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Predicting visual performance from optical quality metrics in keratoconus

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Purpose: The aim was to identify optical quality metrics predictive of visual performance in eyes with keratoconus and penetrating keratoplasty (PK) for keratoconus.
Methods: Fifty-four participants were recruited for this prospective, cross-sectional study. Data were collected from one eye of each participant: 26 keratoconus, 10 PK and 18 normal eyes: average age (mean ± standard deviation) 45.2 ± 10.6 years and 56 per cent female. Visual performance was tested by 10 methods including visual acuity (VA), both high and low contrast (HC- and LC-) and high and low luminance (LL-), and Pelli-Robson contrast sensitivity, all tested with and without glare. Corneal first surface wavefront aberrations were calculated from Orbscan corneal topographic data using VOLPro software v7.08 (Sarver and Associates) as a tenth-order Zernike expansion across three, 4.0 mm and 5.0 mm pupils and converted into 31 optical quality metrics. Pearson correlation coefficients and linear regression were used to relate wavefront aberration metrics to visual performance.
Results: Visual performance was highly predictable from optical quality with the average correlation of the order of 0.5. Pupil fraction metrics (for example, PFWc) were responsible for all of the highest correlations at large pupils for example, with HCVA (r = 0.80), LCVA (r = 0.80) and LLLCVA (r = 0.75). Image plane metrics, derived from the optical transfer function (OTF) were responsible for most of the highest correlations at smaller pupils for example, volume under the OTF (VOTF) with HCVA (r = 0.76) and LCVA (r = 0.73).
Conclusions: As in normal eyes, visual performance in keratoconus was predicable from optical quality; albeit by different metrics. Optical quality metrics predictive of visual performance in normal eyes, for example, visual Strehl, lack the dynamic range to represent visual performance in highly aberrated eyes with keratoconus. Optical quality outcomes for keratoconus could be reported using many different metrics, but pupil fraction metrics, for example PFWc, perform best for highly aberrated eyes.

Key words: aberrations, contrast sensitivity, keratoconus, visual acuity

Corneal topography and whole eye wavefront sensing are powerful techniques for measuring the optical quality of the human eye but the best method for representing optical quality information remains uncertain.[1] While the Zernike polynomial expansion provides a convenient breakdown of optical information into familiar components such as spherical aberration and coma, a large array of numbers must be interpreted to understand optical quality. Moreover, neither the individual components nor simple combinations such as root mean square (RMS) have proved predictive of visual performance.[2] In the absence of retinal or neural disease, optical quality data should be highly predictive of visual performance. Therefore, several groups have attempted to organise optical quality data into single-value metrics that are predictive of visual performance.[3–5] These metrics are based on classical optical concepts such as the shape of the point spread function (PSF), features of the modulation transfer function (MTF) or optical transfer function (OTF), or simply the shape of the wavefront in the pupillary plane. Such metrics have been tested for their ability to predict visual acuity in normal eyes.[6–8] This research has been important as it has identified several optical quality metrics that are suitable for representing the optics of normal eyes; for example, visual Strehl or neural sharpness.[5–7] The ability of optical quality metrics to predict the visual performance of diseased eyes has received little attention.

Diseases of the ocular media may affect retinal image quality by either forward light scatter or wavefront aberrations. Keratoconus is a corneal disease that causes loss of visual performance due to higher-order wavefront aberrations.[9–11] Penetrating keratoplasty (PK) is a standard treatment for improving vision in eyes with keratoconus but visual restoration is incomplete with post-PK eyes still experiencing significant wavefront aberrations.[10,12] Therefore, eyes with keratoconus or having undergone PK for keratoconus represent ideal models for studying the impact of wavefront aberrations on visual performance. The aim of this study was to investigate the relationship between visual performance and optical quality in eyes with keratoconus or penetrating keratoplasty for keratoconus. We did this to determine whether the metrics of optical quality most predictive of visual performance vary between normal and diseased eyes. If so, it becomes important to establish which optical quality metrics are appropriate for use as outcome measures in each disease. We measured visual performance as comprehensively as possible to determine whether different optical quality metrics were important for predicting different aspects of visual performance. This may also provide insight into which measures of visual performance are most sensitive to optical degradation by keratoconus and therefore most appropriate for use as outcome measures for this disease. Optical quality was assessed with corneal topography rather than whole eye wavefront sensing so that measurement was not limited by pupil size. This should not be a disadvantage as it has previously been shown that as wavefront aberrations due to corneal disease increase, corneal first surface wavefront analysis becomes increasingly correlated with whole eye wavefront sensing.[13,14]

METHODS

Patients

This was a prospective, cross-sectional study with recruitment of a convenient sample of participants. People with keratoconus or PK for keratoconus were drawn from the anterior segment clinic of the Flinders Eye Centre at Flinders Medical Centre (FMC) on a consecutive attendance basis. Inclusion criteria for keratoconus were a clinical diagnosis of keratoconus characterised by scissoring of the retinoscopic reflex and corneal topography suggestive of keratoconus (asymmetric bowtie with steepening or skewed radial axes) or clinical signs of keratoconus—stromal corneal thinning by slitlamp evaluation, accompanied by one or more of the following clinical signs: Vogt's striae, iron ring or Munson's sign. Inclusion criteria for those having undergone penetrating keratoplasty for keratoconus were grafted by one surgeon (DJC), with an uncomplicated postoperative course (for example, no rejection, cataract development et cetera) of at least 12 months. Normal participants were drawn from medical students and staff of FMC with the inclusion criteria of age 15 years or older and normal healthy eyes with a VA better than 0.1 logMAR (6/7.5 Snellen equivalent). Exclusion criteria were any ocular pathology (other than keratoconus) for example, cataract or abnormality such as amblyopia and strabismus, any previous ocular surgery (other than penetrating keratoplasty for the PK group), contact lens wear, any neurological problem, systemic disease or taking of any medication that may affect contrast sensitivity, inability to speak English sufficiently to be instructed to perform the tests, insufficient mental ability to perform the tests and physical disability which would make it arduous to perform the tests (for example, wheelchair-bound). The study was restricted to non-contact lens wearers so that the wavefront aberrations being measured with corneal topography were the same as those affecting vision and not neutralised by rigid contact lens wear.

Thirty-six patients with keratoconus and penetrating keratoplasty and 18 people with normal eyes agreed to participate. The keratoconus and PK population consisted of people with bilateral keratoconus, bilateral corneal transplantation for keratoconus and keratoconus in one eye and PK in the fellow eye. One eye from each participant was randomly selected to undergo clinical testing. This led to the inclusion of 26 eyes with keratoconus, 10 eyes with penetrating keratoplasty and 18 normal eyes. The population had an average age (mean ± standard deviation) of 45.2 ± 10.6 years, with no significant difference ($F_{2,51} = 0.5418$, $p > 0.05$) between normal (43.7 ± 9.3), keratoconus (46.8 ± 9.2) and PK (44.0 ± 15.9) subpopulations. The population was 56 per cent female with similar proportions among normal (66 per cent), keratoconus (46 per cent) and PK (60 per cent). Informed consent was obtained from all subjects after the nature of the study had been fully explained. The tenets of the Declaration of Helsinki were followed and the study gained approval from the Flinders Medical Centre Ethics Committee.

A staging system proposed by Krumeich, Daniel and Knulle[15] was used to define keratoconus. This system defines keratoconus as being stage 1, 2 or 3 (eccentric corneal steepening, induced myopia and/or astigmatism less than five dioptres

Vision performance measure	Overall (N = 54)	Normal (N = 18)	Keratoconus (N = 26)	Penetrating keratoplasty (N =10)
High contrast visual acuity (HCVA)	0.14 ± 0.19	-0.05 ± 0.06	0.26 ± 0.16	0.17 ± 0.10
HCVA under glare ($HCVA_{glare}$)	0.26 ± 0.22	0.06 ± 0.07	0.41 ± 0.19	0.27 ± 0.09
Low contrast visual acuity (LCVA)	0.30 ± 0.22	0.10 ± 0.04	0.44 ± 0.21	0.34 ± 0.13
LCVA under glare ($LCVA_{glare}$)	0.34 ± 0.21	0.15 ± 0.04	0.49 ± 0.19	0.41 ± 0.17
Pelli-Robson contrast sensitivity (PRCS)	1.28 ± 0.44	1.62 ± 0.14	1.06 ± 0.35	1.22 ± 0.61
PRCS under glare ($PRCS_{glare}$)	1.15 ± 0.41	1.47 ± 0.14	0.93 ± 0.37	1.17 ± 0.49
Near HCVA	0.31 ± 0.29	0.11 ± 0.06	0.44 ± 0.28	0.35 ± 0.37
Near $HCVA_{glare}$	0.46 ± 0.32	0.22 ± 0.10	0.66 ± 0.28	0.47 ± 0.38
Near low luminance LCVA (Near LLLCVA)	0.62 ± 0.41	0.24 ± 0.07	0.88 ± 0.40	0.72 ± 0.26
Near LLLCVA under glare (Near $LLLCVA_{glare}$)	0.71 ± 0.37	0.42 ± 0.13	0.89 ± 0.37	0.95 ± 0.32

Table 1. Visual performance data in the entire population and broken down by normal, keratoconus and penetrating keratoplasty subjects (mean ± SD)

(Stage 1), less than eight dioptres (Stage 2), less than 10 D (Stage 3), corneal radii less than 48 D (Stage 1), less than 53 D (Stage 2), greater then 53 D (Stage 3), Vogt's striae, no central scars, typical keratoconus topography) or Stage 4, more advanced (with central corneal scars, radii greater than 55 D and unmeasurable refraction). There were 15 eyes at stage one, seven eyes at stage 2, two eyes at stage 3 and two eyes at stage 4. In the PK group, the graft ages ranged from 27 years to 2.5 years since surgery.

Visual performance testing

Data for each participant were collected in a single session. All measurements of vision were performed on natural pupils in standard clinic room lighting, without the use of any dilating or cycloplegic drug. Participants were refracted including determination of near addition and optimally corrected for visual performance testing. The measurements taken were logMAR high contrast visual acuity (HCVA), low contrast visual acuity (LCVA),[16] Pelli-Robson contrast sensitivity (PRCS),[17] near HCVA and near low luminance low contrast visual acuity (near LLLCVA). These five tests were repeated under glare, thus comprising 10 visual performance tests in total.

Visual acuity was measured with a logMAR chart with a high contrast (96 per cent Weber) and a low contrast (18 per cent Weber) side.[18] The logMAR and Pelli-Robson charts were positioned at three metres with luminance of 100 cd/m^2. By-letter scoring, forced-choice testing and fixed error termination rule (five letters for VA and six letters for PRCS), were used to maximise reliability.[19,20] The Smith-Kettlewell Institute Low Luminance (SKILL) card (Smith-Kettlewell Eye Research Institute, San Francisco, CA, USA) was used to assess near visual performance.[21] The SKILL card is a logMAR visual acuity chart with a high contrast (96 per cent Weber) presentation on one side and a low luminance (a dark grey background 10 per cent of the reflectance of white paper) low contrast (14 per cent Weber) presentation on the other side.[21] The test distance was 40 centimetres. The luminance of the high contrast chart was measured at 88.8 cd/m^2 and the low luminance low contrast chart was measured at 6.8 cd/m^2.

The glare source consisted of two projection lamps placed either side of the test chart and monitor. The baseline room illuminance was 200 lux. The illuminance at the eye from the projector source was an increment of 1,000 lux. This arrangement has been reported previously.[22] Natural pupils were used and care taken to ensure neither occlusion of the glare source nor macular photostress occurred.[23] A full list of visual performance tests is presented in Table 1. Photometric testing was performed with an all-in-one photometer and lux meter. (Gossen, Starlite: All-in-one, Nüremberg, Germany).

Optical quality assessment

Corneal first surface wavefront aberrations were calculated from ORBSCAN II (Bausch & Lomb, Rochester, NY) corneal topographic data exported to VOLPro software v7.08 (Sarver and Associates). The Zernike expansion was calculated over three, 4.0 mm and 5.0 mm pupils to the tenth-order. A 5.0 mm pupil was the largest chosen to avoid artifacts associated with the graft-host junction that may occur for larger diameters and the pupil centre was taken from the ORBSCAN map. Thirty-one metrics of optical quality designed to be predictive of visual performance were calculated from the third- to tenth-order Zernike data using GetMetrics v2.02.006 (University of Houston, College of Optometry). These have been described in detail by Thibos and colleagues.[3] In brief, the metrics can be categorised according to their derivation. Pupil plane metrics include wavefront 'flatness' metrics, which quantify the wavefront error in terms of the shape of the wavefront in the pupil, or pupil fraction metrics, which describe the proportion of the pupil, which meets an optical quality criterion. Image plane metrics for a point object describe the compactness of the

Vision performance measure	Highest correlating metrics of optical quality		
	5.0 mm pupil	4.0 mm pupil	3.0 mm pupil
High contrast visual acuity (HCVA)	logPFWc, -0.80	logPFWc, -0.77	logVOTF, -0.76
HCVA under glare ($HCVA_{glare}$)	logPFWc, -0.77	logPFWc, -0.74	logPFCt, -0.70
Low contrast visual acuity (LCVA)	logPFWc, -0.80	logPFWc, -0.78	logVOTF, -0.73
LCVA under glare ($LCVA_{glare}$)	logPFWc -0.77	logPFWc -0.73	logPFCt, -0.64
Pelli-Robson contrast sensitivity (PRCS)	logPFSt, 0.63	logVOTF, 0.58	logVOTF, 0.60
PRCS under glare ($PRCS_{glare}$)	logPFSt, 0.67	logVOTF, 0.67	logVOTF, 0.56
Near HCVA	logPFCt, -0.64	logVOTF, -0.51	logVSX -0.47
Near $HCVA_{glare}$	logPFCt, -0.68	logVOTF, -0.59	logPFCt, -0.46
Near Low Luminance LCVA (Near LLLCVA)	logPFWc -0.75	logVNOTF, -0.72	logVSX, -0.69
Near LLLCVA under glare (Near $LLLCVA_{glare}$)	logPFWc -0.73	logPFWc, -0.70	logVOTF, -0.63

Table 2. The highest correlating optical quality metrics and their coefficients of correlation (R) for each visual performance measure by pupil size. The metrics reported here include pupil plane metrics: logPFCt = log(pupil fraction when a 'good' sub-aperture satisfies the criterion B_{ave} less than 0.25 D), logPFWc = log(pupil fraction when critical pupil is defined as the concentric area for which RMS less than one arcmin), logPFSt = log(pupil fraction when a 'good' sub-aperture satisfies the criteria horizontal slope and vertical slope are both less than one arcmin); image plane metrics derived from the point spread function (PSF): logVSX = log(visual Strehl ratio computed in the spatial domain); and image plane metrics for grating objects based on the neurally weighted optical transfer function (OTF): logVOTF = log(volume under OTF normalised by the volume under MTF) and logVNOTF = log(volume under neurally-weighted OTF, normalised by the volume under neurally-weighted MTF).[3]

point spread function (PSF) or the contrast preserved in the PSF or for grating objects describe attributes of either the modulation transfer function (MTF) or the optical transfer function (OTF). Of the 31 metrics used in this study, 10 were pupil plane metrics, 11 were image plane metrics based on the PSF and 10 were image plane metrics based on the MTF/OTF. These metrics were used to investigate the relationships between visual performance and wavefront error.

Analysis

All variables were tested for distribution normality using the Kolmogorov-Smirnov test ($p < 0.05$). Where distributions were not Gaussian, arithmetic transformation was performed. Many optical quality metrics were positively skewed (27 over a 5.0 mm pupil, 18 over a 4.0 mm pupil and 27 over a 3.0 mm pupil), so a logarithmic transformation was undertaken. Pearson correlation and linear regression were used to test the relationship between optical quality metrics and visual performance measures. All statistical analyses were performed on SPSS for windows (SPSS Inc).

RESULTS

The population had a mean HCVA of 0.14 ± 0.19 logMAR (6/7.5^{--}), which broke down to 0.26 ± 0.16 logMAR (6/12^{++}) for the keratoconus group, 0.17 ± 0.10 logMAR (6/9.5^{+}) for the PK group and -0.05 ± 0.06 logMAR (6/6^{++}) for the normal group. The visual performance of the population is fully described in Table 1.

The relationships between each measure of visual performance and each optical quality metric (at each pupil size) were explored using Pearson correlations. For each visual performance measure, the optical quality metric for each pupil size with the highest correlation coefficient was listed in Table 2. The correlations were highest for HCVA and LCVA measured at distance and lowest for HCVA measured at near. Very high correlations, of the order of 0.7, were also found for LCVA and LLLCVA. Notably, correlations were largely unaltered under conditions of glare, in terms of both strength of correlation and the optical metric most highly correlated.

All visual performance measures were strongly correlated with a number of optical quality metrics. Indeed, averaging across all 10 visual performance measures gives correlations of the order of 0.5 for all optical quality metrics (Figures 1A–1C). Over a 3.0 mm pupil, the results were consistent across all metrics (Figure 1A) with only the best performed metric, volume under the OTF (VOTF) surpassing r = 0.6. The average correlations are slightly higher for metrics calculated over a 4.0 mm pupil (Figure 1B), with a pupil fraction metric (PFWc) achieving the highest average correlation. At 5.0 mm pupils, the best average correlations are achieved with PFWc exceeding 0.7 but several image plane metrics drop away to give poor correlations (Figure 1C).

Eighteen of the 30 correlations listed in Table 2 were for three pupil plane metrics. Three image plane metrics, comprising one PSF metric and two OTF

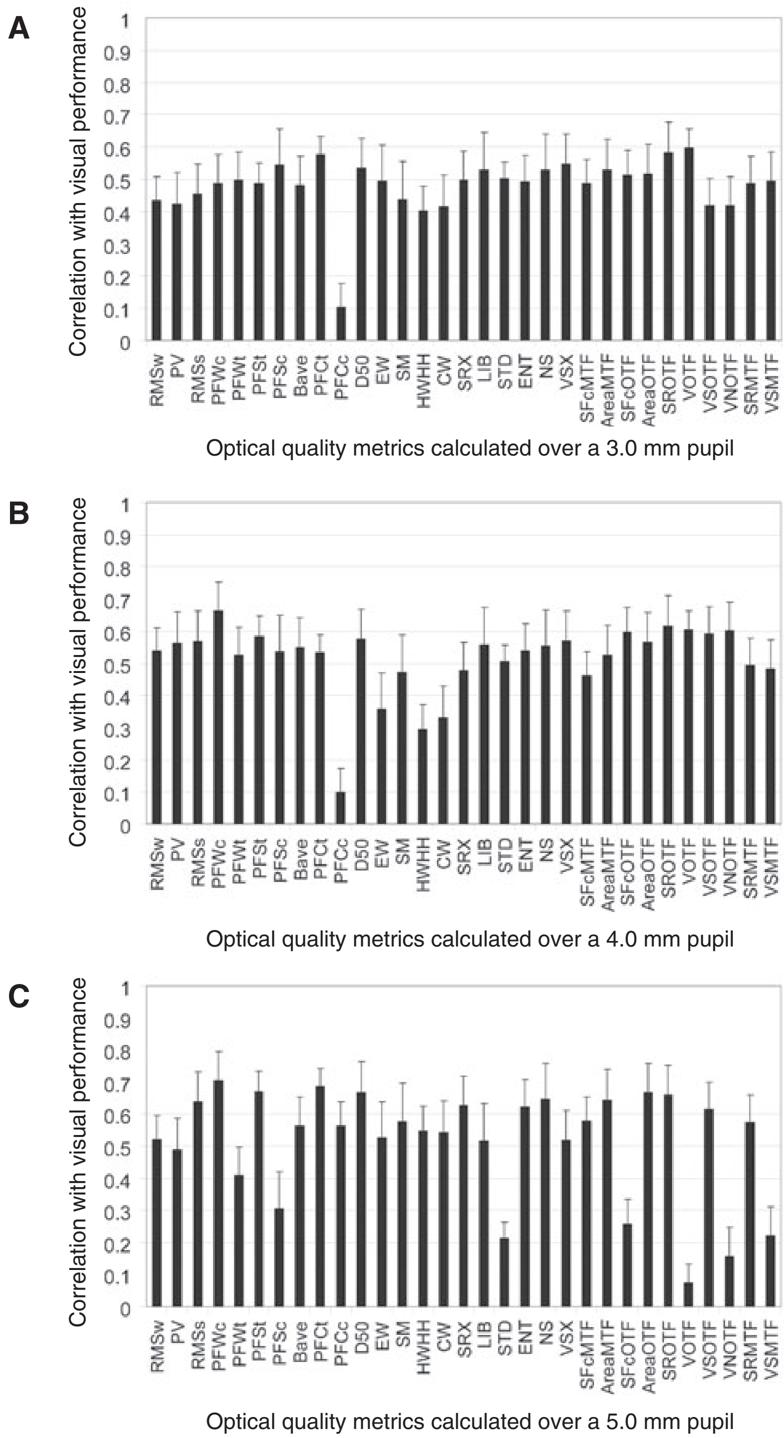

Figure 1. The correlations between each optical quality metric and visual performance averaged across all 10 visual performance measures. A. When calculated over a 3.0 mm pupil, most correlations are of the order of 0.5 with several OTF metrics attaining the highest correlations. B. When calculated over a 4.0 mm pupil, only a pupil fraction metric exceeds a correlation of 0.7. C. When calculated over a 5.0 mm pupil, several image plane metrics lack the dynamic range to perform at the higher levels of aberrations occurring at this pupil size. The highest correlations occur for pupil fraction metrics.

metrics were the other highest correlating metrics. The three pupil plane metrics, which were consistently highly correlated with visual performance, were all pupil fraction metrics. Pupil fraction is defined as the proportion of the pupillary area, for which the optical quality of the eye meets a certain criterion representing good optical quality but not necessarily diffraction-limited: Pupil fraction = Area of good pupil/Total area of pupil.

Pupil fraction can be calculated by two methods:

1. the critical pupil or central pupil method which assumes the pupil centre has good optical quality and expands a sub aperture surrounding the pupil centre until the optical quality criterion is reached (Pupil fraction$_c$ = [critical diameter/pupil diameter]^2) or
2. the tessellation or whole pupil method in which 100 sub-apertures are defined and labelled as good or bad according to the optical quality criterion (Pupil fraction$_t$ = [Area of good sub-apertures/Total area of pupil]).

In this study, one critical pupil fraction and two tessellated pupil fractions achieved the highest correlations. These were:

1. PFWc, which is a critical pupil defined as the concentric area for RMS less than one minute of arc
2. PFSt, which is computed over the tessellated pupil when a good sub-aperture satisfies the criteria horizontal slope and vertical slope both less than the criterion (one arcmin)
3. PFCt, which is computed over the tessellated pupil fraction when a good sub-aperture satisfies the criterion blur average (B_{ave}) less than the criterion (0.25 D).

The metric logPFWc was able to predict over 60 per cent of the variance of HCVA and LCVA with and without glare at 5.0 mm and 4.0 mm pupils: for example, LCVA = 0.02 -0.26 logPFWc, R^2 = 0.61 (Figure 2). The metric logPFSt was the highest correlate with PRCS with and without glare at large pupil sizes. The metric logPFCt was the highest correlate with three glare measures at small pupils.

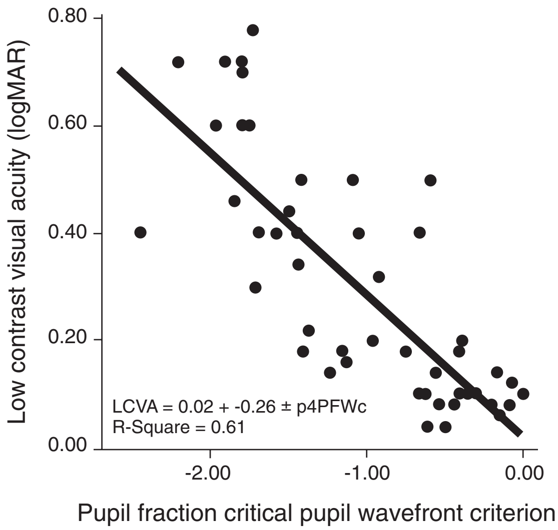

Figure 2. The metric logPFWc (pupil fraction critical pupil wavefront criterion) calculated for a 4.0 mm pupil explains 61 per cent of the variance in low contrast visual acuity. This metric describes size of the concentric area for root mean square total higher order wavefront aberrations less than λ/4.

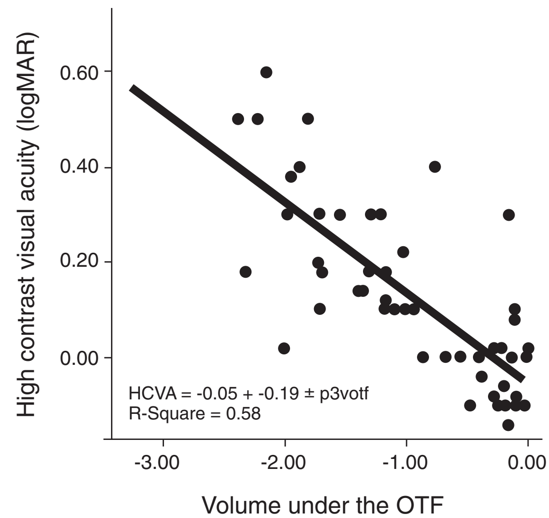

Figure 3. The metric VOTF (volume under the optical transfer function) calculated for a 3.0 mm pupil explains 58 per cent of the variance in high contrast visual acuity

The three image plane metrics with the highest correlations with visual performance comprised one PSF and two OTF metrics, however, the VOTF metric was responsible for nine of these 12 highest correlations including explaining 58 per cent of the variance in HCVA: HCVA = -0.05 - 0.19VOTF (Figure 3). This metric describes the volume under the OTF normalised by the volume under the MTF and the metrics VNOTF, which describes the volume under the neurally-weighted OTF normalised by the volume under the neurally-weighted MTF was also responsible for one of the highest correlations (with LLLCVA at 4.0 mm pupil). The only PSF metric to achieve a highest correlation was VSX, which computes the visual Strehl in the spatial domain (correlated with Near HCVA and Near LLLCVA at 3.0 mm pupil). Although never the highest correlate, several other image plane metrics were consistently strong performers including AreaOTF, which is the area of visibility under the radially averaged OTF and above the neural contrast threshold function is therefore a measure of both contrast attenuation and phase shift and SROTF, which is the Strehl ratio computed in the frequency domain (Figures 1A–1C).

DISCUSSION

Visual performance in eyes with keratoconus and PK for keratoconus was highly related to optical quality. The correlations were high across a range of visual performance tests, optical quality metrics and pupil sizes. At large pupil sizes, pupil plane metrics, specifically pupil fraction metrics provided the highest correlations with each measure of visual performance. Pupil fraction metrics are able to measure over a broad range of aberrations, which may explain their value in diseased eyes. In normal eyes, pupil fraction metrics also correlate well with high and low contrast and low luminance visual acuity.[6,7] Although in one study, the pupil fraction metrics which best correlated with VA were PFSt and PFWc, in the other study, they were PFSt and PFSc, which is a critical pupil fraction using the same slope criteria as PFSt.[6,7] This contrasts with the present study, in which the best performed pupil fraction metrics were PFWc, PFSt and PFCt. The PFSc metric performed well at 3.0 mm and 4.0 mm pupils but not at 5.0 mm pupils.

With small pupils, image plane metrics, especially those derived from the OTF, were the highest correlates with visual performance. At 4.0 mm pupils, the highest correlating metrics were evenly split between pupil fraction metrics and OTF metrics, with the latter proving superior for predicting contrast sensitivity. One may expect metrics of grating image quality based on the MTF or OTF to highly correlate with contrast sensitivity, as they are sensitive to contrast attenuation. The pattern of results shows a clear dependence on pupil size, with OTF metrics performing best at small pupil sizes and pupil fraction metrics performing best at large pupil sizes. As the magnitude of aberrations is dependent on pupil size, this suggests that OTF metrics correlate well with visual performance at low levels of aberrations and pupil fraction metrics correlate well with high levels of aberrations.

These results contrast with those from studies performed on normal eyes.[5–8] In all these studies, most of the optical quality metrics that were highly predictive of visual performance were image plane metrics and chiefly those derived from the OTF. Chen and colleagues[5] found that PSF contrast metrics of 'neural sharpness' and 'entropy' were the most highly predictive and Marsack, Thibos and Applegate[7] found visual Strehl most predictive. This is similar to the present study in that at low levels of aberrations, OTF metrics performed well. The problem with many of these metrics for diseased eyes is that they lack dynamic range; as can be seen in Figure 1C, the correlations for VOTF, VNOTF and several other OTF metrics drop away markedly for the 5.0 mm pupil. Only some of the metrics, particularly the pupil fraction metrics, appear to work well in both our diseased and several normal populations. One limitation of the studies performed on normal eyes is that the only visual performance metric used is visual acuity,[5,7,8] except in the Applegate, Marsack and Thibos study,[6] where low contrast and low luminance visual acuity testing were performed. This was a similar cross-sectional study performed in people with normal eyes (VA better than 6/5.1) but the correlation coefficients were much lower, especially for HCVA and LCVA.[6] This is likely related to the population distributions in the visual performance dimension, which were much narrower for normally sighted eyes and narrowest for HCVA measurement.[6] The high correlations in this study were independent of visual performance test type because the distribution across the visual performance dimension was large for all testing methods.

There are little comparable data from studies with diseased eyes. In our previous study, where we looked at a small number of people who had undergone PK for keratoconus (n = 14), we found very similar results.[12] The highest correlation was between the pupil fraction metrics PFSt and LCVA. Other comparable results included the VOTF metric correlated with contrast sensitivity under glare. The main differences were higher correlations for image plane metrics, including PSF contrast metrics and various OTF metrics. In this way, the previous study had some similarity to the studies on normal populations, which perhaps reflects the better level of HCVA in the PK only population (mean $6/4.8^{-}$) compared to $6/7.5^{-}$ in this study.

These various studies of optical quality metrics and visual performance suggest that most of the metrics that suit normal eyes do not suit diseased eyes and vice versa. The exceptions are pupil fraction metrics, which fare well in all studies although only the PFWc and PFSt metrics were highly correlated to visual performance in all populations. Therefore, if there is to be one optical quality metric to be used in all populations, it must be PFWc or PFSt. Further studies are required in different eye disease populations to confirm this. Therefore, it would seem to be more sensible to organise optical data into visual performance metrics, which suit the population under study. For a keratoconus and PK population, a selection of several optical quality metrics including a pupil fraction metric for example, PFWc or PFSt and an OTF metric for example, VOTF, would be appropriate.

The correlations between measures of visual performance and optical quality metrics were of comparable magnitude across all visual performance methods; albeit slightly lower for HCVA at near and PRCS. This suggests that all measures of visual performance are sensitive to the impact of wavefront aberrations and all are useful as outcome measures for keratoconus. Notably, there were little differences in correlations between measures with and without glare. This suggests that glare testing is of little value in keratoconus, which is consistent with previous studies[24] and with the known mechanism of visual loss in keratoconus being wavefront aberrations and not forward light scatter.[9–11] The impact of glare may have been hampered by the use of natural pupils which stop down under glare and therefore reduce the magnitude of wavefront aberrations present. The use of natural pupils is also a disadvantage because it leads to a range of different pupil sizes being used for visual performance testing; indeed the relationships between wavefront aberrations and visual performance might have been stronger, if the same pupil sizes were used for measuring vision as for calculating optical quality metrics. Ideally, the study design should have incorporated simultaneous recording of pupil size and visual performance. Then optical quality could have been calculated for the actual pupil size used. This was not possible for us to do, so we used a series of fixed pupil sizes to calculate optical quality metrics. This inevitably introduces some noise due to inter-individual variation in pupil size and this would reduce the strength of the correlations between visual performance and optical quality. The calculation of metrics for three different pupil sizes proved highly informative for the impact of the magnitude of aberrations on the correlations between visual performance and optical quality. Notably, the magnitude of the correlations varied little among pupil sizes, being slightly better for the 5.0 mm pupil, implying that this may be closest to the actual pupil sizes of the participants in the study. This study may have found stronger relationships if greater numbers of patients had been recruited and perhaps, if whole eye aberrations had been measured. While this probably does not matter for highly aberrated eyes, our population did include some normal and some diseased eyes with low levels of aberrations, for whom whole eye wavefront aberration measurement may have been more representative of retinal image quality.

In conclusion, it is possible to predict visual performance from several optical quality metrics in keratoconus and PK for keratoconus. Most of these optical quality metrics are not highly predictive of visual performance in normal eyes, with the exception of the pupil fraction metrics PFWc and PFSt.[6,7] Therefore, outcomes research in keratoconus should probably include several optical quality metrics: a pupil fraction metric for example, PFWc or PFSt; and an OTF metric, for example, VOTF.

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