PERFORMANCE OF THE 2WIN PHOTOSCREENER WITH "CR" STRABISMUS ESTIMATION IN HIGH RISK PATIENTS

Short Title: Infrared wand helps the 2WIN photoscreener detect strabismus

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Précis: 2WIN photoscreener with infrared wand CR function correlated with Retinomax and exam in children and adults with or without developmental delays.

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Introduction

Amblyopia is a blinding pediatric disease which is essentially curable if detected early and treated thoroughly[1]. The Amblyopia Treatment Studies by the Pediatric Eye Disease Investigator Group enrolled patients with amblyopic acuity 20/40 or worse typically due to refractive error (1/3), strabismus (1/3) and combined (1/3) etiologies[2]. Strabismus can be constant or intermittent. Strabismus and refractive error are risk factors for amblyopia specifically targeted by objective pediatric vision screeners[3]. However, accurate objective estimation of refractive error and strabismus remains a challenge, especiallly in children.

The American Academy of Pediatrics recommends amblyopia screening in older children by assessing monocular visual acuity[4]. Young children can be efficiently screened by objective measures including instrument-based photoscreening[5]. Photoscreeners employ a flash camera with an acute flash-patient-lens angle of about 1° such that amblyopia risk factor refractive errors can be detected by a light crescent encroaching on the otherwise uniform red pupil reflex; the more light crescent correlated with greater refractive defocus. Some commercial photoscreeners like the iScreen[6] and GoCheckkids[7,8] utilize visible light with central reading centers. Three commercially available photoscreeners (Plusoptix, SPOT and 2WIN) utilize infrared light and internal computer-interpretation to estimate binocular refractive error, pupil size and interpupillary distance. The PlusoptiX models have shown excellent validity and precision to detect amblyopia risk factors[9,10]. Derived from the PlusoptiX, the SPOT photoscreener now marketed by Welch Allyn also shows valid amblyopia risk factor detection[11-13]. The 2WIN remote autorefractor in its initial US validation showed validation comparable to SPOT[9].

Since 2WIN utilizes infrared light, the patient is not aware of the mutiple, rotating photoscreen images being exposed to afford multiaxial estimation of spherical and astigmatic refractive error. 2WIN recently developed a special occluder which is a visible light blocking, infrared transmitting “wand” called “CR.” Corneal reflex Hirschberg images can be taken through the CR wand and used to quantify constant and intermitted horizontal and vertical deviations.

Retinomax (model K + 3, Righton, Tokyo) is a hand held autorefractor with high reliability[14] and determined to be the gold-standard for refractive error in the Multi Ethnic Pediatric Eye Disease study[15].

This manuscript covers validation of the updated 2WIN in a pediatric ophthalmology practice using the new “CR” wand, compared to Retinomax autorefraction and comprehensive examination with cover test.

Methods

This a reliability analysis validating a screening device covered by Institutional Review Board at Providence Hospital with Clinical Trial Registry (NCT03668067). The IRB approved the collection of de-identified data including patient age and neurodevelopment status, the results of 2WIN photoscreening, Retinomax refraction, and gold standard clinical examination of refraction and ocular alignment. The study complies with HIPAA and the Declaration of Helsinki.

Photoscreening and ocular alignment assessment by Corneal Reflex function on a 2WIN photoscreener (Adaptica, Padova Italy, software configuration 2WIN/KALEIDOS 5.0_171018, version 24.0) were included as a components of comprehensive examinations of consecutive new and existing patients in a pediatric ophthalmology and adult strabismus clinic from June through September 2018. The CR 2WIN function combines the photoscreener with an ocular occluder that nearly completely blocks visible light, but transmits the infrared light utilized by the 2WIN photoscreener (Figure 1). The Adaptica Kaleidos fixed-distance tube was not yet available at the time of our study. The 2WIN was used in free space similar to holding and focusing the SPOT or Plusoptix from about 1 meter. A bar on the top of the 2WIN screen turns green when appropriate focal distance is achieved. To exclude potential examiner bias with retinoscopy alone, most of the patients also had refraction estimated by Retinomax K+3 from about 5 cm. De-identified data from the photoscreener refraction and ocular alignment estimates were compared to refraction, strabismus, age, and neuro-developmental status. For the majority of patients, the confirmatory examiner was blinded to the photoscreeners results. The 2WIN photoscreening was performed without

cycloplegia (dry). Retinomax and retinoscopy by one, experienced pediatric retinoscopist (rwa) were performed "dry." Cycloplegia (cyclopentolate 1% 30 minutes before) was used for confirmatory exams. Constant and intermittent strabismus were assessed with prism and cover test and alternate cover test while the patient fixates on a small, high resolution toy.

Refractive variables and strabismus angles from the 2WIN and Retinomax were compared to confirmatory examination. In addition to cylinder power, power vectors were analyzed with J0 representing Cartesian astigmatism (vertical Jackson Cross Cylinder with positive indicating with-the-rule and negative against-the-rule astigmatism)[16] and J45 representing oblique Jackson Cross Cylinder astigmatism.

From varied levels of instrument-estimated refractive errors compared to 2003 AAPOS Uniform Guideline amblyopia Risk factors[17], an ROC curve[18] was derived for 2WIN with and without CR strabismus estimation.

Ocular alignment by cover test was classified as constant deviation or intermittent deviation and compared to the interpretation of CR on the 2WIN.

Correlations were assessed by linear regression and correlation coefficient as well as Spearman coefficient.

Sample size calculation for linear regression with 2 predictors given Statistical power level 0.9, Probability level 0.01, and an anticipated effect size of 0.05 implies a minimal sample size of 351.

Use of the 2WIN with "CR" strabismus estimation is shown in https://vimeo.com/299168395.

Results

Retinoscopic refraction and 2WIN refraction was completed by 371 patients aged 0.6 to 63, median 6.4 years. Fifteen had 2WIN reading on one eye only using the monocular feature enhanced by the infrared wand. Age breakdown and ranges of strabismus and refractive values are shown in Table 1. An additional 64 patients had just the CR corneal reflex alignment compared to cover test (age range 0.6 to 66, median 5.8 years). Three patients could not be screened with 2WIN; one due screener error (battery) and two due to patient's inability to fixate on the camera.

The reasons for new referral to the pediatric ophthalmology clinic included photoscreen referral 43, strabismus 55, ROP/NICU follow up 14, lid/tear duct 11, developmental delay consult 19, amblyopia/glasses 25, acuity screening 3, nystagmus in 1 and Juvenile idiopathic arthritis in 1. Folllow up exams constituted the remaining 199.

Regressions: Figure 2 shows linear regression of cycloplegic refraction right eye (ordinate) for spherical eqivalent compared to 2WIN (solid regression line) and Retinomax (dotted line). Astigmatism components for right eye are classified by cylinder power (Figure 3), J0 vector (Figure 4) and J45 vector (Figure 5) with 2WIN compared to Retinomax. Figure 6 shows cover test (abcissa) compared to the horizontal component of 2WIN CR function for constant strabismus (solid regression line) and intermittent strabismus (dotted regression line). Figure 7 compares those cases with cover test over 10 prism diopters with 2WIN CR function vertical component readings. Table 2 shows linear regression variables, R2 and Pearson's coefficient for refractive and strabismus measurements for right and left eyes.

Refractive readings within 1 diopter of exam for cylinder right eye / left eye were 93%/94% for 2WIN and 89%/90% for Retinomax. Readings for cylinder axis right eye/left eye compared to examination within 10° were 68%/69% for 2WIN and 69%/74% for Retinomax. Readings for right eye/left eye for spherical equivalent within 1 diopter compared to cycloplegic exam were 68%/72% for 2WIN and 69%/68% for Retinomax.

ROC:

Figure 8 shows receiver operating characteristic (ROC) curves for the 2WIN compared to 2003 AAPOS Uniform guidelines[17] (solid lines) and age-stratified 2013 AAPOS guidelines[3] (dashed lines). The prescreening probability of 56% by 2003 guidelines changed to to 45% by the more recent guidelines. 31% of these children aged 0.6 to 5 years had developmental delays. For 2013 guidelines, the preschool (73% sensitivity, 88% specificity) and toddler (78% sensitivity and 82% specificity) resembles 2003 guidelines, but the 2013 infant validity is less (61% sensitivity and 72% specificity). By 2003 guidelines with refractive amblyopia risk factors only, the 2WIN refractive screening achieved 68% sensitivity and 84% specificity. When strabismic risk factors were added, 2WIN refractive screening had 59% sensitivity and 86% specificity. Adding the “CR” corneal reflex strabismus feature to 2WIN produced 69% sensitivity and 88% specificity.

Conclusion

Reliable measurement of refraction and ocular alignment remains a challenge. Of the three commercially available infrared photoscreeners, PlusoptiX and SPOT were mainly designed for pediatric screening while the 2WIN is a component tool from Adaptica emphasizing refraction in adults with photoscreening referral criteria also available for children. 2WIN in a former software release performed similarly to SPOT and slightly less well than PlusoptiX[9].

Objective vision screening is particularly of value for children too young to efficiently perform monocular visual acuity screening, or developmentally delayed individuals, therefore we did not exclude them from our study for which the 2WIN refractive and strabismus functions appeared to perform well. This study addresses “high risk” because it deliberately includes developmental delays and it is performed in the enhanced prescreening probability cohort in the eye office compared to the general population.

Two entirely different refractive techniques were employed to validate the 2WIN; gold standard[3] cycloplegic refraction by an experienced retinoscopist and a Hartmann-Schack autorefractor allowing for the patient’s natural accommodation. The hand held autorefractor Retinomax has proven reliability[19,20] and was therefore adopted as the gold-standard cycloplegic refraction for the MEPEDS and BPEDS studies[15]. This study compared updated software on the 2WIN for estimation of non-cycloplegic refraction to dry and cycloplegic refraction with Retinomax, and compared to experienced phoropter retinoscopy. We found remarkable comparability of the 2WIN to Retinomax with respect to cylinder power, and both vector components of cylinder related to axis. Compared to cycloplegic exam spherical equivalent, both 2WIN and dry Retinomax had good correlation, however the slope of the regression curve indicated that 2WIN exposed from about 1 meter produced less accommodation than Retinomax (Figure 2) despite the video fixation target of the Retinomax attempting to relax accommodation. Photoscreening uses a slightly off-lens-axis flash that produce light crescent in the pupillary red reflex. The further the light reflex encroaches in the pupil, the greater the refractive error. For many photoscreeners, the pupillary crescent appears with ocular defocus of > 1.5D either

hyperopic or myopic. We observed uninterrupted accurate refraction estimate by 2WIN whether outside, or within this refractive range which is a typical photoscreen null zone.

The new visible-blocking, infrared-transmitting wand comes with two round filters in glasses-like frames with a handle. We mainly used only one filter over the non-tested eye. Children would often press the wand up against their “occluded” eye such that the lids would be squished closed. We found it better to advise them to rest the wand against their eyebrow. 2WIN with the CR function gave rapid interpretation of horizontal and vertical alignment in a sequence with both eyes open, then left covered and finally right eye covered. Constant deviations were consistently reported, however on some occasions, we had to hold the wand over the eye several seconds to elicit an intermittent deviation. The wand is not completely visible-light blocking, so bright light sources can appear through the filter- often with a pink tint. We found strong correlation between 2WIN CR measurments and cover test for both constant and intermittent horizontal deviations. The current version of the software estimates large and small values in prism diopters; reliable measurments from 2WIN CR were mainly greater than 10 PD; less than 10 PD probably should presently be considered a null strabismus zone pending future software updates. For our relatively few vertical strabismus deviations greater than 9 prism diopters, the 2WIN CR correlated with cover test.

The infrared wand also assisted refractive estimates for patients with manifest strabismus. The 2WIN refraction function allows binocular testing, but also selected left eye or right eye screening, however the eye must be fixing on the camera. For patients with ocular suppression, applying the infrared wand to the fixing eye allowed accurate refraction of the otherwise deviated eye.

The infrared photoscreener was noted to have yet another helpful role; in extremely photophobic children, such as those with active herpetic keratouveitis, the photoscreener could be aimed and exposed in a nearly dark room affording a clinically useful image of the red refflex without employing any visible light flash. Another advantage of the 2WIN is that is is charged with conventional USB cable.

There were limitations on the current version of the 2WIN. The photoscreener has several buttons required to cycle through various functions. It has a smaller screen than comparable infrared photoscreeners and it is not a touch-screen. The amount of time to acquire an adequate image was similar to the precise Plusoptix if the regular photoscreen function was utilized first on a given patient. However, if CR function was initially employed, then the subsequent photorefract function more readily acquired a readable image quickly- and comparable to characteristic speed of the SPOT. In general, there is a manufacturer-selected choice between photoscreening speed and precision; the new software on the 2WIN performed favorably. The current 2WIN defaults to adult screening. Age-based instrument referral criteria so as to comply with AAPOS 2013 guidelines are available on 2WIN, but through a non-intuitive series of button clicks, and the instrument referral criteria are not easily user-adjusted like the superb ROC-like system on the PlusoptiX. New software updates for 2WIN are addressing these issues to make the device more useful for pediatric screening. 2WIN is able to give reliable refractive data through spectacles. In addition, the portable, luminance and external distraction reducing Kaleidos attachment could make 2WIN additionally efficient for older children in noisy, bright-lit environments.

Although this study had sufficient number of patients including a large number of younger children with developmental delay, the following study limitations were noted: some of the patients were new referrals, but others were already accustomed to wearing their spectacles. Compared to newly-referred hyperopic children, consistent spectacle-wear and/or amblyopia improvement could influence accommodative ability and therefore some components of the refractive and alignment values. The prescreening probability was enhanced by “screening” in a high-risk pediatric eye practice rather than community screening. The confirmatory dry and cycloplegic refractions were not completely masked from the preliminary photoscreening in every case.

In conclusion, the 2WIN performed similarly to the industry-standard Retinomax with respect to astigmatism estimation, and perhaps a bit better than Retinomax for reducing over-accommodation when determining spherical hyperopia. The novel CR function was

reliable for estimating constant and intermittent horizontal deviations greater than 10 prism diopters.

Tables

Table 1:
Patient Characteristics including portion with developmental delays, cover test strabismus of 10 prism diopters (PD) or greater, Ranges of refractive findings for myopia, hyperopia and cylinder for 2WIN photoscreener (dry) and cycloplegic refraction striated by age featuring the 2013 AAPOS uniform vision screening guidelines.

Table 2. Correlation variables comparing 2WIN and Retinomax to retinoscopy and cover test. R2 is correlation coefficient and Pearson is Pearson Product Moment correlation. For strabismus, cover test correlated with 2WIN and CR function.

Figures

Figure 1. Screeners view of the back of the 2WIN utilizing the CR function with the patient holding the infrared-transmitting occluder over the right eye. (Permission given to share image for educational purposes.)

Figure 2. Linear regression for cycloplegic refraction spherical equivalent right eye comparing 2WIN open circles and solid best-fit line versus dry Retinomax solid diamonds and dashed best-fit line.

Figure 3. Linear regression for cylinder power, plus format right eye comparing 2WIN open circles black line versus Retinomax gray diamonds and gray best-fit dashed line.

Figure 4. Linear regression for right eye refraction J0 power vector comparing 2WIN open circles and black best-fit line versus Retinomax solid gray dots and dotted best fit line.

Figure 5. Linear regression for right eye refraction J45 power vector comparing 2WIN open circles and black best-fit line versus Retinomax solid gray dots and dotted best fit line.

Figure 6. Linear regression for horizontal constant and intermittent strabismus deviation in prism diopters comparing 2WIN CR function constant open circles and black best-fit line versus 2WIN CR intermittent strabismus solid gray dots and dotted best fit line.

Figure 7. Linear regression for vertical strabismus (> 10 prism diopters) cover test deviation compared to 2WIN CR function.

Figure 8. Receiver Operating Characteristic (ROC) curves for 2WIN with or without CR strabismus screening function utilizing American Association for Pediatric Ophthalmology and Strabismus (AAPOS) 2003 pre-school uniform refractive ± strabismus amblyopia risk factor (ARF) gold standards on this high risk pediatric cohort shown in solid lines. Age stratified preschool 2013 AAPOS uniform guidelines (shaded, dashed lines) shown for comparison with refractive plus strabismus CR function screening compared to refraction plus cover test ARFs..

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