Clinical Investigation into the Vision Performance Provided by the iZon® Spectacle Lens System

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ABSTRACT

Phase 1

Purpose—To objectively quantify the changes in visual performance derived from wearing wavefront-guided lenses (iZon®).

Methods—Eighty-three normally sighted subjects participated, ranging in age from 18 to 36 years of age (average = 25.6 years). Visual assessment consisted of ETDRS acuity, Glare acuity, Environmental Visual Acuity, Pelli-Robson contrast sensitivity, Regan Contrast acuity, MNRead, and SKILL card. Using a randomized double blind crossover design, we tested visual performance under three lens conditions: baseline (habitual) lenses, conventional lenses with regular refraction, and wavefront-guided iZon® Lenses (with iZonik™ material in the middle of the 3-Layer structure).

Results—The results of the current study demonstrated that a new pair of conventional lenses improved vision for most of the assessment measures. More importantly, the study also demonstrated that the iZon® Lenses almost always afforded the best visual performance; iZon® Lenses produced significantly better vision than the baseline assessments. Additionally, for Glare acuity, Low Contrast acuity, MNRead critical print size, and SKILL cards, the iZon® Lenses produced significantly better vision than the new conventional spectacles.

Summary—The observed improvements in visual function with the iZon® Lenses (3-Layer design) indicate that they will provide patients with generally better vision. Importantly, they deliver significant advantages across a range of visually challenging conditions, including glare, low contrast and low luminance.

Phase 2

Purpose—Given the findings of the first phase of this project, we conducted a second experiment to determine the locus of improved visual function with the iZon® Lens system. We examined: the role of the Z-View® Aberrometer refraction, the role of the multi-layer iZon® construction, and the role of the manufacturing laboratory.

Methods—Fifty-two normally sighted subjects, ranging in age from 18 to 36 years, participated. Four lens designs were tested: 1) conventional lenses—traditional refraction, 2) conventional lenses—traditional refraction made at Ophthonix, 3) conventional lenses—Z-View® refraction made at Ophthonix, and 4) iZon® Lenses—Z-View® refraction.

The study employed a randomized, double blind, crossover design. The assessment battery was the same as the one used in Phase 1.

Results—*The role of Z-View® refraction alone*—We found significant differences between the mean values of lens #2 and lens #3 for Regan Low and Intermediate Contrast acuity, and ETDRS acuity. The conventional lens with the Z-View® refraction showed better acuity. *The role of the iZonik™ material alone*—We found significant differences between the mean values of lens #3 and lens #4 for the SKILL card and MNRead critical print size. The iZon® Lens had better performance for these measures. *The role of the manufacturing process alone*—We found significant differences between the mean values of lens #1 and lens #2 for the Regan high and intermediate contrast acuity thresholds, the SKILL card, ETDRS acuity, Glare acuity, and MNRead critical print size.

Summary—These findings suggest that there is an ordered progression of visual benefits derived from the components of the lenses tested in this phase. For conventional lens material, using the Z-View® refraction is better than traditional refraction. Coupling the Z-View® prescription with single layer Ophthonix lens material added better visual function, and the best overall visual performance was gained by combining Z-View® refraction with the 3-Layer iZon® Lens design.

Conclusions—The results of the current studies clearly demonstrate that the iZon® Lens (3-Layer) system provided the best visual performance across a large number of visual function assessments. Whereas, the improvements in performance were small in magnitude, there was a consistent trend for statistically significant better visual performance with the iZon® Lens (3-Layer).

*Note: The iZon® Lens is wavefront-guided, as opposed to wavefront-corrected. Wavefront-guided refers to the use of wavefront technology to incorporate all 2nd to 6th order aberrations in determining the best sphere-cylindrical fit, as opposed to wavefront-corrected that implies correcting individual aberrations. By utilizing a wavefront-guided approach, the iZon® Lens is optimized and unaffected by gaze angle shifts that could result with the programming required in a wavefront-corrected design.

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The authors thank **Professor Ian L. Bailey** of the School of Optometry, University of California, Berkeley for his review of this manuscript and his helpful suggestions. Dr. Ian Bailey is the Professor of Optometry and Vision Science, School of Optometry, University of California, Berkeley. Dr. Bailey is considered a foremost expert in low vision, and he is the recipient of numerous prestigious awards including the Feinbloom Award, the Prentice Medal, the Glenn Fry Award and the Pisart Award.

Phase 1

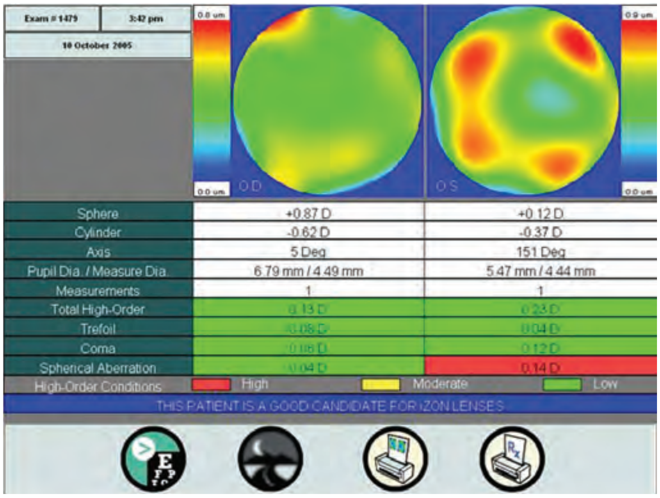
Introduction

The quality of vision is determined by the optical pathway of the eye. This includes factors such as pupil size, and the optical properties of the lens, cornea, aqueous and vitreous. Optical aberrations, in particular, degrade the incoming image quality and as a result, visual acuity and contrast sensitivity may become limited by the retinal image rather than the neural substrate. Typically, the second-order aberrations of defocus and cylinder are measured during conventional refractions, and eyeglasses are prescribed to correct these errors. Although higher-order aberrations are not considered, these optical errors may play a large role in vision. For the average person, higher-order aberrations represent approximately 17% to 20% of the total refractive error.[1] Higher-order aberrations are often the primary source of patients' complaints of poor overall visual quality. Even after an updated refraction and new conventional glasses are prescribed, patients describe "fuzziness" around images, halos and comets from lights at night, and lack of overall clarity of vision, in spite of "seeing" 20/20.

Correcting second-order aberrations using spherical and cylindrical lenses has been practiced for centuries. More recently, technologies have emerged to measure and correct the eye's higher-order aberrations.[2-4] In laboratory experiments, quantifying and correcting low- and higher-order aberrations has been shown to improve visual function.[3,5,6] Until recently, there has been no instrumentation commercially available for clinical measurement of higher-order aberrations, and no options have been available for wavefront-guided lenses. Ophthonix, Inc. (Vista, CA) has recently introduced the Z-View® Aberrometer, a grating-based wavefront aberrometer, designed to rapidly and accurately measure lower- and higher-order aberrations in

Figure 1. Z-View® Aberrometer

Figure 2. Wavefront Maps and Prescription Produced by the Z-View® Aberrometer



patients *(Figure 1)*. The Ophthonix Z-View® Aberrometer is based on a principle of wave optics know as "self-imaging" or the Talbot effect.[7] The second- to sixth-order aberrations, as quantified by the Z-View® Aberrometer, are processed by a proprietary algorithm to determine the best sphere and cylinder back lens surface for each patient (the iZon® Lens) *(Figure 2)*.

In the current study conducted by the authors at the University of Illinois at Chicago, we quantified changes in visual performance derived from patients wearing iZon® Lenses. These lenses are designed to address the visual problems associated with higher-order aberrations including decreased visual acuity, increased glare sensitivity, decreased contrast sensitivity, and nighttime vision problems. In the current study, we assessed the differences in visual performance in normal subjects when wearing iZon® Lenses compared to when wearing conventional lenses with traditional refraction.

Methods

Subjects—We screened 178 normally sighted younger subjects for participation in the study. From this initial group, 93 were identified as candidates for iZon® Lenses. Acceptance of subjects was based on an objective candidacy algorithm designed by Ophthonix to identify those subjects who, based upon their aberration characteristics, would likely benefit from the wavefront-guided iZon® Lens system. Eighty-three subjects completed the entire study. This group was comprised of 37 males and 46 females who ranged in age from 18 to 36 years (average = 25.6 years).

Procedure—This study was approved by the Institutional Review Board at the University of Illinois at Chicago, and informed written consent was obtained

iZon® Lens Candidacy Algorithm

The iZon® Lens candidacy algorithm is based on a distinct clinical investigation conducted by Ophthonix.* This clinical study was designed to develop an empirically derived system that would determine those patients who would most likely benefit from the wavefront-guided iZon® Lenses. The study was conducted at multiple optometric sites in the Southern California area and evaluated subjects' preference for the iZon® Lens compared to a conventional spectacle lens. The multi-layer iZon® Lenses were prescribed from the iZon® Aberrometer, while the conventional single layer lenses were based on manifest refraction. The study was a randomized, double masked design, with 62 subjects who were in good ocular health. Other than the intrinsic differences between the conventional lens and the iZon® Lens systems, all remaining variables were held constant. Subjects wore each lens pair for one week (randomized) and then rated their preference. The data analysis resulted in a regression algorithm that projected preference for the iZon® Lens based on the full 2nd to 6th order refractive profile. The candidacy algorithm is currently employed by practitioners who use the Z-View® Aberrometer to determine which patients will most likely benefit from the iZon® Lens. On average, approximately 65% of patients are candidates.

* iZon® Lens Patient Candidacy Investigation. March 2005. Ophthonix, Inc. Data on file.

after the study was thoroughly explained to each subject. Following acceptance into the study, each subject underwent baseline assessment on the visual test battery described below with their current spectacle lenses (baseline lenses). The subject was then refracted using traditional methods by a licensed optometrist and provided with a typical conventional prescription that accounted for defocus and astigmatism. Wavefront measurements were next taken using the Z-View®.

Two lens designs were tested:

1) **Conventional lenses with lower-order refraction—**sphere and cylinder

2) **iZon® Lenses (3-Layer)—**wavefront-guided sphere and cylinder refraction

Both sets of lenses were made of 1.6-index lens material and contained premium anti-reflective (AR) coatings. The wavefront-guided iZon® Lenses consisted of two 1.6 index lenses with a layer of photo-polymer sandwiched in between *(Figure 3)*. Pupil distance and segmental height were measured, and lenses were mounted in frames and aligned. Identical frames were used for making both pairs of spectacles—one pair made using Z-View® refraction, and the second pair made using conventional refraction.

Experimental Design

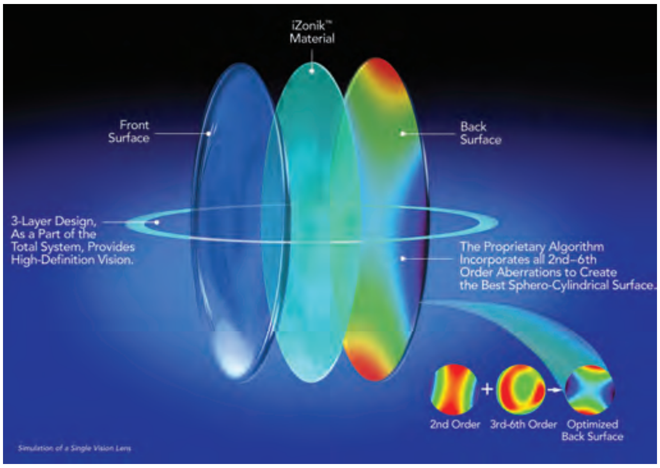
The study employed a randomized, double-blind, crossover design. A subject was given a pair of eyeglasses, with the assigned order randomized. The subject was asked to wear the glasses for two weeks, to use the glasses for all tasks, and to take note of the quality of their vision with the lenses. After the initial two-week period, the subject returned for an assessment. Following this assessment, the subject was given the other eyeglasses, asked to wear them for two weeks and to take note of their vision quality during this time period. After this two week period, the subject returned for a final assessment. Neither the subject nor the experimenter knew the order in which the lenses were worn or which lenses were being evaluated at any time during the data collection.

Assessments

At baseline (with subjects wearing their current lenses) and after each two-week period (with subjects wearing the respective test lenses), the following battery of visual function tests was administered:

Acuity—Visual acuity is a measure that reflects the smallest visual target that can be identified at a distance.

Figure 3. iZon® Lens Structure (3-Layer)



iZon® Lens Structure (3-Layer)

The wavefront-guided iZon® Lens is a unique design, with a three layer structure. The mid-layer iZonik™ material is a photo-polymer that is sandwiched between separate back and front lenses. All three layers are 1.6 index material. The correction for the iZon® Lens is derived from all 2nd to 6th order aberrations of the eye as measured by the Z-View® Aberrometer. The aberrations are analyzed and manipulated by a proprietary algorithm—the second of two used in the iZon® Lens process—to determine the best sphere-cylindrical fit for the back surface. The iZon® Lens is wavefront-guided, as opposed to wavefront-corrected. Wavefront-guided refers to the use of wavefront technology to incorporate all 2nd to 6th order aberrations in determining the best sphere-cylindrical fit, as opposed to wavefront-corrected that implies correcting individual aberrations. By utilizing a wavefront-guided approach, the iZon® Lens is optimized and unaffected by gaze angle shifts that could result with the programming required in a wavefront-corrected design.

In the current study, we used a standard clinical acuity chart (ETDRS and ETDRS Illuminator Cabinet, Precision Vision, La Salle, IL) to measure the smallest letter optotype that could be seen. This chart presents rows of five identical size letters at high contrast *(Figure 4)*. The size of the letter is constant within a line, but the letter size decreases by 0.1 log units between lines. In scoring the chart, each letter is given a value of 0.02 log units. The subject reads the letters beginning with the largest letter at the top of the chart and continues to read progressively smaller letters. The acuity scores are based on the total number of letters read. Visual acuity is reported as log minimum angle of resolution (logMAR). For a letter on the 20/20 line, the stroke width of the elements of a letter is 1 minarc or 0.0 logMAR.

Figure 4. ETDRS Acuity

5 letters per row with proportional spacing
Each letter = 0.02 logMAR
Each line = 0.1 logMAR
20/20 = 0 logMAR

Glare Acuity—The presence of glare reduces visual acuity. In the present study, we assessed the relative effects of glare on acuity for each of the lenses by displaying ETDRS charts on transparencies and back-lighting the charts with a bright light source (440 cd/m2) *(Figure 5)*. Once again, acuity was reported as logMAR of the smallest letter identified.

Environmental Visual Acuity Course—For the standard clinical test of visual acuity, letters of high contrast and uniform font are used, and the subject is stationary and focused on the single task of identifying letters. In the current study, we wished to assess acuity while under more natural conditions, i.e., when the subject was navigating a course and viewing targets of different sizes, fonts, and contrasts. To accomplish this, we designed an "environmental visual acuity" course in the hallways of the University of Illinois Eye and Ear Infirmary building *(Figure 6)*. The subject was instructed to follow a predetermined walking path and asked to read posted signs (such as room numbers, department identification signs, and other directional information signs). The subject stopped walking when they could read a sign, and, if correct, the distance between the subject and the sign was measured using a Leico Disto™ laser distance meter. Based on the size of the letters on each sign and the distance at which they could be read, an equivalent visual acuity in logMAR was calculated. A different course was used in each of the three assessments.

Figure 5. Glare Acuity

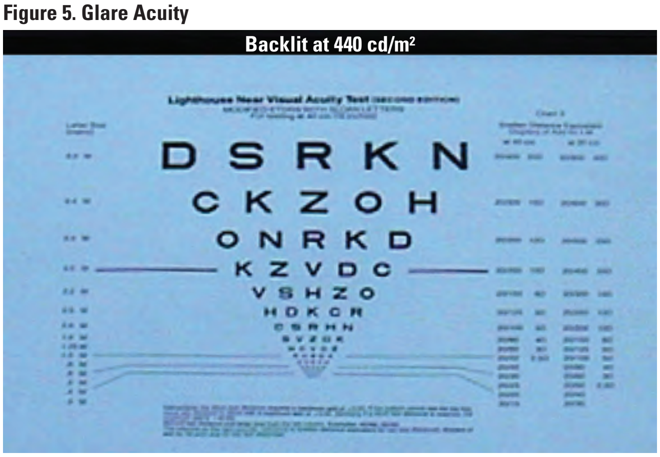
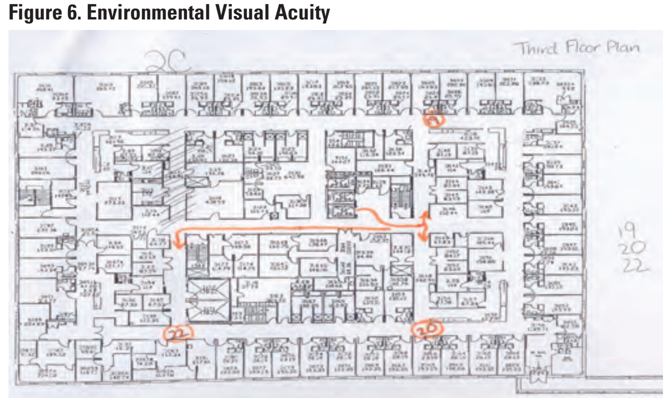


Figure 6. Environmental Visual Acuity



Contrast Thresholds—The contrast of a visual target is commonly measured as the ratio of the luminance of the light elements to the luminance of the dark elements. As this ratio decreases, acuity decreases. The lowest contrast at which a target of a given size can be identified is its contrast threshold. In general, contrast thresholds are higher for smaller targets (higher spatial frequencies) than for larger targets (lower spatial frequencies). In the current study, contrast threshold for letter optotypes was measured using two different charts: the Pelli-Robson (Pelli, Robson, & Wilkins) and the Regan Contrast acuity charts (Regan & Neima).[8,9]

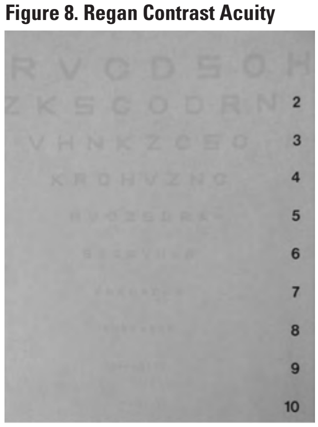
Pelli-Robson Contrast Sensitivity—This chart contains letter optotypes of a single size (2.8 degrees at 1 meter). On each row of the card are two groups of three letters each, with the groups differing in contrast *(Figure 7)*. The contrast of each succeeding group is lower by

50.1% than that of the preceding group, beginning at 90% (Weber contrast) and decreasing to 0.5%. The subject is required to read the letters from high to low contrast until two of the three letters in a group were named incorrectly. The subject's score was based on the previously correctly identified group in log units.

Figure 7. Pelli-Robson Contrast Sensitivity

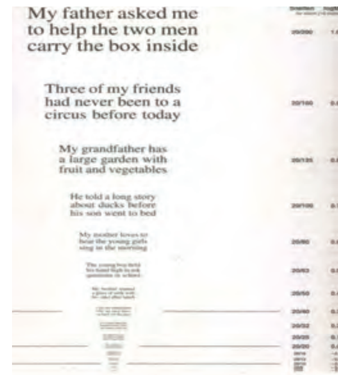
Regan Contrast Acuity—This test consists of charts of letter optotypes that decrease in size by 79% per row from the top to the bottom of the chart *(Figure 8)*. The smallest letters are equivalent to a Snellen acuity of 6/3. The contrast of all of the letters on a single chart is constant at 96%, 11%, or 4%. The subject was required to identify as many letters as possible on each chart. For the purpose of the present study, the results were reported as logMAR equivalents.

Figure 8. Regan Contrast Acuity



MNRead—The MNRead is a test of reading speed as a function of text size. The test contains 19 sentences of different font sizes, ranging from 1.3 logMAR to -0.5 logMAR (Snellen equivalents from 20/400 to 20/6) at a viewing distance of 40 cm *(Figure 9)*. Each sentence contains 60 characters (including spaces), printed as three lines with even left and right margins. The vocabulary was selected from words appearing with high frequency in second- and third-grade level reading material. The results were plotted as reading speed as a function of font size. For smaller text sizes, reading speed is slow, and as text size increases, reading speed increases. At larger text sizes, reading speed reaches an asymptote, and within a range of larger text size, reading speed does not increase further. Three measures of reading are obtained from the MNRead: reading acuity—the average reading speed before speed becomes limited by print size, maximum reading speed—the reading speed at which performance is not limited by print size, and critical print size—the smallest print that supports the maximum reading speed.

Figure 9. MNRead



Statistical Analysis

A one-way repeated measures analysis of variance was performed on the data for each assessment test. The significance of the main effect of lens type was tested. For those results where there was a significant main effect, post-hoc tests of significant differences between means were performed using Tukey tests for all pair wise comparisons.

Results and Discussion

Baseline Findings:

Refractions: Conventional spherical refraction ranged from +3.75 D to -7.00 D (average = -2.3 D), and astigmatic errors ranged from 0.0 D to -3.75 D (average = -0.43 D) *(Figure 10)*. Z-View® low-order refractions ranged from +4.62 D to -6.75 D (average = -2.01 D), and astigmatic error range from 0.0 D to -4.0 D (average = -0.72 D). The differences between Z-View® low-order refraction and conventional low-order refractions averaged 0.18 D (range +1.37 D to -1.25 D) for the spherical correction and -0.30 D (range +0.5 D to -1.75 D) for the cylinder *(Figure 11)*.

The total higher-order aberrations, as measured with the Z-View® Aberrometer, average 0.21 D (range 0.01 D to 0.79 D). The third-order aberrations were distributed as follows: the average trefoil error was 0.11 D (range 0.0 D to 0.44 D), the average coma was 0.12 D (range 0.01 D to 0.64 D), and the average spherical error was 0.08 D (range 0 D to 0.29 D).

Visual acuities with baseline lenses averaged -0.06

Figure 10. Low Order Aberrations Conventional Refraction

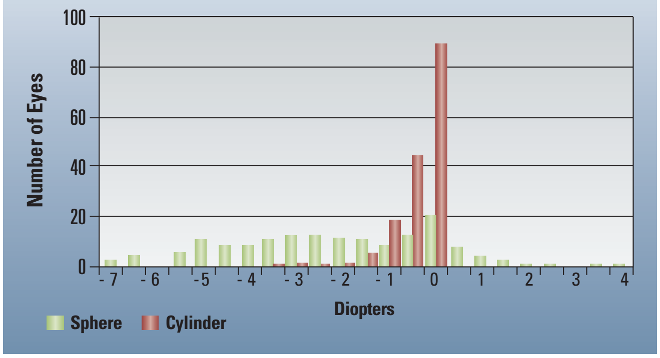
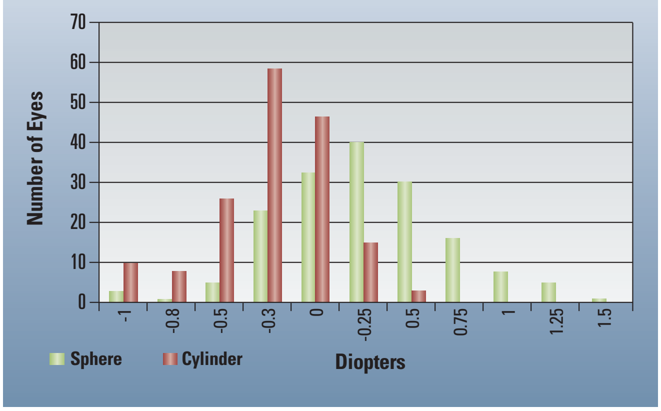


Figure 11. Differences in Low Order Refraction
Z-View® Rx vs. Conventional Rx



logMAR (approximately 20/18.5) and ranged from -0.20 to 0.22 logMAR (approximately 20/13 to 20/33). Baseline Pelli-Robson contrast sensitivity averaged 1.88 and ranged from 1.65 to 2.05.

Effects of Lenses:

ETDRS Acuity—Mean and standard error of the mean (±SEM) ETDRS acuity thresholds (in logMAR) for the three lens conditions are plotted in Figure 12 for the 83 subjects. Smaller logMAR values represent better acuity. The results showed better acuity (lower logMAR values) with the conventional lenses relative to baseline and even greater acuity gain with the iZon® Lenses (3-Layer). iZon® Lenses produced an average gain of three letters over baseline (one line of acuity = five letters). A one-way repeated measures ANOVA yielded a significant main effect ($P< 0.001$) of lens. Tukey post-hoc tests found significant differences between baseline (subjects current Rx lens) and conventional lenses ($P = 0.001$) and between baseline and iZon® Lenses ($P< 0.001$).

Glare Acuity—Average (±SEM) glare acuity thresholds (in logMAR) for the three lens conditions are plotted in Figure 13 for the group of 83 subjects. Smaller logMAR values represent better acuity. The results showed better glare acuity (lower logMAR values) with the conventional lenses relative to baseline and the best acuity with the iZon® Lenses. iZon® Lenses produced an average gain of 2.5 letters in acuity over baseline. A one-way repeated measure ANOVA yielded a significant main effect ($P = 0.001$). Tukey post-hoc tests showed significant differences between baseline and iZon® Lens conditions ($P < 0.001$) and between iZon®

Figure 12. ETDRS Acuity

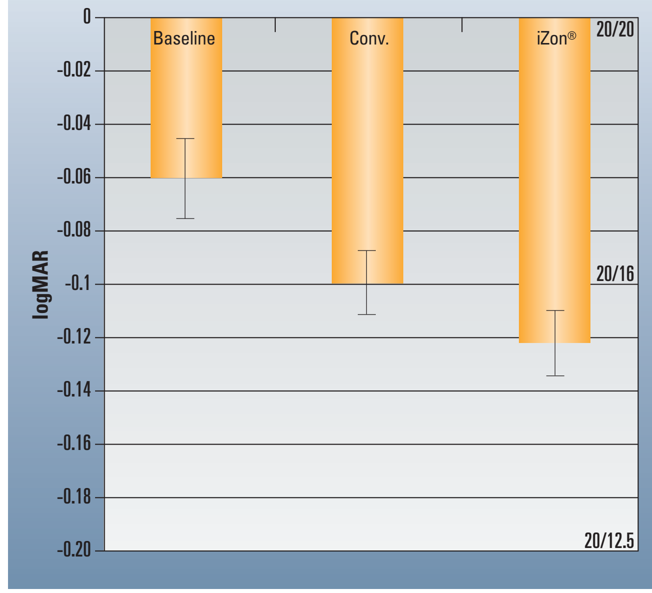
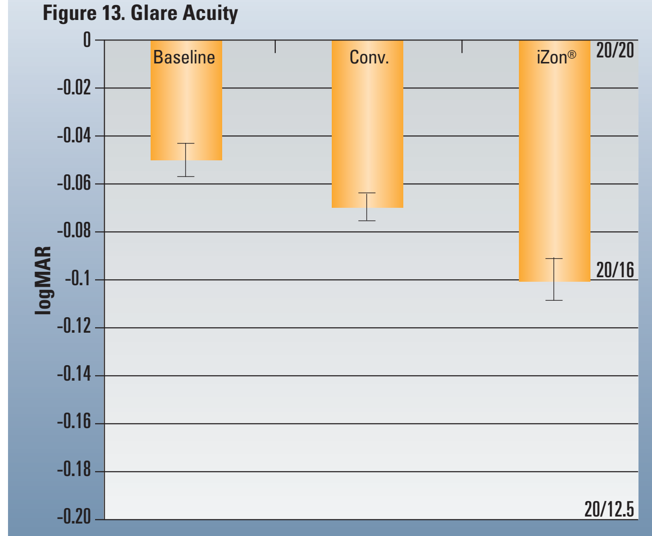


Figure 13. Glare Acuity



Lenses and conventional lenses (P = 0.05). Glare acuity with the iZon® Lenses was significantly better than with either the baseline or the conventional lenses.

Environmental Visual Acuity—A one-way repeated measures ANOVA on ranks failed to yield a significant main effect of lens (P = 0.54) for reading signs accurately while walking through the course. However, when the low-contrast signs (< 35% contrast) were analyzed separately, the average acuity for the baseline condition was 0.14 ± 0.03 logMAR. With the conventional lenses, the average dynamic acuity was 0.12 ± 0.03 logMAR. The best visual acuity was obtained with the iZon® Lenses (0.08 ± 0.03 log-MAR) *(Figure 14)*. Acuity while navigating the course was three letters better with the iZon® Lenses than baseline and this represented an increase (or improvement) of 20% in the distance at which low-contrast signs could be read.

Pelli-Robson Contrast Thresholds—Average (±SEM) Pelli-Robson values for the three lens conditions are plotted in Figure 15 for the 83 subjects. Higher values represent better threshold sensitivity. Values were higher (better visual function) for both the conventional and iZon® Lenses conditions (1.91 ± 0.007 and 1.90 ± 0.008 respectively) compared to the baseline condition (1.88 ± 0.008). A one-way repeated measures ANOVA on ranks yielded a significant main effect of lens (P = 0.001). Tukey post-hoc tests found significant differences between baseline and conventional conditions (P = 0.001) and between baseline and iZon® Lens conditions (P = 0.008).

Regan Contrast Acuity—Average values (±SEM) of high contrast acuity thresholds (in logMAR) for the three lens conditions are plotted in Figure 16. Smaller logMAR values represent better contrast acuity. The results showed better contrast acuity (lower logMAR values) with the conventional lenses relative to baseline, and the best contrast acuity with the iZon® Lenses. iZon® Lenses produced an average gain in contrast acuity equivalent to two letters over baseline (1 line of acuity = 5 letters). A one-way repeated measures ANOVA yielded a significant main effect of lens on acuity thresholds (P < 0.001) for the highest contrast chart. As might be expected, the magnitude of this effect was similar to that seen for the high contrast acuity as measured with the ETDRS chart. Tukey post-hoc tests showed significant differences between baseline and iZon® Lens conditions (P < 0.001) and between the baseline and conventional lenses (P < 0.04).

For the intermediate contrast chart (11%), a one-way repeated measures ANOVA yielded a significant main effect (P < 0.001). The results showed better contrast acuity (lower logMAR values) with the conventional lenses relative to baseline and the best contrast acuity with the iZon® Lenses *(Figure 17)*. This represented a gain of 2.5 letters on the Regan intermediate contrast chart when viewing through the iZon® Lenses.

Figure 14. Environmental Visual Acuity Low Contrast (36%) Signs

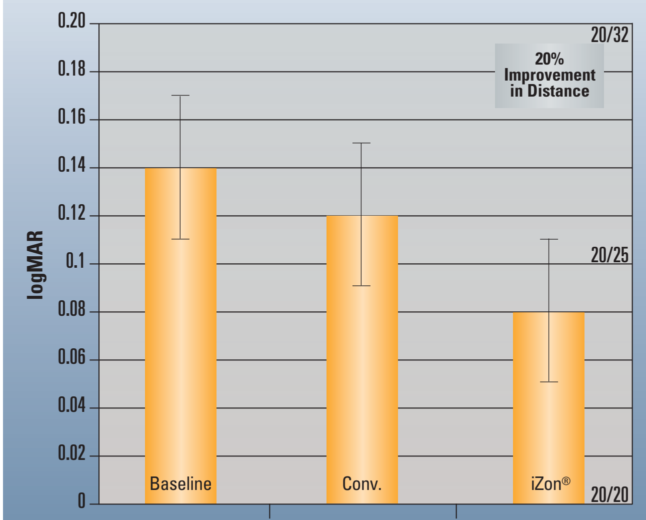


Figure 15. Pelli-Robson Contrast

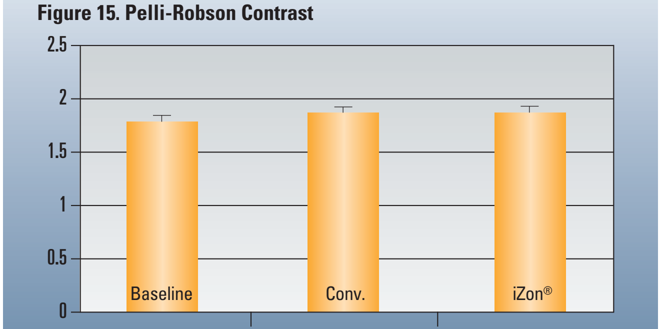


Figure 16. Regan High Contrast (96% Contrast)

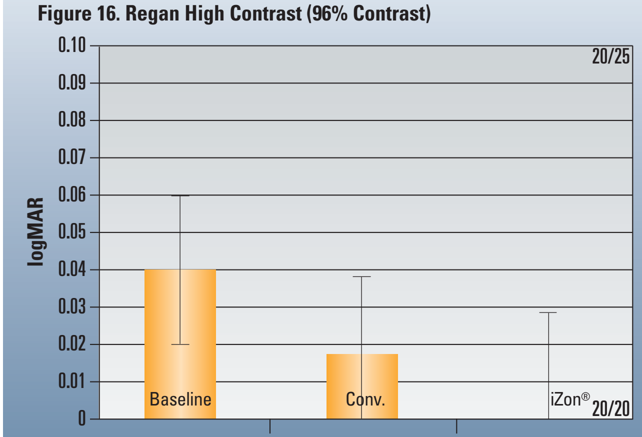


Figure 17. Regan Intermediate Contrast (11% Contrast)

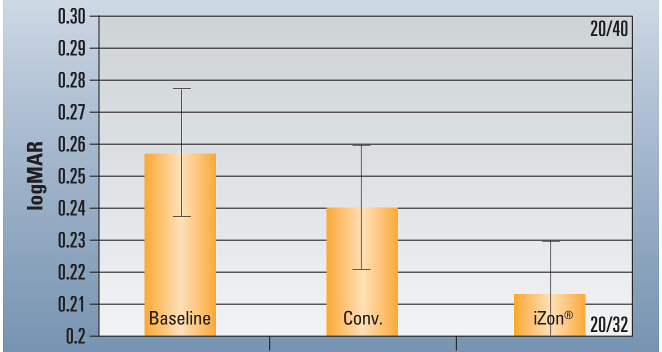
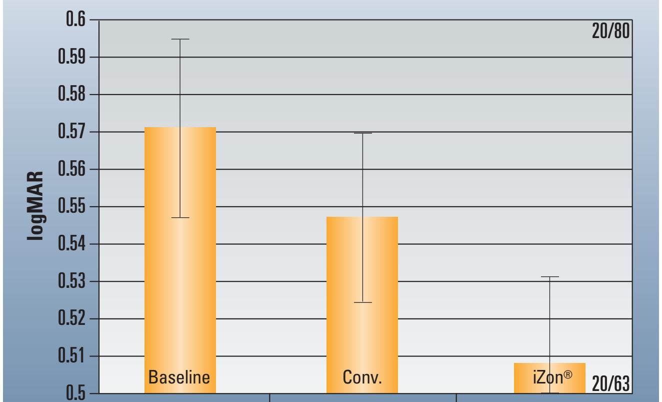


Figure 18. Regan Low Contrast (4% Contrast)



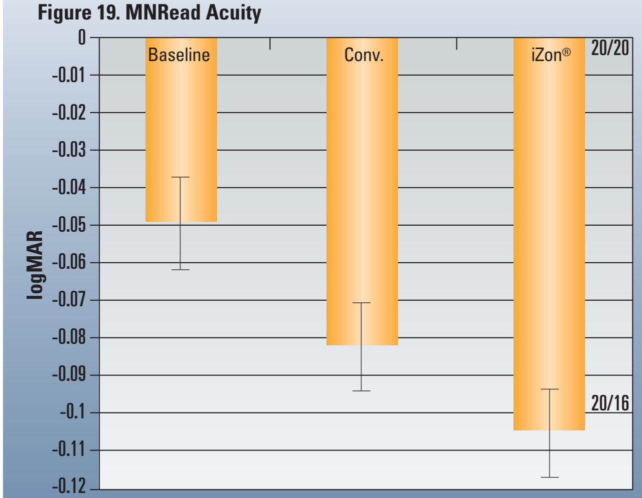
Tukey post-hoc tests showed significant differences between baseline and iZon® Lens conditions ($P < 0.001$) and between the conventional and iZon® Lenses ($P = 0.02$). That is, conventional lenses improved intermediate contrast acuity, but contrast acuity with the iZon® Lenses was significantly better than with either the baseline or the conventional lenses.

As expected, overall acuities were poorest for the low-contrast chart (4% contrast). A one-way repeated measures ANOVA yielded a significant main effect ($P < 0.001$) *(Figure 18)*. The mean contrast acuity with the iZon® Lenses (0.50 ± 0.02 logMAR) was lower (better vision) than average baseline acuity (0.57 ± 0.02 logMAR) and lower than the average acuity of the conventional lenses ($P = 0.006$). For low-contrast acuity, iZon® Lenses performed significantly better than either the baseline or the conventional lenses.

MNRead

Reading Acuity—Average threshold acuity values (±SEM) (in logMAR) for reading under the three lens conditions are plotted in Figure 19 for the 83 subjects. Smaller logMAR values represent better acuity. The results showed better acuity (lower logMAR values) with the conventional lenses relative to baseline and the best acuity gain with the iZon® Lenses. iZon® Lenses produced an average gain of a three letters in acuity over baseline (1 line of acuity = 5 letters). A one-way repeated measures ANOVA yielded a significant main effect ($P < 0.001$). The mean acuity with the conventional lenses (-0.082 ± 0.01 logMAR) and with the iZon® Lenses (-0.104 ± 0.01 logMAR) were lower than that at baseline (-0.049 ± 0.01 logMAR). A gain of approximately 1.5 letters was seen in reading acuity using the iZon® Lenses. This value is similar to other iZon® related gains in acuity seen in our other measures. Tukey post-hoc tests showed significant differences between baseline and iZon® Lenses ($P < 0.001$) and between baseline and conventional lenses ($P = 0.02$).

Figure 19. MNRead Acuity



Maximum Reading Speed—Average (±SEM) reading rates (words per minute: wpm) for the three lens conditions are plotted in Figure 20 for the 83 subjects. Higher reading rates represent better visual performance. Average reading rate was higher with the conventional lenses (281 ± 5.6 wpm) than for the baseline condition (260 ± 4.8 wpm) and the iZon® Lenses (278 ± 5.5 wpm). A one-way repeated measures ANOVA yielded a significant main effect ($P < 0.001$). Tukey post-hoc tests showed significant differences between baseline and iZon® Lens conditions ($P < 0.002$) and between mean baseline and mean conventional lenses ($P < 0.001$).

Critical Print Size—The average (±SEM) smallest font sizes (in logMAR) at which the maximum reading rates were obtained for the three lens conditions are plotted in Figure 21 for the 83 subjects. These data are

Figure 20. MNRead Maximum Speed

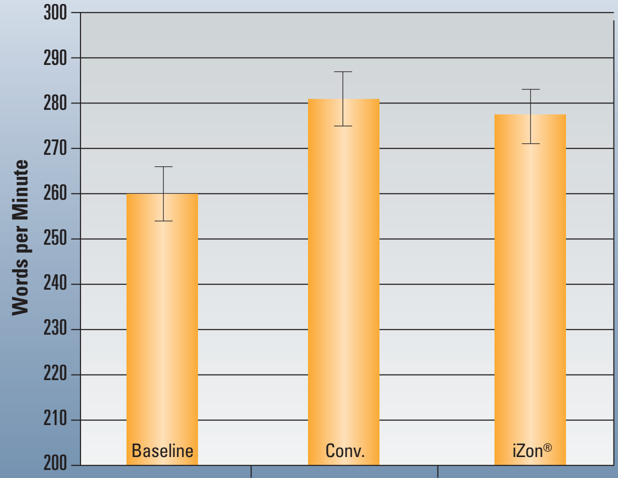
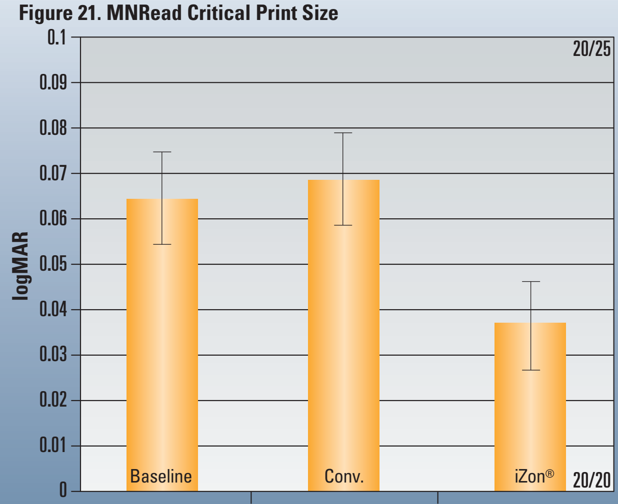


Figure 21. MNRead Critical Print Size



also plotted in logMAR where smaller values represent better performance. The conventional lenses produced CPS values that were statistically equivalent to the baseline values. The iZon® Lenses produced the best performance. A one-way repeated measures ANOVA yielded a significant main effect (P = 0.05). The mean critical print sizes with the iZon® Lenses (0.037 ± 0.01 logMAR) was lower than that at baseline (0.064 ± 0.01 logMAR) and with the conventional lenses (0.069 ± 0.01 logMAR). Tukey post-hoc tests showed that the iZon® Lenses were statistically better than both baseline and conventional lenses. The difference between baseline and iZon® Lens conditions was significant at P < 0.05, and the difference between mean conventional and mean iZon® Lenses was significant at P = 0.04.

Summary—Phase 1

The results of Phase 1 demonstrated that a new pair of conventional lenses improved vision for most of the visual functions assessed. However, the study also demonstrated that, for all but one measure, iZon® Lenses (3-Layer design) produced significantly better vision than the baseline assessments (subjects' current lenses) and frequently afforded better visual performance than the conventional lenses. For every measure, iZon® Lenses produced significantly better vision than the baseline assessments. Specifically, the iZon® Lenses produced statistically better vision than new conventional spectacles on glare, contrast acuity and reading CPS *(Figure 22)*.

Our findings of statistically significant improvement in visual acuity and contrast sensitivity at high- and mid-spatial frequencies are consistent with findings reported obtained using higher-order monochromatic wavefront corrections in experimental laboratory-based systems.[3,5,6] For example, Yoon and Williams found contrast benefits to range from three- to five-fold at mid spatial frequencies to approximately two-fold at higher spatial frequencies (32 c/deg).[6] Guirao *et al.*, found similar average benefits for a large number of normal subjects, although the benefit varied between subjects.[5] Applegate *et al.* reported that the greatest impact of improved optics

Figure 22. Summary (N=83)

Results	ETDRS Acuity	GLARE Acuity	Pelli-Robson Contrast	Regan High 96%	Regan Int 11%	Regan Low 4%	MNRead Acuity	MNRead Speed	MNRead CPS
Baseline (current lenses)	-0.06	-0.05	1.88	0.040	0.257	0.571	-0.049	260	0.064
Conventional	-0.10	-0.07	1.91	0.018	0.240	0.547	-0.082	281	0.069
iZon® (3-Layer)	-0.12	-0.10	1.90	0.000	0.213	0.508	-0.104	278	0.037
Significance of Differences									
iZon® vs. Baseline	0.001	0.001	0.008	0.001	0.001	0.001	0.001	0.002	0.05
iZon® vs. Manifest	0.250	0.05	0.88	0.125	0.02	0.006	0.21	0.69	0.04

Yellow equals best performance Green equals statistical significance at 95% Blue equals statistical significance ≥ 80%

were for mesopic low-contrast stimuli, with photopic high-contrast vision relatively insensitive to corrections.[10]

Having found statistically significant improvement in visual function for the iZon® Lens, questions of clinical significance now can be addressed. The improvements in acuity with iZon® Lenses ranged from two to three letters, or 40 to 60% of a line of acuity. What is the clinical value of this finding? In real world terms, higher visual performance is typically required under conditions of reduced visual salience. For example the following factors can significantly reduce visual performance: small target size, glare caused by reflected sunlight during the day, headlights and illuminated bright signs at night, and low contrast of text and object edges (e.g., stairs). The observed improvements in visual function with the iZon® Lenses (3-Layer design) indicate that they will provide patients with generally better vision. Importantly, they deliver significant advantages across a range of visually challenging conditions, including glare, low contrast and low luminance.

Phase 2

Given the findings of the first phase of this project, we conducted a second experiment to determine the locus of improved visual function with the iZon® Lens system. The variables that were tested included:

1) The role of the Z-View® refraction.

2) The role of the 3-Layer iZon® Lens with iZonik™ material.

3) The role of the manufacturing laboratory.

Method

Fifty-two of the eighty-three subjects from Phase 1 were recruited for Phase 2 and signed informed consent forms to participate prior to the second phase of the study. The average age of this group of subjects was 25 years of age, ranging from 18 to 36 years of age.

Procedure—Four lens designs were tested:

1) **Conventional**: Traditional refraction (with standard lower-order correction of sphere and cylinder), 1.6 Index, premium AR coating—made at a leading commercial laboratory.

2) **Rx-1 Layer**: Traditional refraction, 1.6 Index, Ophthonix AR coating—made at Ophthonix.

3) **Zx-1 Layer**: Z-View® refraction, 1.6 Index, Ophthonix AR Coating—made at Ophthonix.

4) **iZon® (3-Layer design)**: Z-View® refraction, 1.6 Index, Ophthonix AR coating—made at Ophthonix.

Identical frames were used for making all pairs of spectacles.

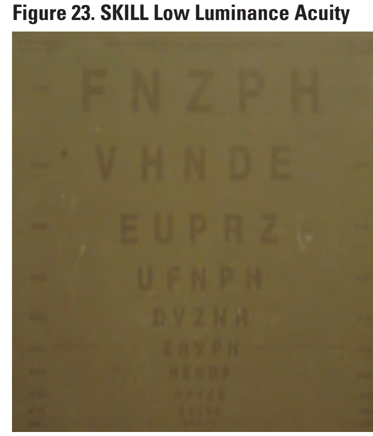
Experimental Design

The study employed a randomized, double-blind, crossover design. Each subject was given a pair of eyeglasses (the assignment of order of the four lenses was counterbalanced across subjects). Each subject was asked to wear the glasses for one week. They were asked to use the glasses for all tasks and to take note of the quality of their vision with the lenses. After the one-week period, the subject returned for an assessment. Following the assessment, the subject was given a second pair of eyeglasses and again asked to wear them for the next week. At the end of that week, the subject returned for a second assessment. This schedule and routine continued until each subject wore all four lens pairs. The lenses were virtually identical in appearance. Visual cues based on the color of the lens substrate or the surface coatings, that might help identify differences between lenses, were extremely subtle. Neither the subjects nor the experimenters knew the order in which the lenses were worn, or which lenses were being evaluated at any time during the data collection.

Assessments

The assessment battery was the same as the one used in Phase 1, with one addition. The Smith-Kettlewell Institute Low Luminance (SKILL) Card was used to measure spatial vision under conditions of reduced contrast and luminance *(Figure 23)*. The SKILL card consists of two acuity charts mounted back to back. One side has a chart with black letters on a dark gray background designed to simulate reduced contrast and luminance conditions, similar to conditions encountered under dim light, veiling luminance, and/or at night. The other side has a high-contrast, black-on-white letter chart. We used the darker side for assessment of lens performance in the present study.

Figure 23. SKILL Low Luminance Acuity



Results and Discussion

Using three planned comparisons (Bonferroni P = 0.0017), we assessed the following for each task:

The role of Z-View® refraction alone—We compared performance when wearing lens #2 (traditional Rx-1 Layer) to performance when wearing lens #3 (Z-View® Zx-1 Layer). The only difference between these two lenses was the procedure for determining

Figure 24. Regan Low Contrast

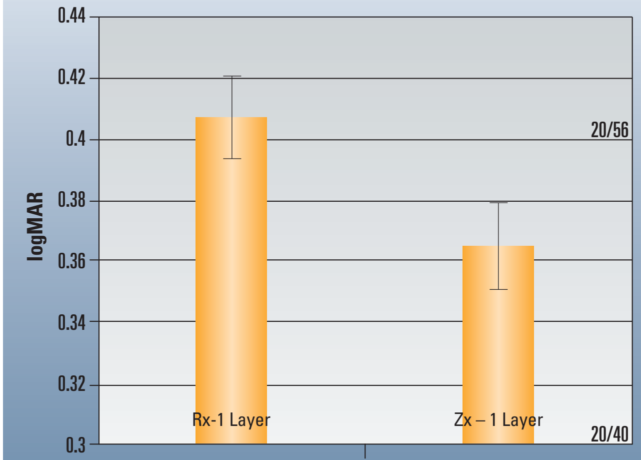


Figure 25. ETDRS Acuity

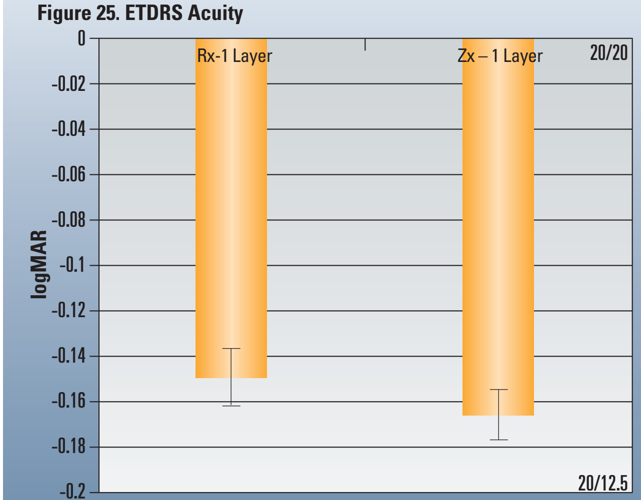
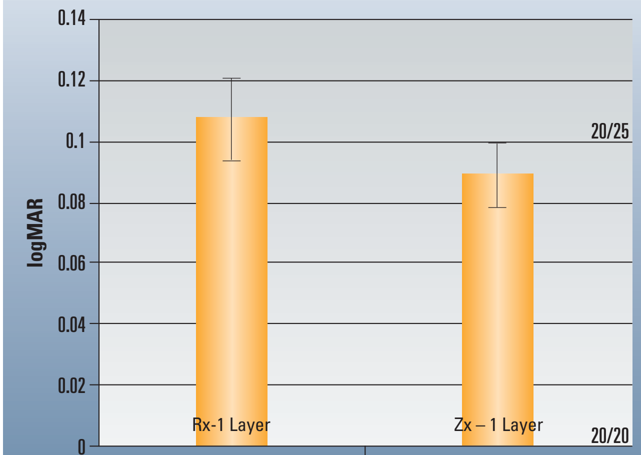


Figure 26. Regan Intermediate Contrast



the refraction.

A significant difference was found between the mean values for the Regan low-contrast acuity thresholds (P = 0.006). The average low-contrast acuity with the Z-View® refraction on a 1-Layer Lens was 0.37 ± 0.014 logMAR *(Figure 24)*. In comparison, when wearing the Rx-1 Layer lenses average Regan low-contrast acuity was worse (0.41 ± 0.13 logMAR). Differences between the means for the ETDRS chart were significant at P = 0.18 and the Regan intermediate contrast chart at P = 0.14 *(Figures 25 and 26)*.

The role of the iZonik™ material alone—We compared performance when wearing lens #4 (iZon® 3-Layer Lens) to performance when wearing lens #3 (Zx-1 Layer). In this comparison, the only difference between these lenses was the material.

A statistically significant difference was found between the mean values for the SKILL Card (P = 0.04) *(Figure 27)*. Average acuity, as measured with MNRead critical

Figure 27. SKILL

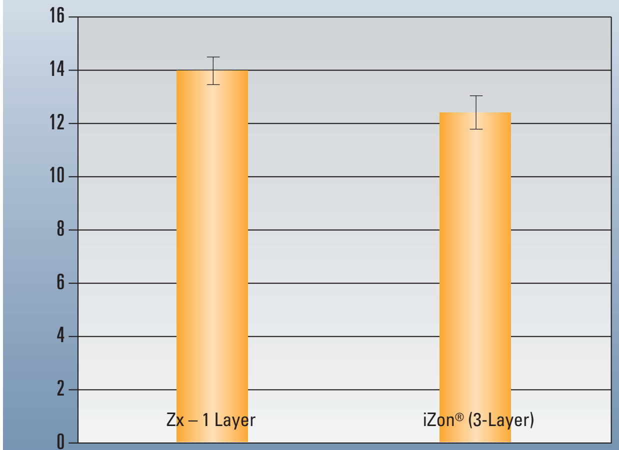
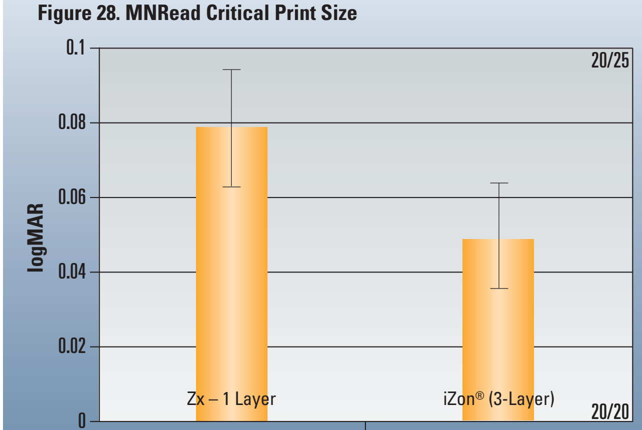


Figure 28. MNRead Critical Print Size



print size (CPS), was statistically different between the two lenses (P = 0.15) *(Figure 28)*.

The role of the manufacturing process alone—We compared performance when wearing lens #1 (Conventional) to performance when wearing lens #2 (Rx-1 Layer). In this comparison, the only difference between these lenses was the lab where the lenses were made.

Significant differences were found between the mean values for the Regan intermediate (P = 0.05) and high contrast acuity thresholds (P = 0.16) *(Figures 29 and 30)* and the SKILL card (P = 0.05) *(Figure 31)*. Additionally, differences between the means reached statistical significance for the ETDRS chart at P = 0.20 *(Figure 32)*, Glare acuity at P = 0.16 *(Figure 33)*, and MNRead critical print size at P = 0.08 *(Figure 34)*.

Summary—Phase 2

These findings suggest that there is an ordered progression of visual benefits derived from the components of the lenses tested in this phase (as illustrated by *Figures 35 and 36*). Using the Z-View® refraction with conventional lens material made at an outside lab resulted in similar or better performance than a traditional refraction coupled with the conventional lens. Coupling the Z-View® prescription with single layer iZonik™ lens material added better visual function on some measures. The best overall visual performance was gained by coupling Z-View® refraction with a 3-Layer lens iZon® Lens design.

Conclusion

The results of the current studies clearly demonstrate

Figure 29. Regan Intermediate Contrast

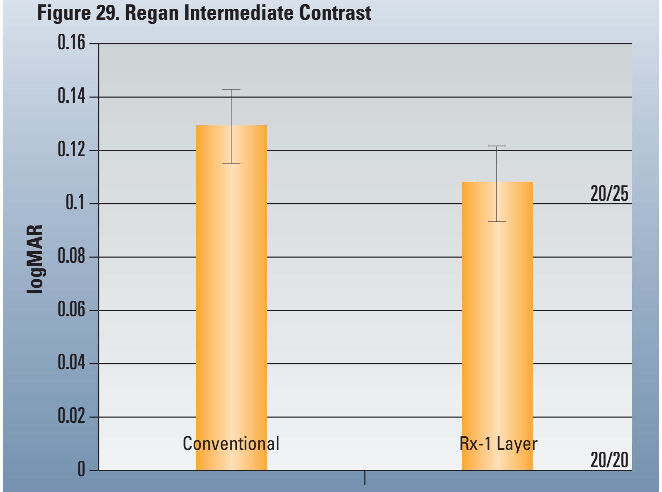


Figure 31. SKILL

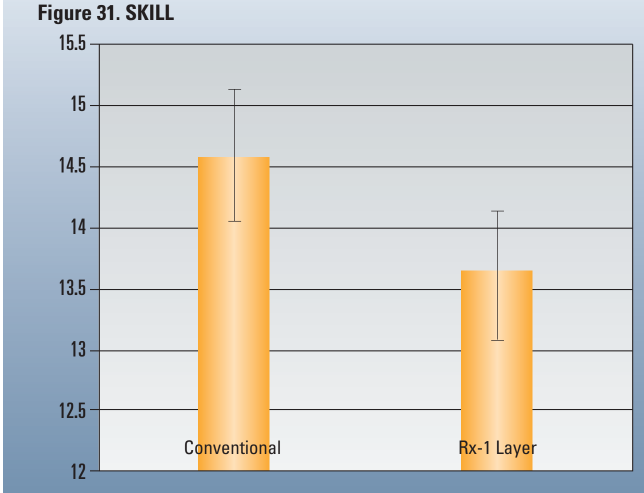


Figure 30. Regan High Contrast

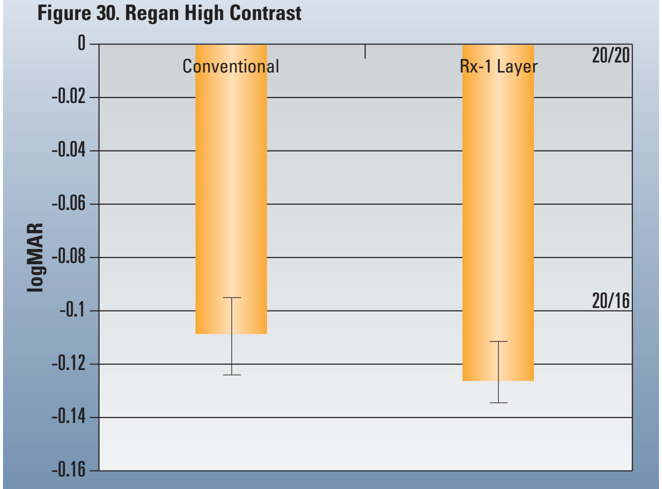
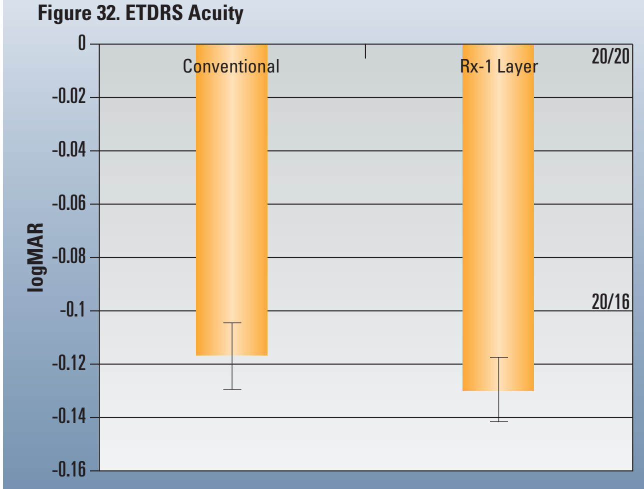
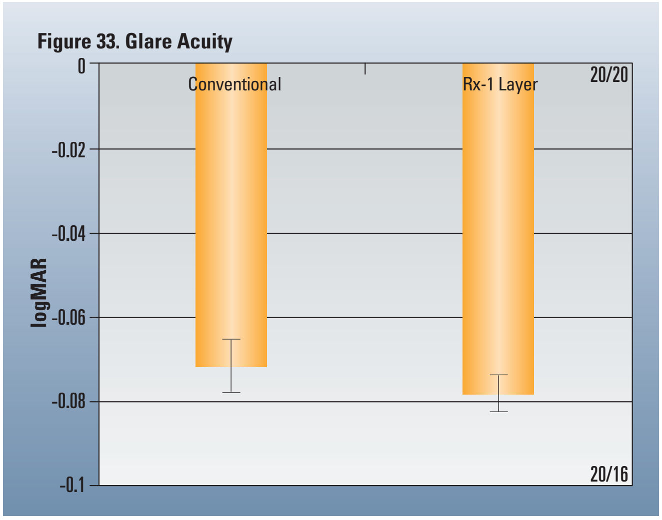
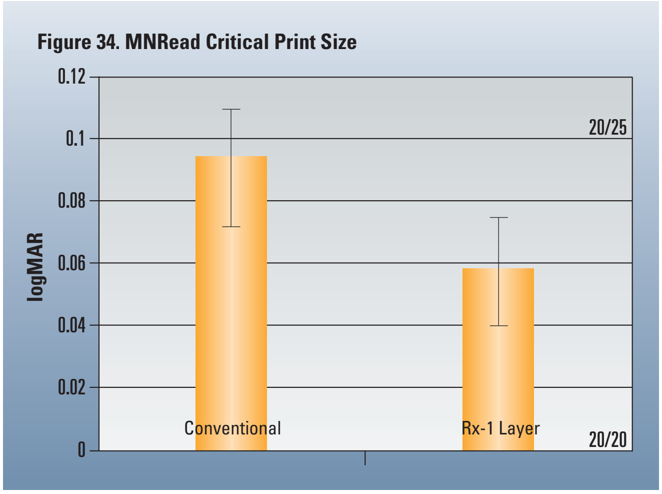


Figure 32. ETDRS Acuity







that the iZon® Lens system (3-Layer Design) provides the best visual performance across a variety of visual function assessments. For every measure, iZon® Lenses (3-Layer) produced significantly better vision than the baseline refractive correction (subjects' current lenses). Additionally, the iZon® Lenses produced significantly better vision than the new conventional spectacles for glare acuity; low, intermediate, and high contrast acuity; MNRead; and SKILL card *(Figure 36)*. These statistically significant improvements, particularly in acuity and contrast sensitivity, are consistent with those visual performance improvements observed in experimental laboratory-based systems using higher-order wavefront correction.

Each of the assessments that we used in this study has a corollary in real-world vision. For example, in the laboratory, glare acuity was best with the iZon® Lenses (3-Layer). Consumers face glare situations each and every day. In the early morning or at sunset, a person may have difficulty seeing an oncoming car with the sun as a backdrop or tracking a golf ball they just struck on a sunny day. Glare acuity can also affect individuals when they are indoors, such as in an auditorium with high-wattage overhead lights. The iZon® (3-Layer) Lens also increased the distance at which signs could be read while navigating an indoor course (Environmental Visual Acuity). In everyday life, when a consumer walks into a supermarket, they are likely to encounter lengthy aisles, with overhanging signs on either end that indicate the grocery items located there. For many, identifying what is at the far end of an aisle may require walking down the aisle to get closer to the sign. The Environmental Visual Acuity test results allowed us to determine how much farther away consumers can read such signs using the iZon® Lens (3-Layer). Based on our research, the iZon® Lens (3-Layer) provided a 20% improvement in viewing distance for reading signs.

Our results also demonstrated that measures of MNRead acuity, (e.g., reading acuity and critical print size) showed the best performance with the iZon® Lens (3-Layer). In every day visual tasks, consumers are faced with reading tiered listings or postings, much like the sentences on the MNRead test. A good example is reading menus, which are frequently tiered. That is, the entrées may be in a large font, bold heading followed by a paragraph listing the specifics of the entrées but in much smaller font (Of course, the price is in the smallest font.). This can be the case whether reading a hanging menu in any fast-food chain, or the menu in a four-star restaurant. Other examples may include reading the credits following a movie. The MNRead test enables us to determine the ability to read such items in terms of general acuity, speed and size.

A significant finding of the present work was the improved acuity under lower contrast conditions afforded by the iZon® Lens (3-Layer). When viewing under high-contrast conditions, resolution is not limited by size within a large range of target sizes. However, as the contrast decreases to an intermediate level (e.g., 11% in the Regan test), an individual has less ability to discern an object against a background. Examples of this are reading a roadside sign that is shadowed by overhanging trees, seeing the edges of stairs or escalators, or stepping onto the jet way when entering a plane. For the lowest contrast conditions (e.g., 4% in the Regan test), one might be faced with reading small letters and numbers on a cell phone, PDA display, or other electronic displays. Due to the spatial size and resolution of these screens, information is commonly displayed at small size and low contrast. The iZon® Lens (3-Layer) was particularly effective at providing the best low contrast acuity.

The SKILL test is ideally suited for evaluating one of the most visually demanding conditions—i.e., identifying dark objects against a dark background. This is often the case when driving at night, especially along a road that has no lights or is dimly lit. If one has ever traveled along a rural highway or dimly lit street, it is not unlikely that they will have encountered an animal or person along the roadside that could not be seen until very close to the car. Sometimes they dart into traffic and require rapid reaction by a driver. The iZon® Lens (3-Layer) system provides the wearer with the ability to see somewhat more effectively in this type of condition than if they were wearing conventional lenses with a manifest refraction.

We also found that the various components of the iZon® Lens system contribute to the overall performance gain, with the whole being greater than the sum of the parts. Using the Z-View® correction with conventional lens materials made at an outside lab resulted in similar or better performance than a traditional refraction coupled with the conventional lens. Coupling the Z-View® prescription with the iZon® Single Layer Lens added better visual function on some measures. The best total vision performance was the Z-View® Rx with the iZon® 3-Layer Lens.

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Figure 35. Planned Comparisons (N=52)

Results	ETDRS Acuity	GLARE Acuity	Pelli-Robson Contrast	Regan High 96%	Regan Int 11%	Regan Low 4%	MNRead Acuity	MNRead Speed	MNRead CPS	SKILL
Conventional	-0.117	-0.071	1.91	-0.108	0.129	0.412	-0.084	278	0.090	14.60
Rx-1 Layer	-0.129	-0.078	1.91	-0.123	0.108	0.407	-0.097	264	0.057	13.65
Zx-1 Layer	-0.146	-0.079	1.91	-0.116	0.089	0.366	-0.105	268	0.079	14.00
iZon® 3-Layer	-0.138	-0.083	1.92	-0.114	0.091	0.366	-0.117	272	0.049	12.40
Significance of Differences										
Zx only Zx-1 Layer vs. Rx-1 Layer	0.18	0.93	0.56	0.63	0.14	0.006	0.58	0.390	0.26	0.53
3-Layer only iZon® 3-Layer vs. Zx-1 Layer	0.07	0.90	0.99	0.80	0.39	0.650	0.67	0.710	0.15	0.04
Oph lab Rx-1 Layer vs. Conventional	0.20	0.16	0.73	0.16	0.05	0.590	0.23	0.005	0.08	0.05

Yellow equals best performance Green equals statistical significance ≥ 95% Blue equals statistical significance ≥ 80%

Figure 36. iZon® Lens System vs. Conventional (N = 83)

	EDTRS Acuity	Contrast Sensitivity	Glare Acuity	Regan High 96%	Regan Inter. 11%	Regan Low 4%	MN Acuity	MN Speed	MN CPS	SKILL*
iZon® System (with 3-Layer Lens) vs. Conventional (with manifest)	0.25	0.88	0.05	0.13	0.02	0.006	0.21	0.69	0.04	0.02

Green equals statistical significance ≥ 95% Blue equals statistical significance ≥ 80% * N=52