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Two-dimensional simulation of eccentric photorefractive images for ametropes: factors influencing the measurement

Yifei Wu, Larry N Thibos, and T Rowan Candy

School of Optometry, Indiana University, Bloomington, Indiana, USA

Abstract

Purpose—Eccentric photorefractive and Purkinje image tracking are used to estimate refractive state and eye position simultaneously. Beyond vision screening, they provide insight into typical and atypical visual development. Systematic analysis of the effect of refractive error and spectacles on photorefractive data is needed to gauge the accuracy and precision of the technique.

Methods—Simulation of two-dimensional, double-pass eccentric photorefractive was performed (Zemax). The inward pass included appropriate light sources, lenses and a single surface pupil plane eye model to create an extended retinal image that served as the source for the outward pass. Refractive state, as computed from the luminance gradient in the image of the pupil captured by the model's camera, was evaluated for a range of refractive errors (−15D to +15D), pupil sizes (3mm to 7mm) and two sets of higher-order monochromatic aberrations. Instrument calibration was simulated using −8D to +8D trial lenses at the spectacle plane for: i) vertex distances from 3mm to 23mm, ii) uncorrected and corrected hyperopic refractive errors of +4D and +7D, and iii) uncorrected and corrected astigmatism of 4D at four different axes. Empirical calibration of a commercial photorefractor was also compared with a wavefront aberrometer for human eyes.

Results—The pupil luminance gradient varied linearly with refractive state for defocus less than approximately 4D (5mm pupil). For larger errors, the gradient magnitude saturated and then reduced, leading to under-estimation of refractive state. Additional inaccuracy (up to 1D for 8D of defocus) resulted from spectacle magnification in the pupil image, which would reduce precision in situations where vertex distance is variable. The empirical calibration revealed a constant offset between the two clinical instruments.

Conclusions—Computational modelling demonstrates the principles and limitations of photorefractive to help users avoid potential measurement errors. Factors that could cause clinically significant errors in photorefractive estimates include high refractive error, vertex distance and magnification effects of a spectacle lens, increased higher-order monochromatic aberrations, and changes in primary spherical aberration with accommodation. The impact of these errors increases with increasing defocus.

Keywords

eccentric photorefractive; photorefractor; vision screening; ray tracing model

Corresponding author: Yifei Wu, wuyif@indiana.edu.

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Introduction

Accurate and precise measurements of refractive state and binocular eye alignment from infants and young children are essential for understanding visual development.^{e.g.1,2} The PowerRefractor (PR, MultiChannel Systems) and its later versions (PowerRef II and PowerRef 3, <https://plusoptix.com>) are examples of commercially available instruments that simultaneously apply the eccentric photorefraction technique to measure refractive state and Purkinje image eye tracking to measure eye alignment.^{1,3,4} These instruments function quickly from a remote working distance of one metre while tolerating some subject head movement, features which are helpful in working with young children. Simultaneous assessment of both eyes also aids in the detection of anisometropia and strabismus when compared with other monocular techniques.⁵

The principle of eccentric photorefraction is based on an analysis of light that has entered the eye and then been reflected from the retina. The reflected light is captured by a camera focussed on the eye's entrance pupil to determine the spatial gradient of luminance in the pupil plane.^{3,6-10} Conversion of the slope of this light intensity profile across the pupil to a dioptric refractive state is based on a group calibration performed on adults.^{3,5} Individual estimates of spherical equivalent refractive state using this technique have been reported to agree with other techniques to within limits of agreement of -1.9D to 1.7D (autorefractors and retinoscopy), with or without cycloplegia, in both young children and adults.¹¹⁻¹³

A number of factors impact the absolute and relative calibration of eccentric photorefraction.^{3,7-9,13-16} Geometric ray tracing along one meridian has demonstrated that the distance of the camera, camera aperture diameter, pupil size, ocular aberrations and light source design (single versus extended source and eccentricity) all affect the conversion factor from light distribution in the pupil to amount of defocus.⁶⁻⁸ Additional considerations when working with clinical patients include the influence of spectacle lenses which alter the apparent size of the eye's pupil by an amount that varies with lens power and vertex distance.

Variability in the empirical calibration of individual subjects has been examined by Bharadwaj *et al.*¹⁴ Those data, gathered using trial lenses, suggested that the combined intersubject and intrasubject variability of the light intensity to refractive state conversion factor can be around $\pm 40\%$ of the mean value. This variability could be due to a number of factors related to the photorefraction technique, the method of calibration and the characteristics of the subject. While there are numerous important advantages of eccentric photorefraction as a vision-screening tool, a deeper understanding of the source of errors in the measurements is required to interpret these data.

The purpose of this study was to simulate the pupil images captured by a photorefractor camera in order to systematically quantify the impact of optical factors on measurements of refractive state. Of particular concern are those factors present when measuring the refractive state of young clinical patients wearing spectacle lenses. These factors included the higher-order aberrations of the young eye,^{7,8,17} changes in primary spherical aberration with accommodation,¹⁸⁻²² corrected and uncorrected defocus and astigmatism,^{23,24} and the

effects of lens magnification and vertex distance. Modelling results are interpreted with reference to empirical calibration data collected from a large group of study participants.

Methods

Elements of the optical model

The eye functions as a dual-pass optical system in eccentric photorefractive. For the purposes of this analysis, the inward (light passing into the eye) and outward (reflected light from the retina) optical paths were simulated separately using sequential ray tracing (OpticStudio, <https://www.zemax.com>). The inward path consisted of: an object plane containing the eccentric light source (LEDs) next to the camera aperture, a one metre working distance to the eye, any lenses as required, the pupil aperture, a Zernike phase plate in the pupil plane to represent the eye's optical system, and a 22.27 mm axial length²⁵ from the pupil plane to the retina through a refractive index of 1.337 (Figure 1, Panels A & C). The outward path included the same elements in the reverse order, with the light passing through the camera aperture to form a focussed image of the pupil plane (Figure 1, Panels B & D). A number of configurations were simulated in both the inward and outward paths, to understand changes in refractive state and higher-order monochromatic aberrations of the eye. Test cases using a more complicated eye model constructed with multiple surfaces (anterior and posterior cornea, anterior and posterior lens)²⁶ did not change the findings qualitatively and so are not reported here.

The source object for the inward path of light in the model had the same dimensions as the LEDs of the commercial photorefractor (Figure 2, Panels A & B, where each white circle represents a single LED). Each individual LED was 5mm in diameter with a 1mm space (border to border) between them in both the horizontal and vertical directions. The image of the LEDs at the retinal plane was then saved for inspection and for use as the source object for the outward path (Figure 2, Panel C). The source characteristic was set as 'uniform' for the inward path of light from the LEDs and 'Lambertian' for the outward path from the retina.

Analysis of simulated pupil images

The pupil image simulations generated by the outward path model were analysed using MATLAB (<https://www.mathworks.com/>). To reduce measurement noise and replicate the approach taken in commercial instruments, the intensities were averaged over a rectangle of width 20 pixels (approximately 16% of the diameter of a 5mm diameter pupil) and height equal to the central 80% of the pupil diameter (Figure 2, Panel E).^{3,5} The mean pixel intensity of each row was then plotted as a function of its distance from the top of the rectangle (Figure 2, Panel F) and the slope of the relationship was determined using ordinary least squares (OLS) regression.

Factors studied

A series of simulations was performed to study the impact of a number of factors on eccentric photorefractive measurements. These factors were modelled as a function of: 1)

defocus of the eye at the pupil plane, 2) the lens power at the spectacle plane, and 3) both together. These three manipulations occur frequently in clinic and research environments.

In the baseline condition used to study the effect of pupil size and refractive error, paraxial defocus was inserted at the pupil plane with effective spectacle plane powers at a 13mm vertex distance of -15D to $+15\text{D}$, to mimic a clinical refraction. This simulation was performed with physical pupil aperture diameters of 3, 5 and 7mm. In addition to defocus, Zernike aberrations were then added in the pupil plane to simulate the typical effect of higher order aberrations of different age groups and changes in spherical aberration with ocular accommodation.¹⁸ A typical set of aberration measurements (2nd to 4th order) from a median participant from two age groups was identified: one pre-presbyopic adult²⁷ and one young infant aged 5–7 weeks¹⁷. A reduced axial length of 14.85mm was used for the infant schematic eye,²⁸ with the refractive index of the media remaining the same as for the adult. Pupil intensity gradients were determined as a function of change in the defocus coefficient (Z_2^0) in the pupil plane, with all the Zernike coefficients scaled for pupil diameters of 3 and 5mm.

Instruments that apply the eccentric photorefractive principle can be calibrated using trial lenses in the spectacle plane to introduce known defocus into the combined eye and lens system.²⁹ However, the lens alters the apparent size of the eye's entrance pupil as seen by the PR's camera, which alters the slope of the luminance gradient thereby producing an error in measured refractive state. The magnitude of this spectacle magnification error was determined for a range of spherical trial lenses (-8D to $+8\text{D}$ power) placed at different vertex distances (3, 13 & 23mm) from the pupil plane of the simulated eye, with a typical adult's aberrations.³⁰ This set of simulations is typical of empirical data collection when trial lenses are used to calibrate the instrument, introduce accommodative demands or correct refractive error, for example. The characteristics of the simulated lenses were based on measurements of real trial lenses. The material was N-BK7 with a refractive index of 1.52. Minor adjustments of the curvature were made to ensure correct lens power in the model.

To study the impact of lenses used to correct spherical and astigmatic refractive errors of the eye, ocular ametropia was introduced in the pupil plane and then corrected with another lens placed in the spectacle plane at 13mm vertex distance from the pupil plane. Retinal image size in corrected ametropia is different from that in emmetropic eyes and, therefore, additional simulations were generated to determine the impact of retinal image size on refractive state measurements using the outward path only. Two focussed retinal images of different sizes were used, equivalent to an uncorrected eye focussed at the camera plane and a corrected $+7\text{D}$ hyperopic eye focused at the camera plane. In the outward path, refractive state was changed at the pupil plane and the 13mm vertex distance spectacle plane in both cases.

The empirical data collection

Empirical calibrations were collected from 226 participants who took part in a number of studies between August 2011 and August 2015. The participants were aged from 1 month to 45 years (median 6.38 yrs, 0.25 quantile 3.04 yrs, 0.75 quantile 23.11 yrs) These data were collected using a consistent protocol.²⁹ Briefly, trial lenses of $+1$, $+2$, $+3$, $+4$ and -2D power

were held over the right eye while the participant viewed a cartoon movie at a distance of 33cm, 50cm or 95cm (example data are presented in Figure 3, Panel A). The induced anisometropia measured by the PowerRefractor was then plotted as a function of trial lens power and the slope of the linear function, the calibration factor, was determined (Figure 3, Panel B). The data collection was repeated for 76 subjects within 30 days of their initial visit.

Empirical measurements from three uncorrected presbyopic subjects were also taken with a PowerRefractor (PowerRef 3, <https://plusoptix.com>) and a wavefront aberrometer (COAS, <http://www.wavefrontsciences.com/>). The complete ophthalmic analysis software (COAS) refraction was calculated for their pupil diameter (4 – 5mm) using 2nd order Zernike aberrations with compensation for longitudinal chromatic aberration, along the same meridian as the PowerRef 3. Subjects fixated the PR camera's light source binocularly at 1m. Measurements of the right eye were taken sequentially with the two instruments viewing through a series of trial lenses placed in the spectacle plane (-4D to +6D in 1 D steps at a 13mm vertex distance). Additional data were collected with the PowerRefractor over an extended range of trial lenses from -13D to +13D to understand the consequences of measuring eyes with refractive error significantly beyond the manufacturer's suggested operating range (-7D to +5D).

Results

Calibration variability for a population of human eyes

Our development of a photorefractive simulation was motivated by the variability in empirical calibrations across subjects displayed in Figure 4. Calibration factors relative to the PowerRefractor's default value of 1 were computed for seven logarithmically spaced age groups. A one-way analysis of variance (ANOVA) revealed a significant effect of age on calibration factor ($F_{6,424} = 8.19$, $p < 0.0001$), with an increase in mean factor occurring over the first 2 postnatal years. One-sample t-tests were used to compare each group's distribution with the instrument's default (equivalent to a value of 1) and significant differences were found in age groups < 6 months ($t_{24} = 4.5$, $p = 0.0001$), 6 months to 1 year ($t_{25} = 5.83$, $p < 0.0001$), 1 to 2 years ($t_{32} = 4.92$, $p < 0.0001$) and 16 to 46 years ($t_{167} = 2.16$, $p = 0.03$). The simulation results presented below reveal numerous factors that may have contributed to the relatively large inter-subject variance evident in Figure 4.

The impact of variation in pupil size and of higher-order aberrations

The impact of pupil diameter on simulated estimations of refractive state is presented in Figure 5. In panels A-C, the slope of the OLS regression fit to the pixel intensity across the pupil is plotted as a function of effective spectacle lens power at a 13mm vertex distance (implemented as paraxial defocus in the pupil plane). Panel A, which includes only defocus (i.e. no higher-order aberrations), demonstrates that calibration curves are non-monotonic functions; pupil image slope is proportional to refractive error over a limited dioptric range before regressing back towards zero slope. Moreover, the rate of change in slope with dioptric refractive error, which is the critical value for instrument calibration, increases as pupil size increases.

These effects of pupil size on the relationship between intensity gradient (y-axis) and refractive error (x-axis), reported previously by Roorda, Campbell & Bobier⁸ using one-dimensional geometric ray tracing, and by Schaeffel, Hagel, Eikermann & Collett³¹ using an artificial eye, have a major impact on instrument calibration for two reasons. Firstly, only the linear portion of the curve on either side of 0D is useful for making unambiguous estimates of refractive state (x-axis) from measurements of intensity gradient (y-axis). For example, an empirically measured slope value of -0.09 intensity units/mm for a 5mm pupil could result from a refractive error of -11 D but be mistakenly interpreted as -4 D (compare the left two vertical arrows in Figure 5, Panel A). The useful range of linear behaviour decreases as pupil size increases, and so the measurable range of refractive errors is more restricted when pupils are large. Secondly, because the calibration curves depend on pupil size, the same example measurement of -0.09 could be interpreted as -2 D refractive state for a pupil diameter of 7mm (compare the right two vertical arrows in Figure 5, Panel A). These pupil size effects are expected because the amount of light entering the eye, and therefore the amount of light reflected from the retina, is proportional to pupil area. Thus the measured intensity slope observed in the pupil plane is, to first approximation, proportional to pupil area. As a result of these effects, manufacturers of these instruments provide limits to the refractive errors that can be detected, and must implement a correction for pupil size in their software.

To compensate for the undesirable effects of pupil area on instrument calibration shown in Figure 5 panels A, B, C, we make use of the fact that, in principle, the measured intensity slope observed in the pupil plane should be proportional to pupil area. Since pupil area can be measured with the photorefractor, a simple and practical compensation procedure is to multiply measured slopes by the ratio of a standard pupil area to the actual pupil area before inferring refractive state. For demonstration purposes, we chose a 5mm pupil diameter and included the typical adult's higher-order aberrations to obtain a standard calibration curve (dark blue curves in Figure 5, Panel B&C). Only the linear portion of the standard calibration (-6 D to 7 D on the x-axis) was fitted with a spline function to include minor features in the function. The inverse of the spline function was then used to estimate refractive state from the corrected values of pupil intensity gradients obtained from the model. The results of this correction procedure applied to the data in Figure 5 panels A, B, C are shown in panels D, E, F, respectively. The abscissa in these panels D-F is the known refractive error introduced into the model, and the ordinate is the difference between the measured refractive state and this known refractive error. Before applying the correction procedure, large errors are evident for pupil sizes smaller or larger than the standard (see connected symbols). The magnitude of these errors is clinically significant: pupil diameter shifts from 3 to 7mm could cause a ± 2 D error in estimating refractive state when using the measured slopes. After the correction procedure is applied (see unconnected symbols), measurement errors are greatly reduced to less than 1D for small and moderate refractive errors. These results confirm that most of the measurement error in the uncorrected case was due to the simple fact that pupil size controls the amount of light entering the eye, and pupil intensity gradients are proportional to the amount of light reflected from the retina.

The presence of ocular higher-order aberrations also affects instrument calibration as shown in panels B and C of Figure 5.⁸ The impact was equivalent to approximately 1D of defocus

at $\pm 4D$ of refractive error, after compensation for differences in pupil area, if the instrument was calibrated for adult eyes and was being used to collect data from an infant (Figure 5, Panels C & F).

Variation in spherical aberration with accommodation

Eccentric photorefractometer instruments have been used to collect data from subjects viewing targets at a range of accommodative demands^{15,32} or with a range of uncorrected hyperopic refractive errors.³³ Because spherical aberration (SA) varies significantly and systematically with accommodation,^{e.g.18} the associated variation in SA is a potential source of error in accommodative response estimates. The Zernike representation of SA includes a defocus component to compensate for the small amount of equivalent spherical defocus present in the Seidel representation of spherical aberration. The simulations were, therefore, performed for aberrations in both Zernike and Seidel form, as the Seidel version incorporates all of the aberration's impact without using defocus compensation.³⁴ Approximately 0.05 microns of Seidel SA change has been measured for an adult accommodation response of 4D with a fixed 4 mm diameter pupil.^{18–22} This is equivalent to Zernike SA of ± 0.005 microns for a 5mm diameter pupil, with ± 0.019 microns of spherical defocus added to unbalance the term and generate the Seidel form. This amount of SA did not induce significant changes in the simulated refractive error estimates, in either Zernike or Seidel format. A larger range of ± 0.7 microns Zernike SA for a 7mm diameter pupil (± 0.18 microns for a 5mm diameter pupil) has been observed in an adult population including LASIK patients.^{35–37} This amount was introduced into a simulation in Seidel format by adding ± 0.71 microns of Zernike defocus coefficient to unbalance the Zernike SA for a 5mm pupil. The Seidel SA shifted the calibration function in the predicted directions for both positive and negative spherical aberration (Figure 6), based on a similar effect in the one-dimensional simulation of Roorda, Campbell & Bobier.⁸ This amount of bias would not be expected when collecting data from most eyes, however, as the extreme values of the higher-order aberrations were mostly likely from post-LASIK subjects.

Spectacle magnification of the pupil image

Introduction of a spectacle lens before the eye will, of course, affect the refractive state of the eye plus lens system measured by the photorefractor. In addition, spectacle lenses influence the apparent size of the eye's pupil image. This spectacle magnification will affect the intensity gradient measured by the photorefractor and is thus another potential source of error when measuring refractive state. Both of these confounding factors (effectivity & magnification) depend on lens power and vertex distance, which are examined in Figure 7. The effect of spectacle magnification on pupil intensity gradients is illustrated in Panel A for two values of vertex distance (0 and 23mm). The abscissa in Figure 7 panels A & B is spectacle lens power. The effective power at the pupil plane of a series of lenses at different vertex distances was also calculated and introduced into the simulation as power in the pupil plane (e.g. $-5.27D$ is the effective power in the pupil plane of a $-6D$ lens at 23mm vd). This adjustment in the pupil plane model for effective power does not recreate the full effect of trial lenses at different vertex distances (Figure 7, Panel A, red versus purple compared to red versus yellow). In theory, the minification effect of minus lenses will make the slopes across the pupil appear steeper and the magnification effects of plus lenses will make the

slopes shallower (equivalent to contracting or expanding the x-axis in Figure 2, Panel F). Including both effective power and magnification effects in the simulation (green) explains the majority of the difference between the lenses at the pupil plane (red) and at the spectacle plane (yellow). For the vertex distance that was simulated, the results indicate that within a moderate range of defocus introduced with lenses ($\sim \pm 4D$), the magnification effect is only up to 1D but this effect increases with higher powers (see also Figure 7, Panel B). These data highlight the importance of considering results relative to one consistent plane and carefully controlling vertex distance when a high power lens is introduced in front of an eye.

Changes in retinal image size

In addition to the pupil magnification effects of spectacle lenses described above, the lenses introduced at different vertex distances in Figure 7 also change the size of the retinal image that becomes the secondary source of light reflected out of the eye. These twin effects present for the inward pass (retinal magnification) and outward pass (pupil magnification) are coupled during photorefractive. In our simulation, however, we have the option of including a corrective spectacle lens in only the inward pass to isolate the contribution of retinal image magnification to measurement error. The results are shown in Figure 8. The '1x retinal image' conditions are outward pass simulations using the focused retinal image of an uncorrected eye focused at the plane of the camera/ LEDs. The 'enlarged retinal image' conditions use the inward pass of a corrected 7D hyperopic eye also focused at the LEDs to create an enlarged retinal image as the source for the outward pass examination. The outward pass refractive errors were implemented in the pupil plane with no lenses or with lenses at a 13mm vertex distance. The enlarged retinal image size resulted in underestimation of refractive state of up to 2D for simulated refractive errors of $-4D$ to $+4D$, as a result of the relative stretching of the retinal image and hence reduction in slope of the reflected light distribution.

In addition to simple myopia and hyperopia, clinical patients could also have uncorrected or corrected astigmatism. Toroidal lenses used to correct astigmatism have a larger magnification along one meridian and therefore they result in a pupil image with an oval shape. Simulations of the impact of astigmatism are shown in Figure 9. For example, in Panel A, '-4D cyl $\times$ 0' represents a lens used to correct astigmatic power with axis 0, at a vertex distance of 13mm. The astigmatic power was simulated using a toroidal lens of +3.80D (thickness = 0) at an axis of 0 deg in the pupil plane, with a vertical power meridian. If data are gathered for only one orientation of LEDs, clinicians and researchers need to be aware that a significant amount of uncorrected astigmatism could affect refraction estimates by more than 1D even when the astigmatic power is along the orthogonal meridian (green versus orange functions in Figure 9). Sampling from multiple meridians is also needed to estimate the full spherical and cylindrical components in combination.²⁴

PowerRef 3 and COAS comparison

Potential sources of measurement error described above were characterised in absolute terms, as the optical system modelled in Zemax was completely defined. In empirical studies, however, knowledge of the optical parameters of individual human eyes and

adjustments made in proprietary software is incomplete, so absolute errors of measurement are difficult to assess. To overcome this problem, we attempted an assessment of the absolute accuracy of a commercial photorefractor (PowerRef 3, <https://plusoptix.com>) by comparing measurements of refractive state with those obtained with a COAS wavefront aberrometer serving as our “gold standard”. Figure 10 presents two sets of measurements collected from each of three quasi-emmetropic, presbyopic subjects. In each set of measurements, the 1st and 2nd PowerRef 3 refraction estimates were the median of 2 seconds of data taken at nonoverlapping times during a 10s measurement, while the COAS estimates were derived from the combination of up to the 6th order Zernike values. Overall, the PowerRefractor estimates were 0.4 to 1D more hyperopic than the COAS measurements, when subjects fixated the 1m target just below the camera aperture. This offset is likely due to an internal offset built into the photorefractor to generate a distance refraction for subjects fixating a near target on the instrument. A previous PowerRefractor model (Multichannel Systems) was found to estimate 0 to 1D more hyperopia than retinoscopy in two other studies.^{13,15} This was the manufacturer’s empirically developed strategy to estimate distance refractive error accurately when the subject viewed the light source during a vision screening. This same offset was observed for six other adults tested with the PowerRef3 and retinoscopy as part of the current study.

Additional measurements of refractive state when trial lenses were held over the right eye while the subjects fixated with their left eye are presented in Figure 11 (the left eye’s refractive state was confirmed to be constant). The differences between the COAS and PowerRefractor measurements across subjects, particularly with trial lenses of higher power, stress the importance of individual PowerRefractor calibration if highly accurate estimates are required. For example, in the left lower subplot from subject 3, the estimated myopic refractive state would have a 1D error if the instrument’s built-in calibration factor was applied to this subject. These PowerRefractor estimates were approximately linearly related when the induced refractive state changes were within the manufacturer’s suggested operating range (-7D to +5D). The non-monotonic trend in pupil image slope, for refractive errors outside this range, can be seen in the simulation results in Figure 5, while Figure 12 demonstrates the same trend in empirical data collected from the presbyopic subjects when refractive error was induced using lenses at the spectacle plane.

Discussion

Although photorefraction is widely used for objective measurement of ocular refractive state, reports in the literature of large variability in instrument calibration between eyes and within the same eye require careful consideration. To improve our understanding of the sources of photorefraction errors that might account for this variability, we modelled an optical system comprised of an eye plus a photorefractor instrument. Our goal was to systematically quantify the impact of pupil size, magnitude of refractive error, astigmatism and higher-order aberrations, spectacle lens power and vertex distance, spectacle magnification, and retinal image size magnification on measurements of refractive state. The effect of these factors on measurement error was partially mitigated by compensating for differences in pupil size that exist between the calibration procedure and actual data

collection. In addition, limiting use to the monotonic portion of the calibration curve is essential for avoiding large measurement errors.

Comparisons with previous studies

The stated linear operating range of the original MCS PowerRefractor photorefraction system was -6D to $+4\text{D}$ ⁵ and the latest Plusoptix version states a slightly wider range of -7D to $+5\text{D}$ according to the manufacturer's instruction manual. Previous studies have discussed the issue of eccentric photorefraction underestimating ametropic power higher than $\pm 4\text{D}$ ^{6,10} and a screening study found the estimated refractive state of some subjects starting to depart at around $+2$ to $+3\text{D}$.³⁸ Care must, therefore, be taken to ensure that an instrument being used for screening does not miss high refractive errors (as demonstrated in the non-monotonic functions in Figure 5 and Figure 12). This effect might explain the false-negative results in detecting hyperopia in cycloplegic eyes, for example estimating $+6.25\text{D}/-1.75\text{D} \times 180$ as $+2.75\text{D}/-0.50\text{D} \times 69$.³³ The manufacturers of instruments that employ the eccentric photorefraction principle must address these effects in developing their instrumentation and software and the user must make themselves aware of them.

The empirical calibration factor data (Figure 4) demonstrate variations in relative calibration factor, over the instrument's linear operating range, of from 0.5 to 1.5. Which factors could contribute to the variability in calibration factors seen within and between participants? Schaeffel, Mathis & Bruggemann¹ suggested the operating range of the PowerRefractor is related to pupil diameter: -7D to $+5\text{D}$ for a 4mm pupil and -4D to $+3\text{D}$ for a 7mm pupil. The simulation results in Figure 3 are consistent with these recommendations and demonstrate the compensation that manufacturers need to achieve for the effect of pupil size. While cycloplegia relaxes accommodation to reveal the full refractive error, a number of studies have suggested that it did not help make screening more efficient.^{11,33,39–41} The balance between preventing accommodation to reveal full refractive error and maintaining sensitivity of the instrument in the presence of large pupils needs to be considered carefully in developing these screening approaches.

The simulations of typical higher-order aberrations of two age groups did not affect the refractive error estimates significantly (Figure 5), although they did introduce a 1D shift in the defocus estimate at the edges of the range of -6D to $+4\text{D}$. While eccentric photorefraction instruments have been calibrated at intermediate to far distances,^{5,13} clinicians need to be aware of potential changes in SA with accommodation when a fixation target is placed at near.¹⁹ The current simulations did not predict significant effects of higher-order aberrations in a normal population at a moderate accommodative demand.

The simulations with -8D to $+8\text{D}$ trial lenses at three vertex distances (Figure 7) suggest that both their effective power at the pupil plane and magnification effects impact the refractive error estimates.⁴² For example, moving a $+7\text{D}$ lens between the spectacle plane (e.g. 13mm vertex distance) and the pupil plane could cause up to a 10% difference in the estimate. Some studies have used spectacle lenses when testing patients with large amounts of ametropia.^{43,44} These spectacles can bring the retinal defocus back into the linear operating range of the eccentric photorefractor, but they will also introduce magnification or minification of the pupil image depending on the lens power and vertex distance (Figure 7).

The simulations using retinal images of two different sizes and the outward pass only (Figure 8) suggest that lenses could affect the refractive state estimation by up to 2D. For example, high powered positive spectacles to correct hyperopia will magnify the retinal image of the LED array, making the calibration function shallower, and therefore, underestimate refractive state with moderate changes in accommodation (Figure 8, 'enlarged retinal image' vs '1x retinal image').

While the simulations performed here addressed a number of important clinical factors, the model has limitations in not including additional factors that may affect the calibration of photorefractometry: for example, any difference in the position of the retinal layers that reflect the near infrared light compared with the photoreceptors initiating the visual response,^{45–47} the Stiles-Crawford effect (the directionality of photoreceptors will diminish light emerging through the edges of the pupil),⁷ the pigmentation and reflectance of the retina for different ages and races,^{e.g.9,14,48} and nonlinearities in the camera's imaging process. For example, increased reflectance of the retina would have a multiplicative effect on the pupil intensity gradient and therefore impact the refractive error estimate if not compensated. The simulations, therefore, do not provide specific adjustments to refractive error estimates to be applied, but are instead providing insight into the variation in the calibration function. The model also did not incorporate factors related to subjects' responses to different visual stimuli in the absence of cycloplegia.^{5,41,49} The best type of target to relax accommodation and reveal the refractive error closest to the cycloplegic refraction was not addressed here. When thinking about clinical application, these instruments are also designed to use Purkinje image eye tracking to document eye alignment. While this is an important benefit when screening for strabismus, it must be remembered that the photorefractometry data will be collected from off-axis eccentric gaze in cases of significant strabismus. In that case coma and astigmatism are likely to be more significant, and therefore affect the estimate of refractive error.^{50–52}

Users of these instruments need to be aware of these factors and to try to maintain a consistent approach to the measurements, for example, by using stable room lighting, consistent target distances, small vertex distances and minimal lens tilt. For the measurements taken in the current study from corrected high hyperopes, the corrections were kept at their habitual vertex distance and pantoscopic tilt, with trial lenses for calibration placed immediately in front of the spectacles. Almost all measurements were taken by two individuals: one placing the lenses, and the other adjusting the head and spectacle position slightly. The interpretation of data collected using eccentric photorefractometry then depends importantly on whether group means/medians or data from individual participants are required and then whether the data have been calibrated for individuals. Individual calibration using lenses may not be practical or essential in vision screening if there is going to be a referral for those that fail a reasonable criterion. An additional screening through lenses (e.g. +5D) should be considered to avoid underestimating high refractive error that falls outside the linear operating range of the technique (Figure 5, panel A). For researchers or clinicians considering performing individual calibrations, the approach should be consistent for calibration and formal measurement. Based on the simulations conducted here and by others, one can be relatively confident when refractive state is close to emmetropia at least, although anyone wanting to

assess focus accurately in space needs to be aware of any offset in the software in commercial photorefractors (Figure 11).^{13,15} When the underlying refractive error or trial lens is of higher power there are numerous factors that affect the estimate and, for refractive states beyond the linear operating range, eccentric photorefraction is likely to include significant error in its estimate. Calibration functions obtained in one set of conditions but applied in a different set may cause significant bias in the refractive state estimates, particularly for larger amounts of defocus. Overall, the technique is valuable, however, because it takes fast, remote measurements of both eyes simultaneously and can be combined with Purkinje image tracking to assess eye alignment. Manufacturers of these instruments will address some of this variability in their software, but the user of the instrument needs to be careful to understand the capabilities and limitations of the instrument they are using.

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Figure 1.

Illustration of the inward (Panel A) and outward (Panel B) paths when the eye is focused at the camera aperture plane. Under this condition, the theoretical pupil image captured by the camera would be black as the light all returns to the light source with no light entering the camera. Panels C & D simulate an eye focused in front of the camera plane. In this case some of the light exiting the pupil is captured by the camera, therefore the lower part of the pupil image appears brighter than the upper part. In the case of an extended light source consisting of multiple LEDs, these distributions of light will be combined at each location in the pupil, creating an intensity gradient.

Figure 2.

A) The PowerRefractor LED light source. Only one portion of the array of LEDs (the area enclosed by the red triangle) is used to obtain an eccentric photorefraction measurement for each meridian (vertical in all cases here); B) The LED array used in the model for the inward path of the simulation; C) The simulated retinal image formed by the inward path, which is used as the source object in the outward path (3D myopic eye with 5mm pupil diameter); D) An empirical PR image of myopic eyes; E) A simulated pupil image of a 5D myopic eye with a 5mm pupil diameter. The yellow rectangle shows the area used to estimate refractive state. The granular appearance is due to a finite number of rays traced in

the simulation; F) Average relative pixel intensity (blue function) as a function of height in the yellow rectangle in panel E, (green functions represent 95% limits of the distributions across each row). The red line presents an ordinary least squares (OLS) regression fit to the pixel intensity data, representing the relationship between pupil position and average intensity. The slope of this line is used to estimate refractive state.

Figure 3.

A) The measured refractive state of the two eyes of a participant while lenses of different powers were held over the right eye (smoothed over a 0.5s window). B) Induced anisometropia measurements as a function of trial lens power. The slope of the linear regression provides the relative difference in calibration factor between the instrument's value (equivalent to slope = 1) and the calibration for the tested participant (fitted slope value = 0.80, $r^2 = 0.99$).

Figure 4.
Box plots (median and interquartile range) of the empirical PowerRefractor relative calibration factors for different age groups.

Figure 5.

The impact of pupil diameter on the slope of the light distribution across the pupil simulation. The slope of the OLS regression (e.g. Figure 2, panel F) is plotted as a function of effective refractive error at a 13mm vertex distance (the refractive error was actually introduced in the pupil plane). A) Simulations of an adult eye, with the impact of paraxial defocus only. The dashed lines demonstrate how a single slope value could be associated with multiple different values of refractive state; B) Simulations of an adult eye, including a typical adult's higher-order aberrations; C) Simulations of an infant eye, including a typical six-week-old's higher-order aberrations, for comparison with adult simulations from panel

B. D) The shift in refractive state estimation for different adult pupil sizes (derived from panel A), and after an adjustment for the ratio of the pupil area, compared with the adult 5mm function E) The impact of adult higher order aberrations derived from panel B and after adjustment for the ratio of pupil sizes, compared with the adult 5mm function F) The impact of 6-week-old higher order aberrations derived from panel C and after adjustment for the ratio of pupil sizes, compared with the adult 5mm function .

Figure 6.

A typical adult with a 5mm diameter pupil and coefficients introducing ± 0.18 microns of Zernike and Seidel spherical aberration. The right side of the graph shows the impact on refractive state estimations, relative to the standard adult function used in the previous analyses.

Figure 7.

A) The effect of trial lenses simulated at the pupil plane (1) and at a 23mm vertex distance (2), plus the optical effects of adjusting effective power at the pupil plane (3) and then adding the effect of lens magnification to the pupil image directly. B) Simulations of trial lenses at 3, 13 & 23mm vertex distances or their effective power at the pupil plane. The right side of each panel shows the impact on refractive state estimations.

Figure 8.

The impact of a change in retinal image size on refractive state estimations. In each case, the inward pass is focussed at the retina, but one version is for an uncorrected eye (1x) and the other is for a corrected 7D hyperopic eye (enlarged). The right side of the graph shows the impact on refractive state estimation.

Figure 9.

Calibration function simulating -8D to 8D trial lenses for an eye with A) 4D of uncorrected and B) 4D of corrected astigmatism at four meridians. The trial lenses were placed at 23mm to permit the lens correcting the astigmatism to be placed at 13mm . The right side of each panel shows the impact on refractive state estimations.

Figure 10.

Comparison of refractive state measured by the Plusoptix PowerRef 3 and a COAS aberrometer, for three almost emmetropic, presbyopic subjects. Subject 3 had a set of repeat measurements collected the following day. A) The two columns of data represent within-subject repeatability measures in the same visit. With two PowerRef 3 estimates from each measurement. B) Bland-Altman plot of repeated measurements using PowerRef 3. C) Bland-Altman plot of the first measurement from PowerRef 3 and COAS vertical meridian.

Figure 11.
Comparison of COAS and PowerRef 3 measurements with trial lenses.

Figure 12.

Refractive state measurements (D) from the PowerRef 3 while different trial lenses were held at a vertex distance of approximately 13mm. The lens power was increased in both directions until no data could be collected with the instrument.