

# Penetrating Keratoplasty for Keratoconus: The Nexus Between Corneal Wavefront Aberrations and Visual Performance

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## ABSTRACT

**PURPOSE:** To compare the visual and optical performance after penetrating keratoplasty (PK) for keratoconus to normal patients and to examine the relationship between corneal wavefront aberrations and visual performance in patients with PK.

**METHODS:** Visual performance testing, with optimal refractive correction, included low contrast visual acuity (LCVA) and Pelli-Robson contrast sensitivity with and without glare, and high contrast visual acuity. Corneal first surface wavefront aberrations were calculated from EyeSys topography data using VOL-Pro software v7.00 for a 4.0-mm pupil as a 10th order Zernike expansion and converted into single value metrics. Normal patients were compared to patients with PK using analysis of variance, and linear regression was used to compare wavefront aberration metrics to visual performance.

**RESULTS:** Patients with PK ( $n=14$ , age  $41.6\pm 7.0$  years) and normal patients ( $n=14$ , age  $36.7\pm 9.0$  years) were of similar age ( $F_{1,26}=2.54$ ,  $P=.12$ ). Normal patients saw significantly better on all visual performance measures and had better optical performance for total higher order root-mean-square corneal wavefront aberration (mean $\pm$ SD): PK,  $0.67\pm 0.41\ \mu\text{m}$ ; normal,  $0.09\pm 0.02\ \mu\text{m}$  ( $F_{1,26}=28.41$ ,  $P<.001$ ) and across all Zernike orders and modes. Wavefront aberrations in PK eyes were dominated by trefoil  $0.35\pm 0.27\ \mu\text{m}$ , coma  $0.47\pm 0.37\ \mu\text{m}$ , spherical aberration  $0.17\pm 0.10\ \mu\text{m}$ , and tetrafoil  $0.12\pm 0.07\ \mu\text{m}$ . The relationships between corneal wavefront aberration and visual performance metrics were strongest for LCVA= $0.30-0.98$ Pupil fraction for wavefront (tessellation)  $-0.04$ Half width at half height,  $R^2=0.75$ .

**CONCLUSIONS:** In this series, patients with PK had poorer visual performance compared to normal patients, which is due to increased corneal wavefront aberrations. Outcomes research in corneal transplantation should include measurement of wavefront aberrations and visual performance in the contrast domain. [*J Refract Surg.* 2006;22:926-931.]

Penetrating keratoplasty (PK) remains the surgical option of choice for keratoconus<sup>1</sup> despite the availability of alternatives.<sup>2,3</sup> High contrast visual acuity (HCVA), also known as best spectacle-corrected visual acuity, has been the usual visual outcome measure for PK,<sup>4,5</sup> but the inadequacy of HCVA as an indicator of visual quality is widely appreciated.<sup>6,7</sup> Although PK has been demonstrated to be an effective treatment for keratoconus, as measured by an improvement in HCVA,<sup>8,9</sup> contrast vision outcomes have not been so well studied. Sub-normal contrast sensitivity after PK for keratoconus has been shown previously.<sup>10-14</sup> Low contrast visual acuity (LCVA) in PK has undergone minimal investigation with one study reporting abnormal values<sup>15</sup> and another showing no difference from normal eyes.<sup>16</sup> Glare testing after PK has been the subject of several small studies with inconsistent findings—some show glare losses in keratoconus greater than in patients with PK, others the opposite.<sup>11,12,17,18</sup> This inconsistency is at odds with the clinical impression that patients benefit from PK and seems worthy of further investigation.

Few reports have been made regarding wavefront aberration outcomes of PK. In small numbers of cases, total higher order root mean square (RMS) wavefront aberrations have been shown to be elevated in eyes with PK compared to normal eyes.<sup>10,15,19</sup> Subnormal visual performance in eyes with PK is likely due to higher order wavefront aberrations. Therefore, the purpose of this study is to examine the visual and optical performance after PK for keratoconus, to compare these results to normal patients, and to examine the relationship between corneal wavefront aberrations and visual performance in eyes with PK.

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### PATIENTS AND METHODS

Informed consent was obtained from all patients 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. Inclusion criteria were age  $\geq 15$  years and normal healthy eyes with an HCVA  $> 0.1$  logMAR (6/7.5 Snellen equivalent) for the control group, or having undergone PK for keratoconus, grafted by one surgeon (D.J.C.), with an uncomplicated postoperative course (eg, no rejection, cataract development, etc) of at least 12 months and habitually corrected with spectacles only (for the PK group). Exclusion criteria were any ocular pathology or abnormality such as amblyopia and strabismus, any previous ocular surgery (other than PK for the PK group), contact lens wear, any neurological problem, systemic disease, or medication regime that may affect contrast sensitivity. The study was restricted to non-contact lens wearers only so that the wavefront aberrations being measured with corneal topography were the same as those affecting vision, and not neutralized by rigid contact lens wear. Patients with PK for keratoconus were drawn from the anterior segment clinic of the Department of Ophthalmology at Flinders Medical Centre on a consecutive attendance basis. Control patients were drawn from medical students and staff of Flinders Medical Centre.

Data were collected on the visual performance of 14 eyes of 14 PK patients and 14 eyes of 14 normal patients. Data for each patient were collected in a single session. All patients were refracted and optimally corrected with trial frame lenses prior to visual performance data collection. The measurements taken were logMAR HCVA, LCVA,<sup>6</sup> Pelli-Robson contrast sensitivity,<sup>20</sup> LCVA with glare, and Pelli-Robson contrast sensitivity with glare.<sup>21</sup> Both HCVA and LCVA were measured on a computerized monitor-based system.<sup>22</sup> The program uses the psychophysical "staircase" method, using a forced-choice protocol, to determine the acuity end-point, which is taken as the average of 13 staircase reversals. This offers excellent reliability and validity and is free from learning effects. The program uses the same 5 $\times$ 4 letters used in Bailey-Lovie logMAR charts and the results are given in logMAR.<sup>22</sup> Low contrast visual acuity is analogous to HCVA testing except that the target optotypes are reduced in contrast. Twenty-five percent (Weber) contrast optotypes were used, as this has been reported to be the most suitable contrast level for detecting visual loss in early cataracts under glare conditions and thus may be suitable for other eye conditions.<sup>23</sup> Testing was conducted at 3.0 m and the monitor had a maximum luminance of 185 cd/m<sup>2</sup>. Low contrast visual acuity was also measured under glare conditions.

Glare testing was conducted with a light source directed at the patient. The glare source consisted of two projection lamps placed on either side of the test chart and monitor. The baseline room illuminance was 200 lux at the eye. The illuminance at the eye from the projector source was an increment of 1000 lux. This arrangement has been previously reported.<sup>21</sup> Natural pupils were used during visual performance testing. Care was taken to ensure occlusion of the glare source or macular photostress did not occur.<sup>24</sup>

The Pelli-Robson contrast sensitivity chart was chosen for its superior validity and reliability compared to sinusoidal grating charts such as the Vistech and FACT.<sup>20,25</sup> The Pelli-Robson chart was positioned 3 m from the patient and had a maximum luminance of 100 cd/m<sup>2</sup>. The test was scored by the modified method of letter-by-letter scoring,<sup>26</sup> and results were given in units of log contrast sensitivity (logCS). Contrast sensitivity was also measured under the same glare conditions as LCVA with glare.

The results were reported as raw measures and three derived measures of contrast and glare loss. Taking the simple arithmetic difference between glare and no glare, or high and low contrast, demonstrates the effect of contrast or glare independent of baseline HCVA or contrast sensitivity. This facilitates comparison of groups of disease versus no disease where matching for HCVA is not possible. Low contrast loss (LCL) is defined as the difference between the high contrast HCVA and LCVA:  $LCL = LCVA - HCVA$ .<sup>21</sup> Low contrast visual acuity glare loss ( $GL_{LCVA}$ ) is defined as the difference between the LCVAgl and LCVA:  $GL_{LCVA} = LCVAgl - LCVA$ .<sup>22</sup> Pelli-Robson Contrast Sensitivity glare loss ( $GL_{PRCS}$ ) is defined as the difference between PRCS and PRCSgl:  $GL_{PRCS} = PRCS - PRCSgl$ .<sup>21</sup>

Corneal first surface wavefront aberrations were calculated from EyeSys corneal topography data (EyeSys Vision Inc, Houston, Tex) using VOL-Pro software v7.00 (Sarver & Associates, Carbondale, Ill). A 10th order Zernike expansion was used. A 4.0-mm pupil was chosen to avoid artifacts associated with the graft-host junction that may occur for larger diameters, and pupil center was assumed to be at the corneal vertex. Corneal topography was used for wavefront aberration calculation rather than whole eye wavefront sensing because we had a convenience sample with these data. For each eye enrolled in the study, the average 3rd to 10th order Zernike coefficients were reduced to a single value by each of 33 optical quality metrics. Detailed descriptions and mathematical formulations for these single-value metrics used were recently published by Thibos et al.<sup>27</sup> In brief, the metrics can be categorized according to their derivation: pupil plane metrics, point spread func-

TABLE 1  
**Visual Performance of Normal Eyes and Eyes That Underwent Penetrating Keratoplasty (PK)\***

	Group		
	Normal (N=14)	PK (N=14)	
Age (y)	36.7±9.0	41.6±7.0	$F_{1,26}=2.54, P=.12$
Spherical equivalent refraction (D) (range)	-0.70±2.00 (0.00 to -7.00)	0.45±0.79 (+1.37 to -0.62)	$F_{1,26}=1.794, P=.20$
Astigmatism (D) (median, range)	0.00 (0.00 to -2.00)	-3.12 (0.00 to -7.25)	$F_{1,26}=11.37, P<.01$
Raw Vision Measures			
High contrast visual acuity	-0.16±0.05	-0.03±0.11	$F_{1,26}=16.84; P<.001$
Low contrast visual acuity	-0.11±0.07	0.10±0.11	$F_{1,26}=40.87; P<.001$
Low contrast visual acuity under glare	-0.10±0.08	0.10±0.14	$F_{1,26}=21.25; P<.001$
Pelli-Robson contrast sensitivity	1.78±0.11	1.46±0.14	$F_{1,26}=41.25; P<.001$
Pelli-Robson contrast sensitivity under glare	1.68±0.05	1.45±0.13	$F_{1,26}=38.59; P<.001$
Difference Measures			
Low contrast loss	0.05±0.04	0.14±0.06	$F_{1,26}=19.94; P<.001$
Glare loss (low contrast visual acuity)	0.02±0.08	-0.01±0.08	$F_{1,26}=0.51, P=.48$
Glare loss (Pelli-Robson contrast sensitivity)	0.10±0.13	0.03±0.11	$F_{1,26}=1.84, P=.19$

\*Values represented as mean±standard deviation.

Note. The normal group scored better than the PK group on all raw scores and for low contrast loss.

tion (PSF) metrics, or optical transfer function (OTF) metrics. These metrics were used to investigate the relationships between visual performance and wavefront error as they have been previously shown to be highly predictive of visual performance.<sup>6,28</sup>

One way analyses of variance (ANOVA) were used to compare groups. Pearson correlations and linear regression were used to explore the relationships between single-value wavefront aberration metrics and visual performance measures. All statistical analyses were performed on the SPSS software package v12.0.1 (SPSS Inc, Chicago, Ill).

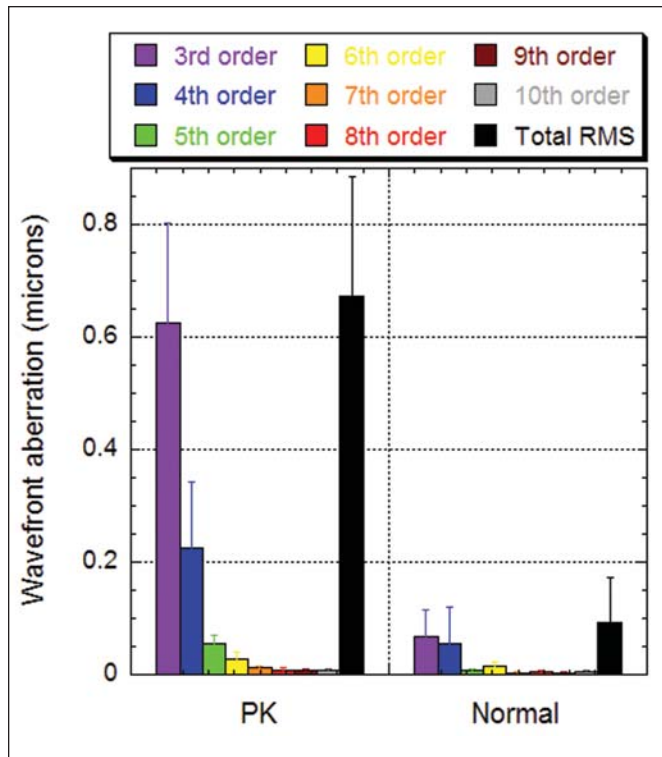
### RESULTS

The results of visual performance of the normal control group and the PK group are listed in Table 1. The groups were similar for age, but the normal controls performed better than the PK group on all raw vision measures. However, as the groups were not matched for HCVA ( $F_{1,26}=16.84; P<.001$ ), they were also compared using three difference measures. Only one significant difference was identified: the PK group had a greater low contrast loss than the normal group ( $0.14±0.06$  vs  $0.05±0.04$ ,  $F_{1,26}=19.94; P<.001$ ), that is the measurement of LCVA identified loss of vision in the PK group not predicted by HCVA testing. Glare testing did not

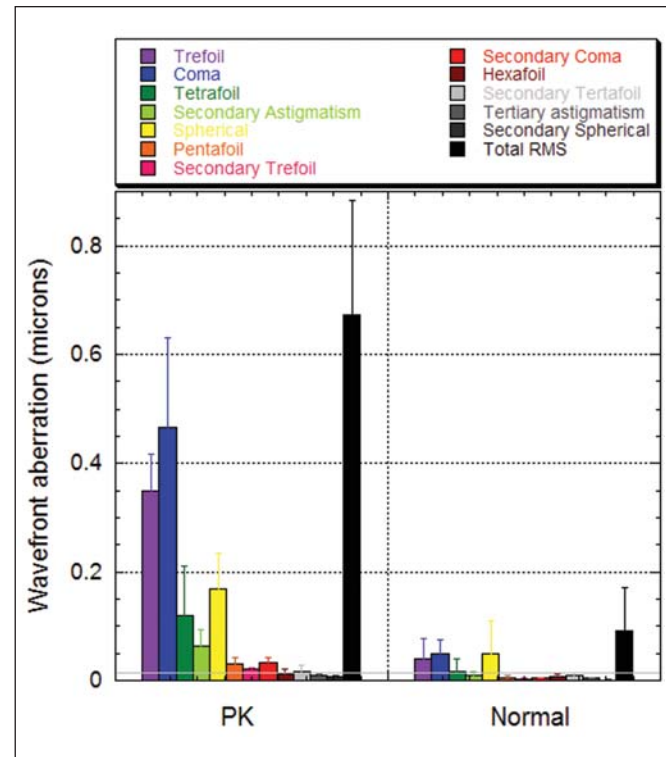
provide any such useful information.

The visual performance differences were also reflected in wavefront aberration differences. Corneal wavefront aberrations calculated for a 4.0-mm pupil were compared by order in Figure 1 and by mode in Figure 2. The normal group had significantly less higher order corneal wavefront aberrations than the PK group for total higher order RMS (mean±standard deviation): PK,  $0.67±0.41$  μm; normal,  $0.09±0.02$  μm ( $F_{1,26}=28.41, P<.001$ ) and for each order (3rd, 4th, 5th, 7th, and 9th,  $P<.001$ ; 6th and 8th,  $P<.05$ ) except 10th ( $P>.05$ ) (see Fig 1). The normal group had less higher order wavefront aberrations than the PK group for each polar mode tested except hexafoil ( $Z_{66}$  by Campbell's scheme for representing Zernike polar modes)<sup>29</sup> ( $P>.05$ ), significant at  $P<.001$  for all modes except secondary astigmatism ( $Z_{42}$ ), pentafoil ( $Z_{55}$ ), secondary trefoil ( $Z_{53}$ ), and secondary spherical aberration ( $Z_{60}$ ), which were significant at  $P<.01$  and secondary tetrafoil ( $Z_{64}$ ) and tertiary astigmatism ( $Z_{62}$ ), which were significant at  $P<.05$  (see Fig 2). Corneal wavefront aberrations in PK eyes were dominated by trefoil ( $Z_{33}$ ) (mean±SD)  $0.35±0.27$  μm, coma ( $Z_{31}$ )  $0.47±0.37$  μm, spherical aberration ( $Z_{40}$ )  $0.17±0.10$  μm, and tetrafoil ( $Z_{44}$ )  $0.12±0.07$  μm (see Fig 2).

The single-value metrics of wavefront aberration



**Figure 1.** The penetrating keratoplasty (PK) group had significantly more higher order corneal wavefront aberrations (calculated for a 4.0-mm pupil) than the normal group at all orders except 10th order (values are means, error bars are +1 standard deviation).



**Figure 2.** The penetrating keratoplasty (PK) group had more higher order corneal wavefront aberrations (calculated for a 4.0-mm pupil) than the normal group for all modes tested except hexafoil (values are means, error bars are +1 standard deviation).

were correlated to the visual performance measures, except for the glare loss measures. Pearson correlation coefficients ranged from 0.27 to 0.72 for correlations between visual performance measures and RMS of each order up to 9th order. Similar correlations occurred between visual performance measures and Zernike modes. Stepwise multiple linear regression was used to identify which of the 33 single-value wavefront aberration metrics, alone or in combination, best predicted each measure of visual performance. The relationships were strong with coefficients of determination ranging from 0.50 to 0.75 for the five raw measures; the linear regression equations are listed in Table 2. The visual performance measure best explained by a single wavefront metric occurred for LCVA and Pupil fraction for wavefront (tessellation) (PFWV(t)):

$$LCVA = 0.18 - 0.77PFWV(t), R^2 = 0.68.$$

This relationship is shown graphically in Figure 3.

### DISCUSSION

In this series, PK patients had inferior visual and optical performance compared to normal patients. The normal control group performed significantly better on

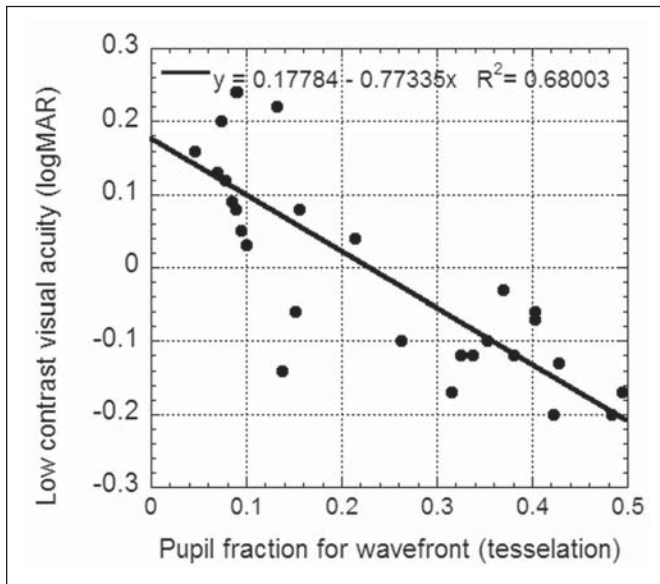
all raw measures of visual performance. However, this may reflect that the normal and PK groups were not matched for HCVA. When adjusting for unequal HCVA by using the difference measures low contrast loss and glare loss, the normal group was only significantly better on low contrast loss (logMAR drop between HCVA and LCVA). This suggests that HCVA is an effective measure for distinguishing between normal and PK patients, but that contrast testing provides additional information. Low contrast visual acuity in PK patients has previously been shown to include sub-normal values<sup>15</sup> and to be indistinguishable from keratoconus eyes in others.<sup>16</sup> Sub-normal contrast sensitivity after PK for keratoconus has also been shown previously.<sup>10-14</sup> Our data support these findings, demonstrating that spectacle-corrected patients with fully healed PK have contrast sensitivity and LCVA inferior to normal patients. Those studies in which PK patients have been shown to have greater deficits in contrast sensitivity than keratoconus patients were either in the early postoperative period<sup>13,30</sup> or during a rejection episode.<sup>31</sup> Studies where PK eyes were indistinguishable from normal eyes were confounded by the inclusion of eyes with rigid contact lens correction, which would reduce corneal wavefront aberrations in the PK eyes.<sup>16</sup>

TABLE 2

**Linear Regression Equations Demonstrating Which Single-Value Wavefront Aberration Metrics Best Explain the Variance in Each Visual Performance Measure**

Visual Performance Measure	Linear Regression Equation	R <sup>2</sup> %
High contrast visual acuity	= -0.23 -0.10Square root of the 2nd moment	50
Low contrast visual acuity	= 0.30 -0.98Pupil fraction for wavefront (tessellation) -0.04Half width at half height	75
Low contrast visual acuity under glare	= -0.18 +0.02Square root of the 2nd moment	54
Pelli-Robson contrast sensitivity	= 1.22 +1.56Area of visibility for rOTF +0.08Half width at half height	68
Pelli-Robson contrast sensitivity under glare	= 2.57 -0.15Entropy -0.35Volume under the neurally weighted OTF +0.02Peak-valley +0.08Half width at half height + 0.12Spatial frequency cutoff of radially averaged MTF	73
Low contrast loss	= -0.13 +0.02Entropy	44
Glare loss (low contrast visual acuity)	Not significant	0
Glare loss (Pelli-Robson contrast sensitivity)	= -0.01 +0.25Volume under OTF normalized by the volume under MTF	36

Note. The metrics reported include pupil plane metrics (Peak-valley, Pupil fraction for wavefront [tessellation]), point spread function metrics (Square root of the 2nd moment, Half width at half height, Entropy), or metrics derived from either the modulation or the optical transfer functions (MTF/OTF) (Area of visibility for rOTF, Volume under the neurally weighted OTF, Spatial frequency cutoff of radially-averaged MTF). Detailed descriptions and mathematical formulations have been published by Thibos et al.<sup>27</sup>



**Figure 3.** The single-value wavefront aberration metric Pupil fraction for wavefront (tessellation) explains 68% of the variance in low contrast visual acuity. This metric is calculated by tessellating the pupil area into 1% sub-apertures and determining the fraction of the pupil area for which the optical quality of the eye is good enough to meet a certain criterion (eg,  $\lambda/4$ ).

Contrast vision decrements were reflected in increased higher order wavefront aberrations, which were at levels comparable to previous studies.<sup>10,15,19</sup> Eyes with PK had increased higher order wavefront aberrations for all Zernike modes and orders, with the trefoil and coma terms, and to a lesser extent spherical

aberration and tetrafoil terms, accounting for the majority of the wavefront error. Single-value wavefront aberration metrics explained up to three-quarters of the variance in low contrast visual performance, but only half of the variance in high contrast visual acuity. This indicates the importance of measuring contrast vision to detect aberration related visual loss, but also indicates the importance of using single-value wavefront aberration metrics, which are predictive of visual performance. Thirty-three wavefront aberration metrics were used in this study and for each visual performance test the metric that best correlated with visual performance was different. This indicates that numerous single value metrics predictive of visual performance exist. Indeed, the relationships between wavefront aberration and visual performance metrics may have been stronger if whole eye aberrations were measured, and if the same pupil sizes were used for visual performance and optical measures.

Because the two glare loss measures did not yield any vision losses in the PK group, which were not identified with LCVA or PRCS testing alone, the main mechanism of visual loss in PK seems to be wavefront aberration rather than light scatter.<sup>15</sup> This same clinical set-up finds large glare losses in cataract because the main mechanism of optical disturbance from cataract is forward light scatter.<sup>21</sup> Because wavefront aberration is the mechanism, visual performance must be pupil dependent. Therefore, the use of natural pupils, which will constrict in a bright glare source,<sup>32</sup> reduces

the chance of finding decreased visual performance under glare due to a reduction in higher order aberrations. This likely explains the insignificant tendency ( $F_{1,26}=1.84$ ,  $P=.19$ ) for Pelli-Robson contrast sensitivity to decrease less in the presence of glare in PK eyes ( $0.03\pm 0.11$ ) compared to the normal group ( $0.10\pm 0.13$ ) (Table 1). Previous small studies that found glare losses in PK greater than those seen in keratoconus included cases in the postoperative recovery period, which may have had graft edema, which would cause glare loss.<sup>11</sup> Although our data suggest glare testing is not generally useful for measuring visual performance in eyes with PK, it may still be useful in the presence of apical corneal scarring or graft edema, eg, in the first month after surgery<sup>30</sup> or after a rejection episode.<sup>31</sup>

Penetrating keratoplasty may provide vision superior to keratoconus, but it does not provide levels of vision as good as normal eyes. The pursuit of improvement in the surgical management of keratoconus requires optical and visual performance testing to establish these improvements. Based on these findings, studies of surgical treatments for keratoconus should include a measure of visual performance in the contrast domain and wavefront aberrations preferably reported as a single-value metric predictive of visual performance.

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