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Pediatric Vision Screener 2: pilot study in adults

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Abstract. Amblyopia is a form of visual impairment caused by ocular misalignment (strabismus) or defocus in an otherwise healthy eye. If detected early, the condition can be fully treated, yet over half of all children with amblyopia under age 5 escape detection. We developed a Pediatric Vision Screener (PVS) to detect amblyopia risk factors. This instrument produces a binocularity score to indicate alignment and a focus score to indicate focus. The purpose of this study is to assess the performance of the PVS by testing adults who were fully cooperative for testing. The study group includes 40 subjects (20 controls, 20 patients) aged 22 to 79 years. 12 patients had constant strabismus (8 to 50^{Δ}), and eight had variable strabismus (12 to 55^{Δ}). All controls had binocularity scores >50%. Binocularity was <50% in 11/12 patients. The patient with binocularity >50% had a well-controlled intermittent exotropia and was not at risk for amblyopia. Focus scores were highly sensitive for good focus but not specific. The PVS shows high sensitivity and specificity for detection of strabismus in adults. Future studies will determine whether this performance can be achieved in preschool children, who are at greatest risk for vision loss. [DOI: 10.1117/1.1805561]

Keywords: amblyopia; strabismus; vision screening; polarization optics; birefringence.

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1 Introduction

The developing human visual system requires focused images and precise binocular alignment to attain optimum visual acuity and stereopsis at maturity. When an eye is unable to focus properly in childhood, the result may be irreversibly poor vision in adulthood. If the two eyes are misaligned in childhood, one eye may be suppressed centrally by the still-flexible central nervous system to avoid double vision or visual confusion, again causing poor vision in adulthood. Vision loss in an otherwise structurally sound eye, known clinically as amblyopia, has a prevalence as high as 5%.[1]

If detected early in life, amblyopia is remarkably responsive to treatment. Unfortunately, children respond best to treatment at an age when they are also most difficult to examine, and as many as half of children with amblyopia escape detection before age 5.[2] Large-scale specialist examinations for amblyopia risk factors have effectively eliminated the most severe forms of amblyopia in Scandinavia,[3] but this approach is not practical in most health care systems. Potentially cost-effective strategies for detecting amblyopia, including a variety of devices and protocols designed for use by nonprofessionals, have failed to attain adequate sensitivity and specificity to warrant mass screening of preschool children.[4]

Photorefraction is currently the most widely applied automated approach for detecting the optical performance of the eye for mass screening purposes. In this approach, the eye is illuminated with a point source or extended light source, and a 2-D image of the returning light distribution in the pupillary plane is recorded for subsequent characterization of the image. Photorefraction can detect poor focus and irregularities of ocular media, but sensitivity and specificity for detection of amblyopia risk factors have been limited in studies to date, and the devices require complex or bulky optical apparatus.[5–8]

We have developed a Pediatric Vision Screener (PVS) to detect amblyopia risk factors automatically in a series of measurements over a brief interval.[9] In this study, the clinical performance of the PVS was evaluated in cooperative adult subjects in anticipation of future studies in less-cooperative children. The device showed high levels of sensitivity and specificity for ocular misalignment.

1.1 *Device Operation*

The PVS design has been described in detail elsewhere.[9] Briefly, the eyes are scanned with binocular retinal birefringence scanning (BRBS)[10] to detect alignment, and with binocular focus detection to detect focus.[11] The device was mounted on a stand for ease of testing (see Fig. 1). Data were obtained as a series of five measurements in a total of 2.5 sec, with the final results averaged.

For data acquisition, adult subjects were seated in a dim room, with the chin in a chin rest to facilitate head positioning. The fixation target was the focus detection laser diode itself, a near-infrared blinking point source presented in combination with a synchronized beeping tone. Data were inspected online and saved to disk for off-line analysis. The fast Fourier transform (FFT) power spectrum of the BRBS signals was obtained to determine the power at both the scanning frequency of the spinning mirror and twice the scanning fre-

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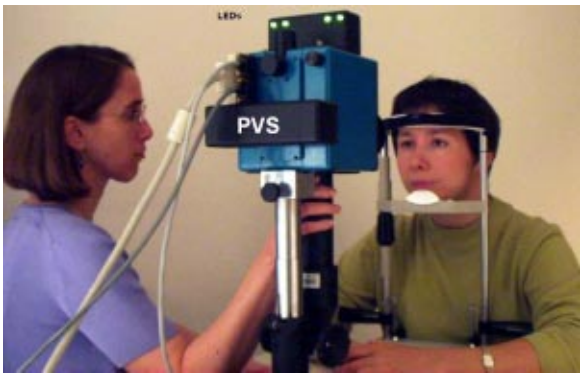

Fig. 1 Prototype Pediatric Vision Screening device (PVS). The subject is asked to view a blinking target within the aperture of the device. To facilitate testing, the device is mounted on a stand, and the subject's head is placed in a chin rest. Neither the stand nor the chin rest is required for testing. Light emitting diodes (LEDs) indicate passing score.

quency. The percentage of power at twice the scanning frequency indicated the fixation of each eye. The results were displayed as separate plots for the right and left eyes. To determine power at 400 Hz (the modulation frequency of the focus laser), the FFT power spectrum of the focus detection signals was obtained. The results were displayed as a pair of peaks for each eye—one representing the center (C) of the bull's-eye photodetector, the other the annulus (A).

1.2 *Volunteer Testing*

To determine whether the PVS could identify strabismus and/or defocus, measurements were obtained from adults with strabismus and concurrent controls. Subjects were excluded if they had glaucoma, age-related macular degeneration, cataract, nystagmus, retinal disease, or cognitive deficits. An orthoptist performed a ''gold standard'' examination, measuring best-corrected visual acuity, distance refraction, binocular vision, and ocular motility. Ocular alignment was expressed in prism diopters, a clinically used unit of measure approximately equal to 0.5 deg in the range of interest. Residual distance refraction was measured with vision correction in place. The study was approved by the appropriate institutional review boards, and informed consent was obtained from all subjects.

Based on the results of the orthoptic evaluation, subjects were classified as either control, constant strabismus, or variable strabismus. Subjects were considered ''control'' if they claimed no major ocular problems and if both eyes had <3.00 D of myopia and <0.50 D of hyperopia, with <1.25 D of anisometropia and no strabismus. Contact lens and glasses wearers were grouped with ''control'' (low refractive error) subjects if residual refractive error met control criteria. Subjects were classified as having ''constant strabismus'' if they had clinically documented ocular misalignment of any angle that was always present. Subjects were classified as having ''variable strabismus'' if they had ocular misalignment, but were able to compensate for this either through intermittent fusional eye movements or by using a compensatory head position to achieve binocularity.

Subjects were asked to fixate first centrally with both eyes, then centrally with each eye separately, the untested eye being covered with a clinical occluder. They were then asked to fixate centrally and in four ordinal directions alternately, 1.5 deg from the central fixation light. This protocol allowed testing for repeatability, for detection of cross talk between channels, and for identification of false positive responses. Five readings were obtained for each direction of fixation.

1.3 *Data Analysis*

Characterization of the BRBS output has been previously detailed.[9,10] Briefly, a binocularity score was calculated from an entire sequence of readings as the percentage of attentive readings with bilateral fixation. The ability to detect fixation of each eye made it possible to identify inattentive measurements in which neither eye was looking at the target. Thus, the percentage of attentive readings overall was designated as the yield (Y) of the sequence. The instrument also produced a signal-to-noise (STN) relationship determined by the percentage of information in the frequencies of interest. The STN, expressed as a percentage, is not the same as the classic signal-to-noise ratio (SNR), which is expressed as a logarithm. The use of a percentage rather than a log allowed yield and STN to be combined into a single product, designated as the quality score, QS=STN*Y. A binocularity score of 50% was set as the threshold between a pass and refer. That is, a subject with binocularity $<50\%$ would be referred for a specialist eye examination; a subject with binocularity $>50\%$ would not.

Characterization of the focus output has also been explained in detail previously.[11] Briefly, the output of the bull's-eye photodetector consists of a central component C and an annular component A. The ratio C/A is maximum when the eye is in perfect focus; as focus declines, C/A approaches 1.0. To compensate for variations in fundus reflectivity, the normalized ratio $(C-A)/(C+A)$ was calculated; this ratio ranges from 0 for complete defocus to 1 for perfect focus. The pass versus refer threshold for focus was not determined *a priori*.

For comparison of binocularity scores, a one-way analysis of variation (ANOVA) test was performed. Sensitivity and specificity for detection of amblyopia risk factors was also determined. For studies of age and eye color in the focus detection system, the values obtained from both eyes of each subject were averaged. To allow for statistical analysis, two groups were formed for the parameter of eye color. Brown eyes were compared against all lighter eye colors (blue, green, gray, and hazel). For the focus detection studies, paired data were analyzed with the student t-test. Results were considered statistically significant if the p value was <0.05.

2 Results

The 40 subjects ranged in age from 22 to 79 years. The study population included 10% African American, 8% Asian, 78% Caucasian, and 5% Hispanic subjects. Of the 20 strabismus patients, 12 had constant strabismus (with misalignment ranging from 8 to 50 prism diopters). The other eight patients had variable strabismus, six with intermittent strabismus (20 to 55

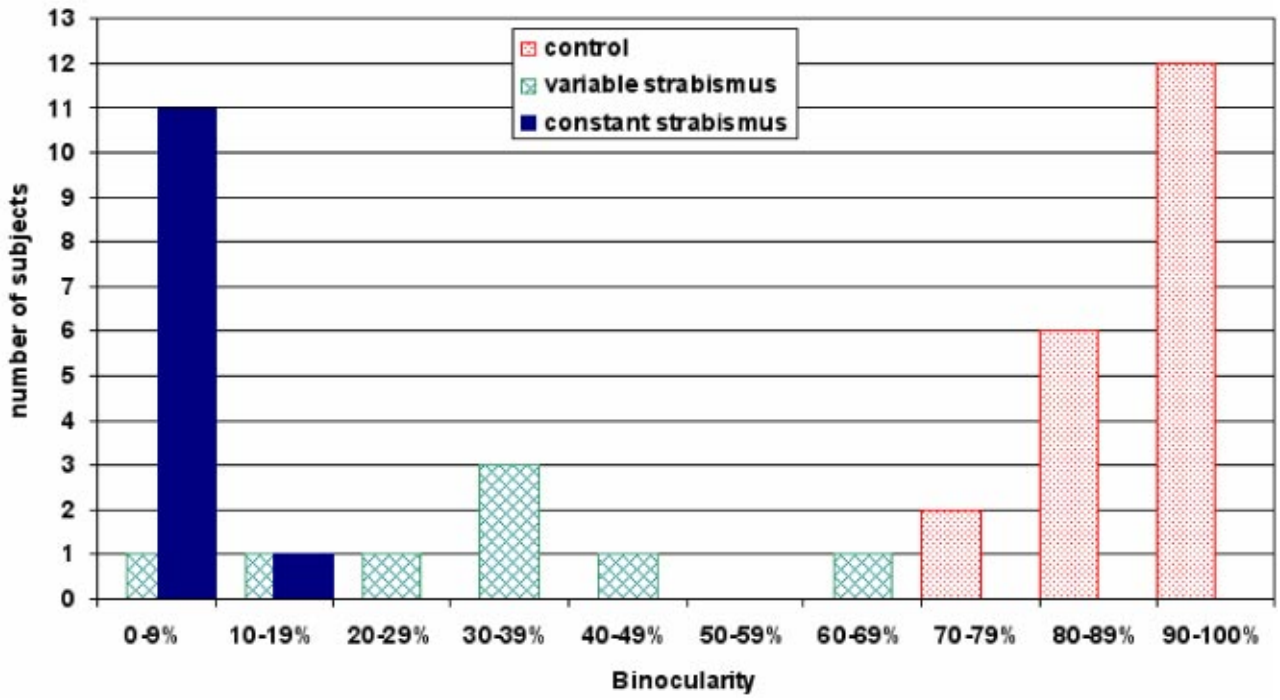

Fig. 2 Histogram detailing binocularity scores of all subjects.

prism diopters) and two with strabismus of 12 to 16 prism diopters who were able to fully align the eyes by adopting an (anomalous) compensatory head position.

2.1 *Binocular Alignment*

For all subjects, central fixation was never detected during 1.5 deg of paracentral fixation in four ordinal directions, and cross talk (detection of fixation in an occluded eye while the other eye focuses on the fixation target) never occurred.

The binocularity scores of all subjects are presented as a histogram in Fig. 2. Binocularity was >70% for all controls and <20% for all patients with constant strabismus, including the subject with only 8 prism diopters of misalignment. In subjects with variable strabismus, Binocularity ranged from 0 to 67%, but was <50% in all but one subject, a 25-year-old woman with well-controlled intermittent exotropia, high-grade stereopsis, and no amblyopia. The clustering of the groups is more clearly shown as a box plot (Fig. 3), with highly significant differences by ANOVA ($p<0.001$). As shown by the receiver operator curve in Fig. 4, all thresholds above 10% resulted in zero false positives. The best balance of sensitivity and specificity occurred when a threshold binocularity score was set to 60%.

Quality score (QS) averages for all three populations are shown in Fig. 5, with the error bars representing one standard deviation. QS was lower in variable strabismus patients than in controls or constant strabismus patients ($p=0.0058$). QS was not dependent on gender or eye color. QS showed a non-significant trend toward being lower in African American subjects, but the African American subjects were variable strabismus patients, who as a group had significantly lower QS as indicated above.

2.2 *Focus Detection*

Focus score did not correlate with eye color (Fig. 6, $p=0.93$). Focus score also did not correlate with age [$R^2=0.09$ for C/A, $R^2=0.10$ for normalized $(C-A)/(C+A)$], as shown in Fig. 7, but there is a suggestion that it becomes more difficult to obtain high signal strength after age 50. Focus scores for each eye were plotted as a function of accommodative demand, which is the reciprocal of the distance to the fixation target (2 diopters) added to the clinically measured residual distance refraction (Fig. 8). The best sensitivity

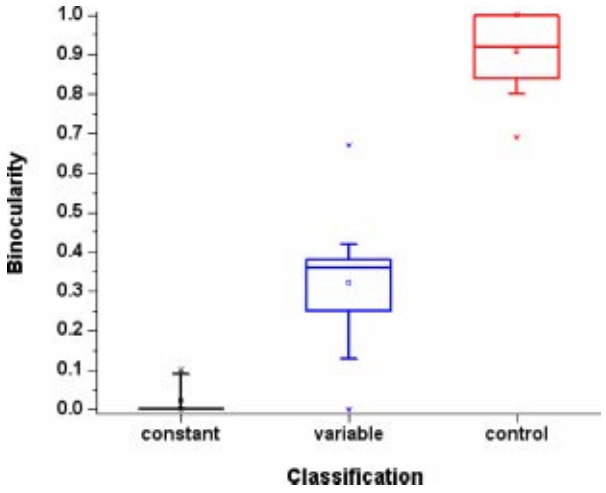

Fig. 3 Box plot of binocularity scores for controls, patients with variable strabismus, and patients with constant strabismus. □ are mean values; * are extreme values; and horizontal lines represent 25, 50, and 75 percentile values.

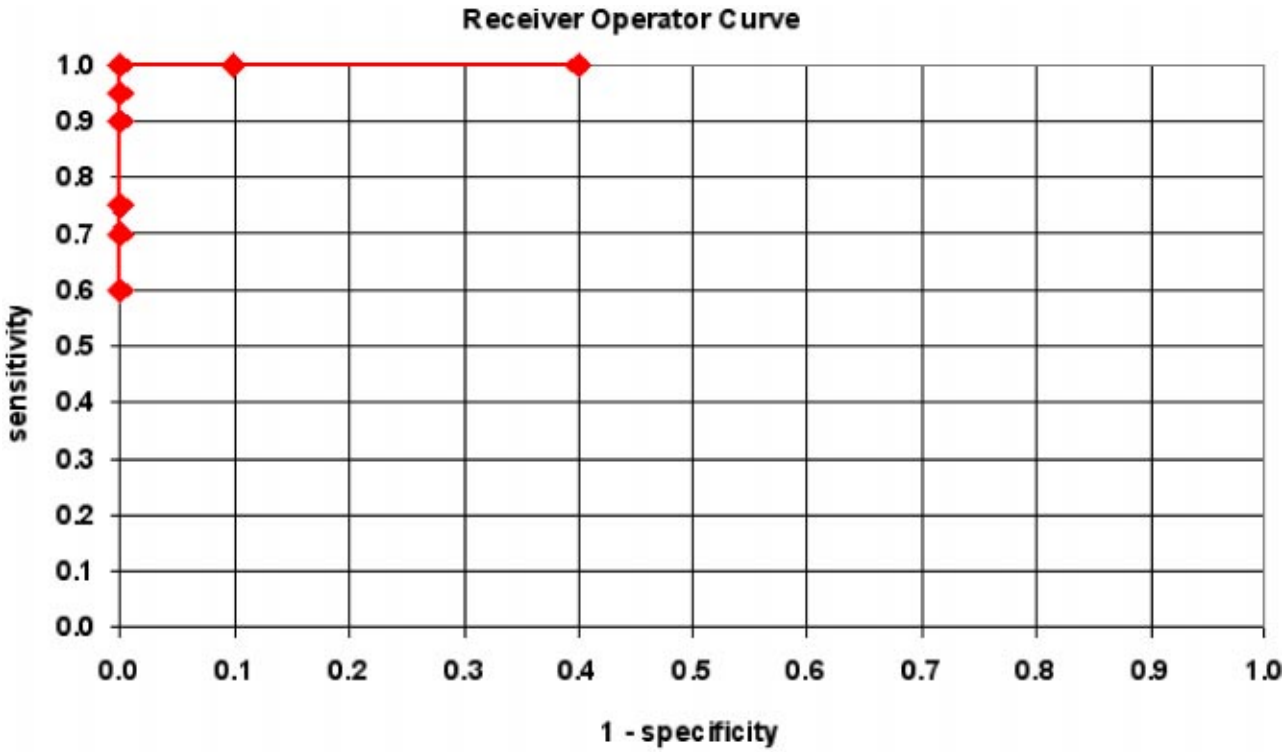

Fig. 4 Receiver-operator curve for the Pediatric Vision Screener. The diamonds indicate pass/refer thresholds of 10 to 90%. No false positives were generated at these values.

was obtained above a threshold of 2.6, as no subject with high residual distance refraction obtained a focus score >2.6. In contrast, a score of less than 2.6 did not identify focus versus defocus.

3 Discussion

Ophthalmologists continue to be frustrated by silent visual impairment from amblyopia, which remains a leading cause of vision loss in childhood despite a readily available and effective treatment. The principal reason for the persistence of amblyopia is the failure of health care systems to detect amblyopia risk factors in preverbal children. Specialist eye examinations of all children have effectively prevented amblyopia in Scandanavia,[3] but would be a costly and complex endeavor worldwide. Thus there is a need for an automated, inexpensive method of amblyopia detection that is rapid enough to screen large numbers of children and sufficiently sensitive to detect essentially all patients at risk, while avoiding large numbers of unnecessary referrals caused by false positive test results.

Good binocular alignment was appropriately detected in all control adults, while all adults with constant strabismus received a ''refer'' score. The Pediatric Vision Screener thus shows promise as a tool for detection of patients at risk for amblyopia. Patients with constant strabismus are at greatest risk for amblyopia and were most effectively detected. Pa-

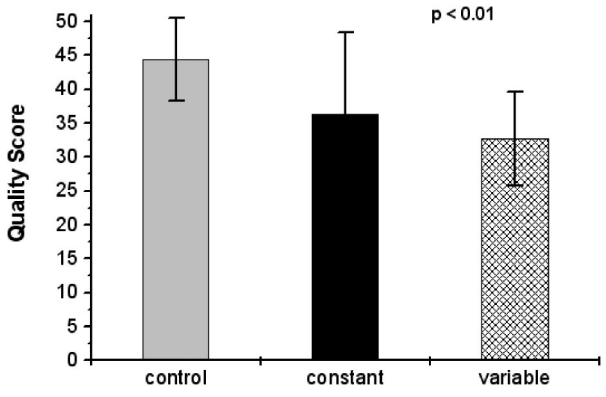

Fig. 5 Quality scores for controls, patients with constant strabismus, and patients with variable strabismus. Error bars represent one standard deviation.

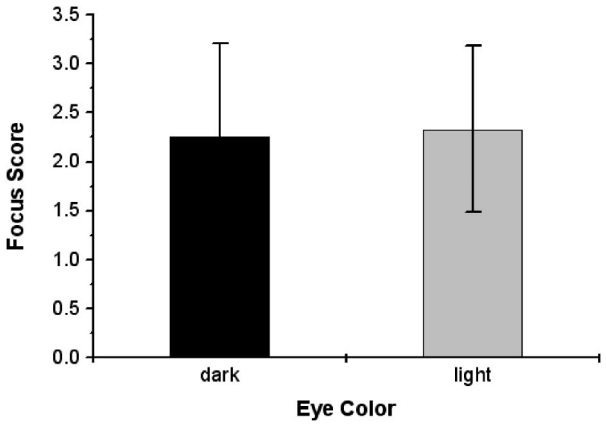

Fig. 6 Average focus score for light (blue, green, hazel, and gray) and dark (brown) eyes. Error bars are one standard deviation.

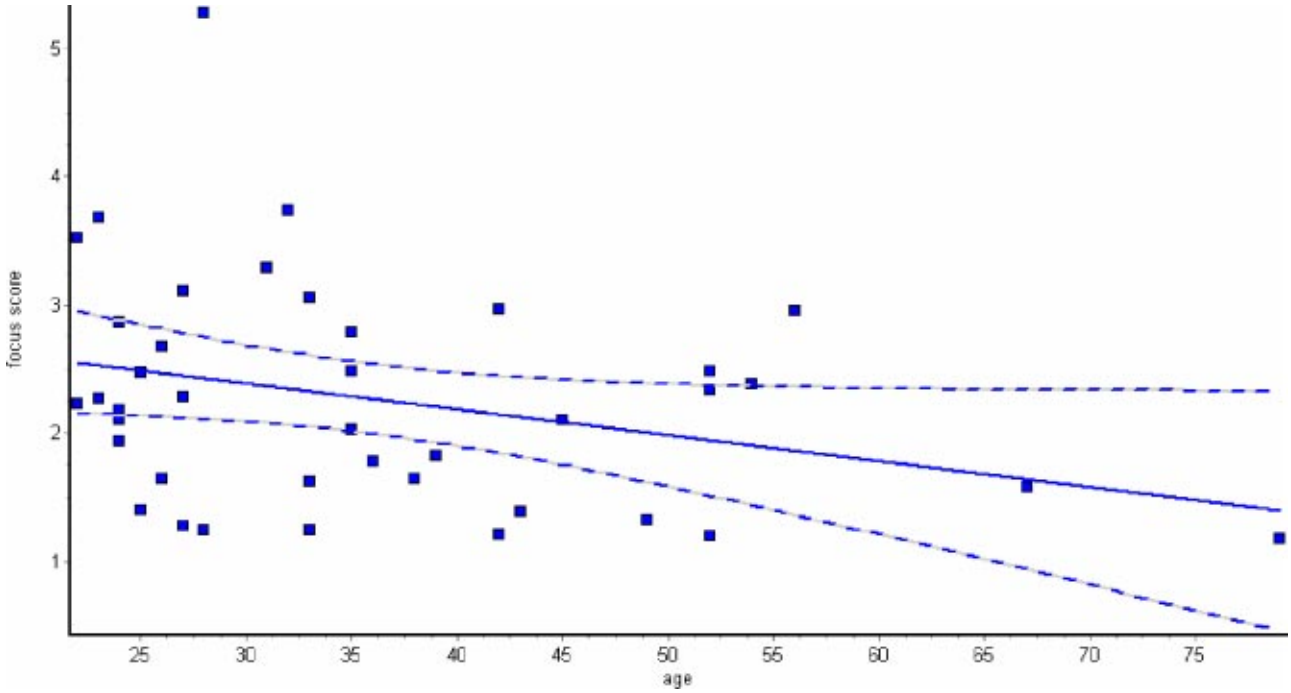

Fig. 7 Focus score versus age for 40 subjects. Solid line is a linear regression, while dashed lines represent 95% confidence levels.

tients with variable strabismus have binocular vision at least part of the time and are thus at lower risk for amblyopia, depending on the percentage of time the eyes are misaligned. One subject with variable strabismus did not receive a refer score at the 50% binocularity threshold. This was a 25-year-old woman with well-controlled intermittent exotropia, best corrected visual acuity of 20/20 in each eye, and high-grade stereopsis. She showed no evidence of having acquired amblyopia througout life. In a screening environment, a child with well-controlled intermittent exotropia and no anisometropia is at essentially no risk for amblyopia. Therefore a high binocularity score is appropriate in this subject. The

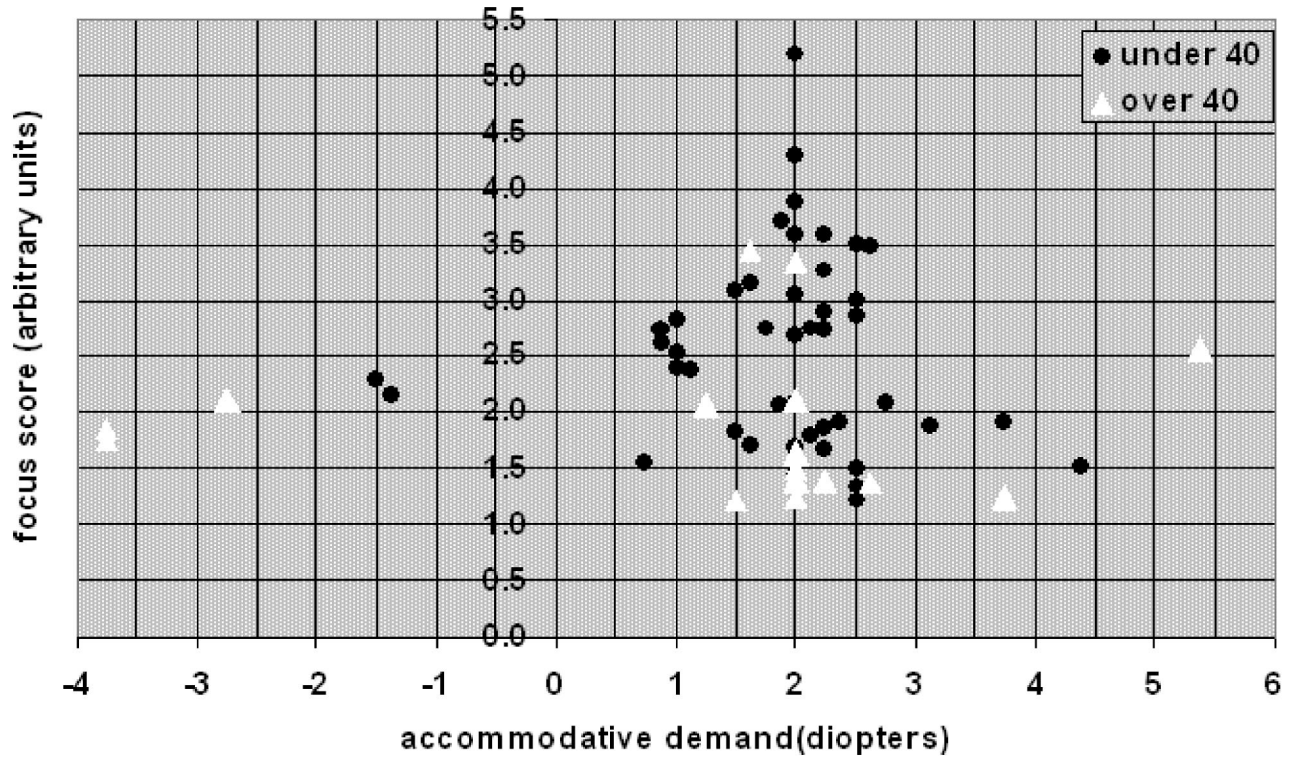

Fig. 8 Focus score versus accommodative demand, all eyes. Black circles represent subjects under age 40, white triangles are subjects over age 40.

short testing time of 2.5 sec will allow patients with mild intermittent tropias to pass, therefore avoiding unnecessary referrals.

In the present study, the smallest angle of strabismus tested was 8 prism diopters, which is larger than the 0.75 prism diopter theoretical threshold of BRBS.[9] Further study of a wider range of strabismus subjects using the present device is currently ongoing to validate the sensitivity of the device. Eye color had little influence on the BRBS scores. Although pigmented eyes show lower reflectivity in the IR, BRBS depends on a ratio of signals for accuracy. This ratio was preserved despite the lower signal strength.

Early in the study, five subjects were tested while wearing their eyeglasses. Although the antireflective coatings could have birefringent properties that might have influenced the results, the instrument was able to determine alignment appropriately. In a screening application, glasses would not be worn, and thus lens coatings would not affect measurements.

The focus detection system output was compared with inferred near focus, which was derived from the residual distance refraction. The underlying assumption was that subjects were capable of sufficient accommodation to bring the near target into focus. Presbyopic individuals, however, are not able to accommodate to a near target. While presbyopia may partially explain the large number of adults with apparently minimal residual distance refraction but low focus scores, this should have caused a more dramatic reduction in focus signal strength with increasing age (Fig. 7). In addition, the variability in focus scores was also present in subjects under age 40, who generally are not presbyopic (Fig. 8, circles). The use of a near-IR point source as the fixation target may have interfered with accommodation in presbyopic and nonpresbyopic subjects.[12] Some subjects reported that they were unable to determine whether the laser point-source target was sharply in focus, making it difficult for them to control accommodation.

Another confounding factor that may have lowered the apparent performance of the focus detection system is the longitudinal chromatic aberration of the eye, which placed the point of best focus at a different effective distance from the point of fixation. Some perceptive subjects noted that it was necessary to choose between accommodation (best point-source focus with some doubling of the faint BRBS ring) and convergence (single BRBS ring but blurred point source). The next prototype of the Pediatric Vision Screener, currently under development, will incorporate an extended target located at the most appropriate distance from the eye in an attempt to remedy this difficulty.

Ideally, to evaluate the strict optical performance of the focus detection system, residual distance refraction could be measured binocularly at 40 cm as the subject attempted to accommodate to, and converge on, a near-IR point source of light. Such measurements are difficult to obtain clinically. For the present study, it was decided that the most consistent measurement could be obtained at a distance, without use of cycloplegic agents. Future studies involving pediatric patients will likely determine focus scores in comparison with cycloplegic refraction, which provides the most consistent, objective measurement.

The focus detection system thus appeared to be sensitive for distance defocus at a relatively high threshold, but subthreshold measurements did not appear to be specific for poor focus. Despite these limitations, it is possible to conclude from the present study that there was no systematic, subject-dependent bias detected in the focus scores. The true utility of focus scores in detection of amblyopia risk factors will best be studied in a pediatric population, and these studies are currently ongoing in our laboratory.

Considering the 5% prevalence of amblyopia, there may be millions of children under age 5 worldwide who are suffering preventable vision loss due to the simple lack of detection. Yet amblyopia is rare enough that any attempt at mass screening for the condition will need to show exquisite sensitivity and specificity, and low per-subject cost, if it is to be economical to administer. A test for this condition must in particular be highly specific to avoid referrals of large numbers of unaffected subjects for comprehensive eye examinations. The PVS, with automated, remote detection of alignment (and in the future of focus as well) in a testing time of a few seconds, shows potential for such performance in preschool children. Additional testing in children will be required to determine whether the device can function as robustly with subjects who are less cooperative and less understanding than adults.

Acknowledgments

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References

1. J. Sjöstrand and M. Abrahamsson, ''Risk factors in amblyopia,'' *Eye* **4**, 787–793 (1990).
2. L. Köhler and G. Stigmar, ''Vision screening of four-year-old children,'' *Acta Paediatr. Scand.* **62**(1), 17–27 (1973).
3. G. Kvarnstrom, P. Jakobsson, and G. Lennerstrand, ''Visual screening of Swedish children: an ophthalmological evaluation,'' *Acta Ophthalmol. Scand.* **79**(3), 240–244 (2001).
4. K. Simons, ''Preschool vision screening: rationale, methodology and outcome,'' *Surv. Ophthalmol.* **41**(1), 3–30 (1996).
5. S. P. Donahue, T. M. Johnson, W. Ottar, and W. E. Scott, ''Sensitivity of photoscreening to detect high-magnitude amblyogenic factors,'' *J. AAPOS* **6**(2), 86–91 (2002).
6. R. A. Kennedy and D. E. Thomas, ''Evaluation of the iScreen digital screening system for amblyogenic factors,'' *Can. J. Ophthalmol.* **35**(5), 258–262 (2000).
7. K. S. Morgan and W. D. Johnson, ''Clinical evaluation of a commercial photorefractor,'' *Arch. Ophthalmol. (Chicago)* **105**(11), 1528–1531 (1987).
8. P. Y. Tong, R. E. Bassin, E. Enke-Miyazaki, J. P. Macke, J. M. Tielsch, D. R. Stager, G. R. Beauchamp, and M. M. Parks, ''Screening for amblyopia in preverbal children with photoscreening photographs: II. Sensitivity and specificity of the MTI photoscreener,'' *Ohio Nurses Rev.* **107**(9), 1623–1629 (2000).
9. D. G. Hunter, D. S. Nassif, N. V. Piskun, R. Winsor, B. I. Gramatikov, and D. L. Guyton, ''The pediatric vision screener 1: instrument design and operation,'' *J. Biomed. Opt.* (in this issue).
10. D. G. Hunter, A. S. Shah, S. Sau, D. S. Nassif, and D. L. Guyton, ''Automated detection of ocular alignment using binocular retinal birefringence scanning,'' *Appl. Opt.* **42**(16), 3047–3053 (2003).
11. D. G. Hunter, K. J. Nusz, N. K. Gandhi, I. H. Quraishi, B. I. Gramatikov, and D. L. Guyton, ''Automated detection of ocular focus,'' *J. Biomed. Opt.* (in this issue).
12. K. R. Aggarwala, S. Nowbotsing, and P. B. Kruger, ''Accommodation to monochromatic and white-light targets,'' *Invest. Ophthalmol.* **36**(13), 2695–2705 (1995).