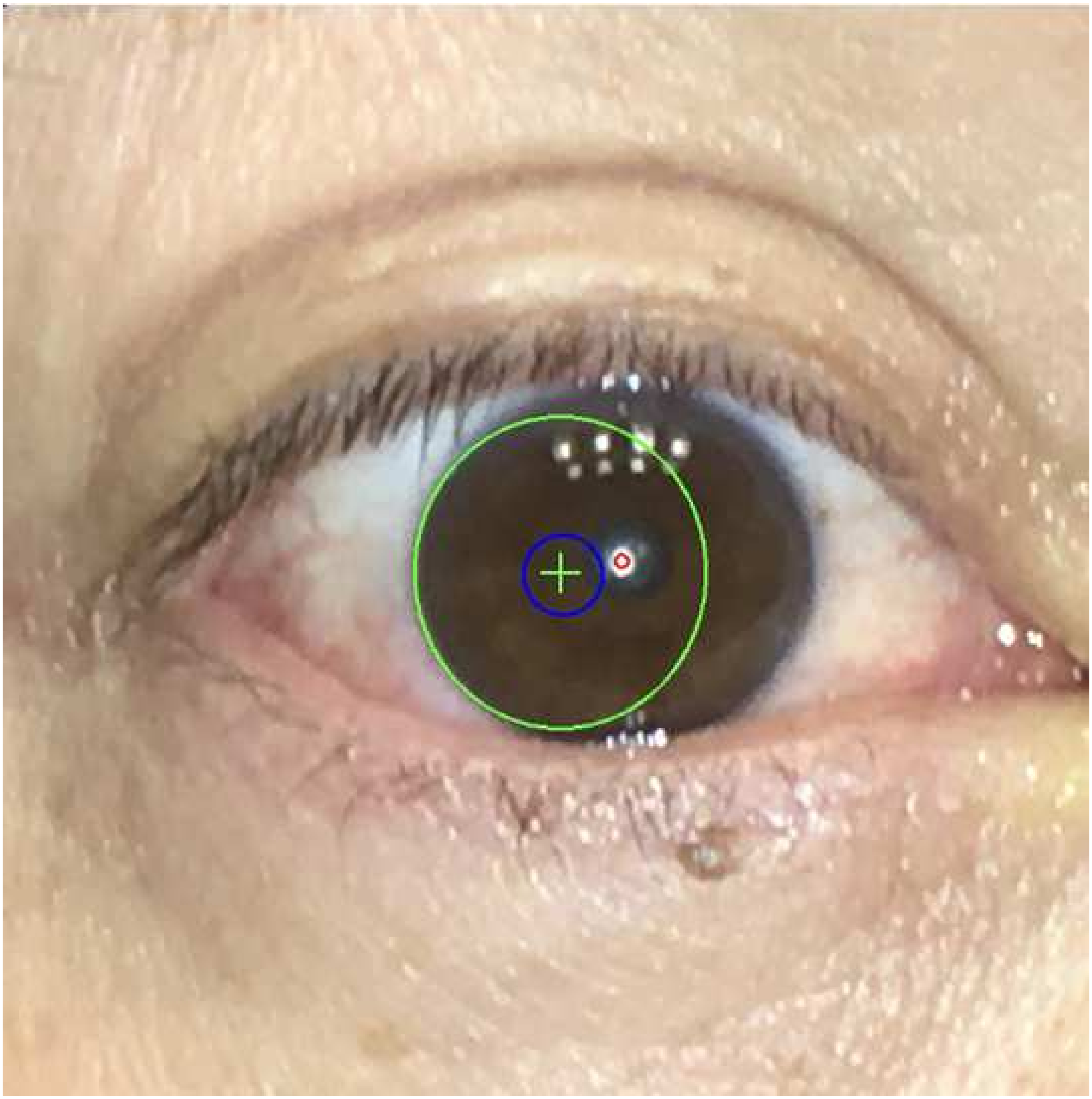

Figure 5

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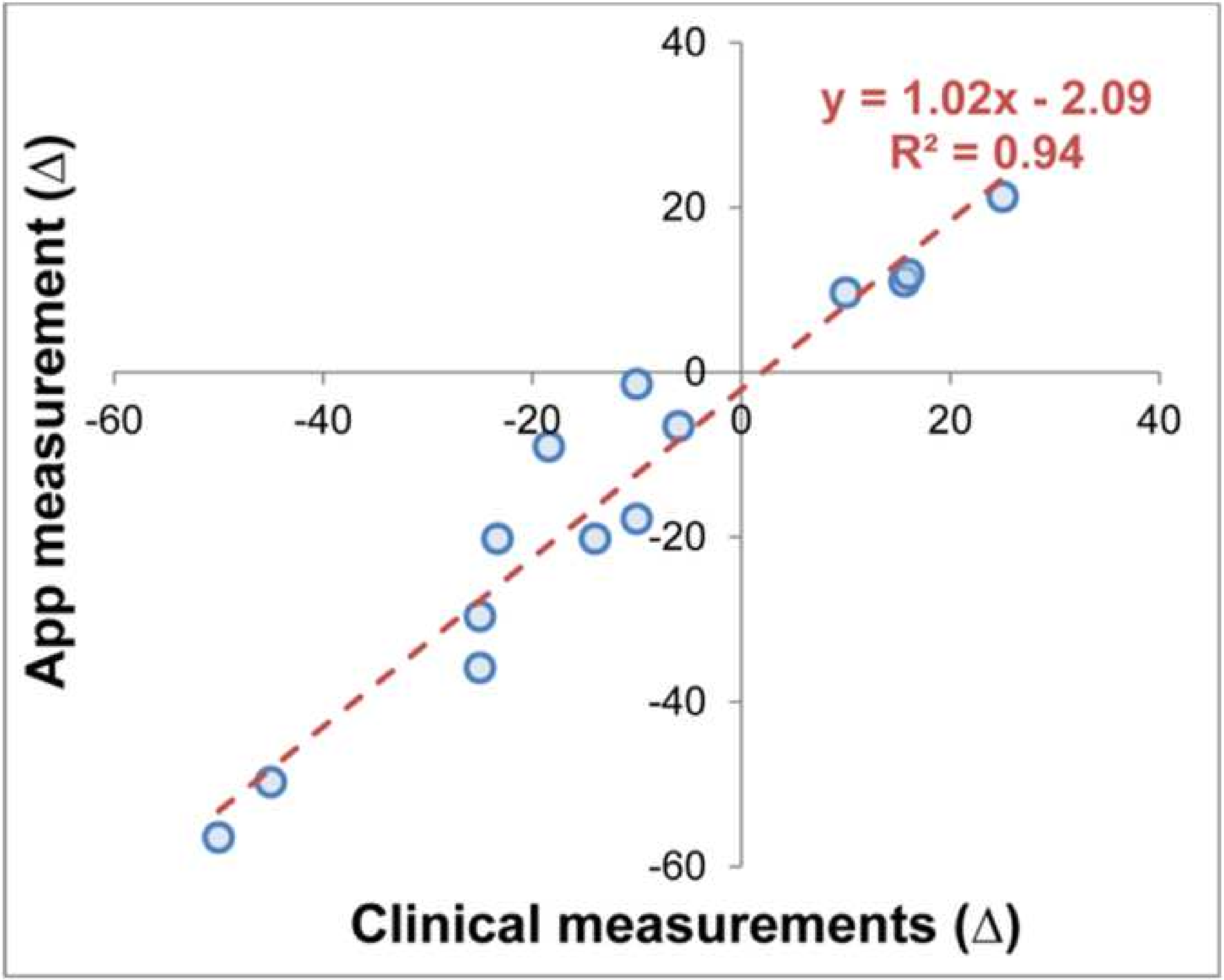

Name of Material/Equipment	Company	Catalog Number	Comments/Description
EyeTurn	EyeNexo		Smartphone app for measureing eye misalignme

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Date:	02/12/2019

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Dear Editor,

We greatly appreciate the very detailed review made by the reviewers and the editorial member. We have addressed them in the revision and we are making point-by-point responses as follows. Changes to the manuscript are tracked.

We have obtained permission from Translational Vision Science and Technology to re-use some of the data we presented previously.

Sections we want to be filmed are highlighted in yellow.

Regards,

Gang Luo

Editorial comments:

Changes to be made by the Author(s):

1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues. The JoVE editor will not copy-edit your manuscript and any errors in the submitted revision may be present in the published version.

Checked.

2. Please provide an email address for each author.

Provided

3. Please include a single line space between each step, substep and note in the protocol section. Please use Calibri 12 points

We are using single line spacing setting.

4. Please rephrase the Short Abstract/Summary to clearly describe the protocol and its applications in complete sentences between 10-50 words: “Here, we present a protocol to …”. Please do not use the term video tutorial. This is a text manuscript.

Revised.

5. Please rephrase the Long Abstract to more clearly focus on the the goal of the protocol i.e., technique described in the manuscript which can be performed with the help of the smartphone app.

Revised.

6. Please ensure the Introduction to include all of the following:
a) A clear statement of the overall goal of this method

Added to the end of Introduction

b) The rationale behind the development and/or use of this technique

c) The advantages over alternative techniques with applicable references to previous studies
Rationale and advantages added to the second paragraph of Introduction.

d) A description of the context of the technique in the wider body of literature

Described in the first paragraph of Introduction.

e) Information to help readers to determine whether the method is appropriate for their application

Added to the last paragraph of Introduction.

7. JoVE policy states that the video narrative is objective and not biased towards a particular product featured in the video. The goal of this policy is to focus on the science rather than to present a technique as an advertisement for a specific item. Please revise parts of the introduction/discussion to bring out clarity.

Revised. “highly consistency” has been removed.

8. Please explain the Hirschberg method as well since the app is dependent on this.

Explanation added to second paragraph of Introduction.

9. Please include an ethics statement before the numbered protocol steps, indicating that the protocol follows the guidelines of your institution’s human research ethics committee.

Included.

10. The Protocol should be made up almost entirely of discrete steps without large paragraphs of text between sections. Please move lines 63-68 to the introduction section instead or convert to action step.
11. Please ensure that all text in the protocol section is written in the imperative tense as if telling someone how to do the technique (e.g., "Do this," "Ensure that," etc.). The actions should be described in the imperative tense in complete sentences wherever possible. Avoid usage of phrases such as "could be," "should be," and "would be" throughout the Protocol. Any text that cannot be written in the imperative tense may be added as a "Note."
12. The Protocol should contain only action items that direct the reader to do something.
13. Please present this as a study from beginning to end. Before the start of the measurement please include Section 1 which should show patient recruitment, how many patients were recruited, inclusion/exclusion criteria, age/sex specific bias if any, etc. Section 2 will then be preparation prior to the experiment. Please write the steps in the order of it being performed.

Comments 10-13 addressed.

14. Please add more details to your protocol steps. Please ensure you answer the "how" question, i.e., how is the step performed? Please do this for the all the steps.

Made clearer.

15. For all software steps, please include all the button clicks in the software, knob turns, etc.

Done

16. 1.1. Launch the app by clicking on the app icon in the smartphone. 1.2 how is this done? 1.4: Flashlight of the smartphone? How far is the smartphone from the patient? The fixation target placement should be the part of the preparation step. 1.6: How do you ensure that the analysis is complete? How to do visually verify that there are no errors in the detection. How do you correct if there are errors?

An erroneous example is given to explain how to do quality check. Distance to a patient is already described.

17. 2: For 2.1: Please explain what Kappa angle is. Please provide citations. 2.2-2.3: How is this done?

As Strabismus, tropia, phoria, angle Kappa is a basic concept in ophthalmology. We expect the targeted readers should know about these concepts.

18. 3: 3.3.: This step is performed prior to the start of the experiment. 3.4: How do you identify the dominant eye? How do you cover with an occluder?

Revised description. Dominant eye is not required.

19. There is a 10-page limit for the Protocol, but there is a 2.75-page limit for filmable content. Please highlight 2.75 pages or less of the Protocol (including headings and spacing) that identifies the essential steps of the protocol for the video, i.e., the steps that should be visualized to tell the most cohesive story of the Protocol.

Protocols 1, 4, 5 are highlighted for filming.

20. Please remove the embedded figure(s) from the manuscript. All figures should be uploaded separately to your Editorial Manager account. Each figure must be accompanied by a title and a description after the Representative Results of the manuscript text.

Fixed.

21. Figure 1: Please do not show the face of the participant.

We can provide photo right release form. We want to show an appropriate size of human face. Too small or too large may cause the test fail.

22. Figure 2, Figure 3: How do you ensure there is no error in the detection. Please include a comparison with some other tests as well.

An erroneous example is given to explain how to do quality check

23. In the result section, please include how many patients were analyzed with this app and include some statistics to show the rate of error. Please also include a comparison between clinical data/other techniques, etc. and this test result to show that this indeed is one of the ways to analyze this.

Provided.

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25. As we are a methods journal, please revise the Discussion to explicitly cover the following in detail in 3-6 paragraphs with citations. Presently there are no citations in the discussion section.
a) Critical steps within the protocol
b) Any modifications and troubleshooting of the technique
c) Any limitations of the technique
d) The significance with respect to existing methods
e) Any future applications of the technique

Added existing methods to the end of Discussion. The other items are already addressed.

26. Please include more citations to show a through review of the literature present in this field of eye research.

More references added.

27. Please revise the table of the essential supplies, reagents, and equipment. The table should include the name, company, and catalog number of all relevant materials in separate columns in an xls/xlsx file.

In our case, the only supply is the smartphone.

Reviewers' comments:
Reviewer #1:

Manuscript Summary:
No concerns for the manuscript, just a note, there were only two sentences (one in the introduction and one in the discussion) regarding taking measurements in different head tilts. There was no information regarding testing for head turns which should be noted.

Co-author Kevin Houston performs test in some patients with their head tilted or turned side way on patients with cranial nerve palsy. This is not described in this paper. So the mentioning is removed.

Reviewer #2:

Manuscript Summary:
User instructions for a smartphone app that measures ocular alignment.

Major Concerns:
* To be accepted by the eye care community, you need to use standard terminology for cover testing; otherwise you risk losing credibility. You might have a academic clinical BV optometrist help you here, and one who knows both the optometry and ophthalmology lingo (as they are not the same). Terminology I would suggest using.
1. Cover-uncover test is performed under binocular viewing conditions and detects if strabismus is present or not. (optometry often says "unilateral cover test", but these are the same; I lean toward cover-uncover because many optometrists have started to use the term because of involvement in the PEDIG network). Or put unilateral cover test in parenthesis after cover-uncover test.
2. SPCT - the simultaneous prism and cover test is primarily done by peds ophthalmologists (and PEDIG optometrists) and is the measurement of the size of tropia under binocular viewing conditions. US ophthalmologists use this measure all of the time for pre- and post-op strabismus measures because this is the patient's "walking-around-in-real-life strabismus magnitude". This magnitude can be smaller, and sometimes is considerably smaller than what one measures on the PACT. Typically, this is only measured on CONSTANT tropias (hard to do if patient has a low-frequency intermittent tropia; need the eye to be deviated to do the measurement.)
3. PACT - prism and alternating cover test - this is the prism neutralization of the magnitude of the ocular deviation (which can be a constant strabismus, intermittent strabismus, or a phoria). Only gives magnitude and direction info. The PACT is often larger than the SPCT because the patient is dissociated for this PACT measure, and other times the PACT and SPCT are the same.

Both cover-uncover (as in SPCT) and alternate cover (as in PACT) can be performed when using the app. Different covering methods put patients in different viewing conditions. The app can measure alignment in those condition. Revision makes it clearer.

Minor Concerns:

Title: instead of saying "measure ocular misalignment" which not all people have - misaligned eyes (particularly because most people with think that means strabismus. Thus, you are not alwasy measuring strabismus, but trying to determine if present and then measuring it. Thus, how about: "Using the Eye Turn smartphone app to evaluate ocular alignment." I would argue that "evaluate" could encompass both 1) is strabismus present? and 2) what is the magnitude of the deviation (strab or phoria). But totally up to the authors - just a suggestion

We accepted the suggestion on “evaluate” and “alignment”. We do not use the app name, EyeTurn, in the title, because JOVE editor clearly stated we should not use the product name.

Keywords: Consider adding "prism and alternate cover test (PACT)"; also Simultaneous prism cover test?

Added.

Abstract:

* line 25 "eye center" - seems like there might be a better word, albeit this is good for lay persons

Rephrased to “iris center”.

* Line 28: what does "highly consistent "mean? - I have no idea in this context. And should this be in the abstract or in the introduction, instead? I would argue the intro. But I guess you could leave it, reference it, and then explain what you mean.

We do have a reference to our published paper, Ref 12. Also data are added to show the consistency.

* line 29: "cover test" is not sufficiently descriptive - is it the SPCT or the PACT?
* Line 29: There is no such thing as the "prism test" ---presumably referring to the PACT here?

Cover test includes cover-uncover and alternate cover tests. Both SPCT and PACT counterpart tests can be performed using the app. It is explained now in revision.

* Line 42: Strabismus is not the "leading" risk factor - abnormal refractive error is. However, if you change the word "the" to "a" then the sentence is now accurate. Quick fix! A good reference to considering adding: is Tarczy-Hornoch K, Varma R, Cotter SA, McKean-Cowdin R, Lin JH, Borchert MS, Torres M, Wen G, Azen SP, Tielsch JM, Friedman DS, Repka MX, Katz J, Ibironke J, Giordano L; Joint writing committee for the Multi-Ethnic Pediatric Eye Disease Study and the Baltimore Pediatric Eye Disease Study Groups. Risk factors for decreased visual acuity in preschool children: The Multi-Ethnic Pediatric Eye Disease and Baltimore Pediatric Eye Disease studies. Ophthalmology 2011;118(11):2262-73. PMCID: PMC3208077

The citation is added.

* Line 51: what does "highly consistent" mean - this is totally vague

Data added to show the consistency. Also refer to published paper Ref 12.

* Line 53: we do not talk about minus or plus to describe strabismus - so suggest you just say "magnitudes of strabismus up to 60Δ" or "magnitudes of esotropia and exotropia up to 60Δ". The latter is better since we don't know about hyper- or hypotropia yet.

Corrected.

* Line 59: it was not clear to me what was meant by "with and without eye covering (to break fusion" here. It was not until I read the rest of the paper that I understood. Better clarity would be helpful

Rephrased.

* Lines 62-8: Should the patient be standing or sitting? Glasses on or glasses off? Presumably before administering drops in eyes? (Some US ophthalmology practices measure alignment after dilation.) I would add all of these, particularly if dilation would affect readings. Even if dilation is not a problem, if cylco'd then accommodation paralyzed so could miss some esotropias.

For varied purposes, we have used the app to test patients when they were standing, sitting, or even lying on bed (patients with stroke). We have also used the app to test patients with visual field loss, including hemianopia and tunnel vision. The purpose of this manuscript is just to show how to use the app as a tool to evaluate alignment, but not to teach users how to interpret the results or how to make diagnosis. It is physicians who should decide whether glasses or dilation drop should be used.

* Line 79-80: Why not put a small letter (and perhaps an adjacent picture for young kids) on the phone routinely. The thing is, that if you miss an accommodative ET because you did not use an accommodative target, there is no way for you to know that you missed that kid.

This is a very good point. That is why we suggest that a fixation target can be used. Again, the app is just a measuring tool. The user should decide the viewing conditions under which the app can be used.

* Lines 83-86: These directions make sense to me as an eye care professional because I know what a limbus and corneal reflection are (if I pair these directions with the photo), but these are not likely to work well for a non-medical professional (for example, vision

screening situation)
Added iris outer boundary to explain limbus.

* Line 94: "latest" means? The last one that was photographed?

* Page 2 far fixation 2.5. This seems like it could be tricky. How do you get the phone between the patient's eyes and yet have the patient fixate in primary gaze at distance? The patient has to look around the phone, so likely to look off to the side or above the phone, and if they do this by a large degree, then the patient is no longer in primary gaze. Seems like there should be more explicit directions to examiner and the patient so that this does not happen. There is also the possibility of the head and body of the examiner in the way fixing a straight-ahead target in primary gaze. Same thing happens when we try to do PACT at distance - have to be very careful we don't block the fixation target.
As it is said in the protocol, patients should look above the phone. They don't have to deviate from primary gaze point. Tester can just place the phone a little bit below the eyes. Revision is made to make it more explicit.

It will be even clearer in video how this can be done. This is exactly the point to publish this paper on JoVE.

* Line 119. First, I was confused because it says "cover test" but a cover test is not done - instead, occlusion is done. (Cover testing implies that there are multiple covers of either eye, of at least more than a single cover.) The measurement is really based on the refixation movement required for the eye to fixate after dissociation by the occlusion of one eye. So, I think your title could be more descriptive.
* Frankly, you could measure constant strabismus like this as well, right? Have you tried this? Is there a difference in accuracy? If both of these ways of measurement are equally accurate, then you can actually get both the SPCT and the PACT measures. Your binocular measure is the counterpart of the SPCT and his occlusion method would be the counterpart to the PACT. Sometimes the SPCT and the PACT are the same and sometimes they are different.

One can do cover-uncover and alternate cover test with the app. The two cover methods corresponds to SPCT and PACT, respectively. The instruction is revised to make it clear. Again, different cover methods may put patient in different viewing conditions. Users should make the decision what to use. We have done different cover tests using the app. The difference depends on patients.

* If in the development of the instrument, you only compared your photographic results to those from the PACT (in free space with prism or neutralized in the major amblyoscope), this could have contributed to any differences found (when your method was smaller than the PACT or the major amblyoscope measure).

As our published paper (Ref 12) shows, the app measurement is highly consistent with PACT measurement, as the slope of the linear regression of app versus prism is 1.01.

* This reminds me - I think I saw reference to using a Maddox rod measure comparison for the occlusion method you have here for phorias. Just a reminder you can only do that for phorias, because if someone with strabismus has anomalous correspondence then the MR measure will differ from that obtained on the PACT or in the major amblyoscope. You probably already considered this, but thought I would mention anyways.

Again, the app is just a measurement tool. It is up to clinicians to interpret the results based on viewing condition and other medical history.

* Line 129-31. I am not familiar with the "common" technique of moving the fixation target for this purpose and I am not sure that it even makes sense to me why this would be. However, I do feel that you should not use the words "phoria posture"; "phoric posture" is jargon used by some eye care providers (others will say, what the heck is "posture") and if the patient is dissociated you don't know whether it is a phoria or a tropia, and furthermore, this procedure has been described as being appropriate for intermittent tropias. Does not make sense for the intermittent tropia to go to its' "phoria posture." Bottom line - you just want to dissociate the patient. If you want to encourage dissociation, instead I would do the PACT for 15-25 seconds or so (and the magnitude may increase as the time increases) and then stop and do the test as described. So, do the ACT for a prescribed time or XX number of alternately covering the eyes, then stop but with the occluder covering one eye, make sure patient fixating, push the button, and uncover the eye to complete the measurement.

It is removed, to avoid confusion.

* Line 196 - I do not understand "perform cover test or measure binocularly"

Rephrased

* Line 202 - patient is singular

Corrected

* Line 206 - insert "correctly" before "determine"?

Fixed.

* Seems like you would have a reference (or several) for the Hirschberg test in your references, since this is proposed as the replacement? Particularly references that provide data on the accuracy of the Hirschberg and any limitations of the test. e.g., Can be difficult to estimate magnitude accurately, particularly with dark irises if only using

transilluminator because hard to see pupil/iris border because so dark (albeit if use direct ophthalmoscope then that particular thing is no longer an issue. But not everyone uses or has a direct ophthalmoscope - I am thinking when screening).

Two more references are added.

* What is "HOR" in the figures?

It means Horizontal measure. Explained in reivison.

Luo, Gang

From: Debbie Chin <dchin@arvo.org>
Sent: Tuesday, December 17, 2019 12:07 PM
To: Luo, Gang
Subject: RE: permission to use some results from TVST paper

Dear Dr. Luo,

Thank you for your email. As a TVST author, you retain the right to reuse material from your TVST article in your future work, with appropriate attribution. You do not need to ask for permission to reuse your own material. You are welcome to take some of the data from your TVST article and re-plot it in a new figure for a new article.

Best regards,

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From: Luo, Gang <Gang_Luo@MEEI.HARVARD.EDU>
Sent: Monday, December 16, 2019 12:34 PM
To: Debbie Chin <dchin@arvo.org>
Subject: permission to use some results from TVST paper

Hi Debbie,

We published a paper on TVST early this year, "Pundlik S, Tomasi M, Liu R, Houston K, Luo G. Development and Preliminary Evaluation of a Smartphone App for Measuring Eye Alignment. Translational Vision Science & Technology. 2019;8(1)". In that study we evaluated a smartphone app for measuring strabismus. Now we are writing a new manuscript to be submitted to another journal, describing in more details about the protocol using the app. We hope that by following the protocol, people would be more likely to achieve similar accuracy as we showed in the TVST paper. I am writing to request a permission to use some of the relevant data published on TVST in the new manuscript. We will re-plot the used data in a new figure. I wish the permission can be granted.

Regards,

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