Title: First Photochromic Intraocular Lens (Focus Acrylic® eclipse) – Clinical Experience in Humans

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Synopsis:

A new photochromic hydrophobic acrylic intraocular lens (Focus Acrylic® eclipse, Model 603, by eyePx LLC) was implanted in 35 cataract patients with Focus Acrylic eclipse in one eye and Focus Acrylic Yellow (Model 602, eyePx LLC) in the opposite eye. The follow-up time is 12 months. The Focus eclipse lens appears safe and efficacious in comparison with Model 602. In addition, the scotopic vision with Focus Acrylic® eclipse appears better than that with Focus Acrylic® Yellow (Model 602), especially under low-level light conditions.

ABSTRACT

Purpose: To evaluate the intra-individual comparison of best-corrected visual acuity (BCVA) of Focus Acylic® eclipse (the study IOL) vs. Focus Acrylic Yellow Model 602 (the controlled IOL) in human eyes in scotopic and photopic conditions.

Materials and Methods: Prospective comparative study of 35 patients (20 females and 15 males, ages from 51 to 80) with bilateral implantation with a photochromic hydrophobic acrylic IOL, Focus Acrylic® eclipse (Model 603, eyePx LLC.) randomly selected for one eye and Focus Acrylic Yellow (Model 602,) in the opposite eye. Standard phacoemulsification technique was used for cataract removal. All IOLs were implanted with the Epsilon EL22 injector using the cartridge from Opthec OD501 through a clear corneal incision of about 2.8 mm. BCVA was measured using Snellen Charts under various lighting conditions for both study IOLs and control IOLs. For comparison reasons, four healthy subjects (without cataract) were also tested for their BCVA in various lighting conditions.

Results: 32 of 35 patients completed the 1 month and 12 months follow-up examination. Three patients did not return for follow-up and were excluded from the study. The postoperative scotopic vision (BCVA in Log MAR) of both the study IOL and the control IOL increased as the illumination levels increased; BCVA of the study IOL was found to be better than that of the control IOL, especially in low level illumination conditions (11 Lux to about 500 Lux). At high illumination levels (from 500 Lux to 1,200 Lux), there is no significant improvement in BCVA within each IOL type and the difference in BCVA between the study IOL and the control IOL also decreases. In the photopic environment, a subset of the population (15 subjects) wearing UV-blocking sunglasses was associated with a more significant reduction in BCVA in the control IOL than in the study IOL.

Conclusions: This preliminary study demonstrates that in the indoor environment, Focus Acrylic® eclipse outperforms Focus Acrylic Yellow in postoperative scotopic vision (BCVA in Log MAR), especially under low level illumination conditions. In addition, Focus Acrylic® eclipse appears to be as safe and effective as the control IOL.

INTRODUCTION

It is common for the human crystalline lens to gradually yellow with age.[1-3] There is a hypothesis that the gradual darkening of the human crystalline lens with age may provide a mechanism for blocking harmful violet and blue light from reaching the retina, thus protecting eyes from age-related diseases, such as macular degeneration. Based on this hypothesis, yellow intraocular lenses which block both the violet and blue light have been developed for cataract surgery. These lenses include AcrySof® IQ Aspheric Natural (model SN60WF, Alcon Laboratories, Fort Worth, TX, USA) and Focus Acrylic Yellow lens (model 602, eyePx LLC., Bourg la Reine France). These yellow IOLs are believed to provide additional protection for the retina compared with clear UV-blocking IOLs. Although no human clinical study has provided direct evidence for this additional benefit of yellow IOLs, there are studies which indirectly indicate that blocking both violet and blue light may reduce the risk for macular degeneration or its progression. [4-10]

While yellow IOLs are marketed as providing additional benefits to cataract patients for retina protection, there have been concerns that a yellow IOL may compromise scotopic vision, such as night driving. At least for now, ophthalmologists are divided on the optical performance of a yellow IOL (Holladay JT. Blue Blocker: Optical Downside? ***Yes***, and Cionni RJ. Blue Blocker: Optical Downside? ***No***. Papers presented at the AAO/SOE Joint Meeting, New Orleans, LA, USA, October 25, 2004).[11-14] The concern that a yellow IOL compromises night vision is based on the fact that the rod-mediated scotopic sensitivity increases from the violet light range to the blue light range and peaks at 507 nm (still in the blue light range). A yellow IOL which blocks the blue light inevitably decreases the scotopic sensitivity of cataract patients. Thus, their night vision may be compromised. Because of this loss of available light, Dr. Mainster and others believe that an ideal IOL should block UV and violet light but not blue light.[11-12] For this reason, IOLs which block UV and violet light but transmit blue light have recently been developed by Bausch and Lomb. Nevertheless, such a violet-light-blocking IOL only reduces, but does not eliminate, the negative impact of colored IOLs on scotopic sensitivity under weak lighting conditions.

To overcome the difficulty of blocking harmful violet and blue light without compromising scotopic vision, researchers at EyePx LLC have successfully adopted a new IOL with photochromic properties. This new photochromic IOL is based on Medennium's (Irvine California) existing patented photochromic technology. The proprietary hydrophobic acrylic material has a refractive index of 1.49. Focus Acrylic® eclipse is colorless and behaves as a normal UV blocking IOL in the absence of UV light. When exposed to UV light, such as found in sunlight, the IOL turns yellow in a few seconds. Once the UV stimulus is gone, the IOL switches back to a colorless form, again in a few seconds.[14] This way, the yellow color of the Focus Acrylic® Eclipse can be repeatedly turned on by the presence of UV light (daytime outdoors) and turned off (i.e. made colorless) by the absence of UV light (Figure 1).

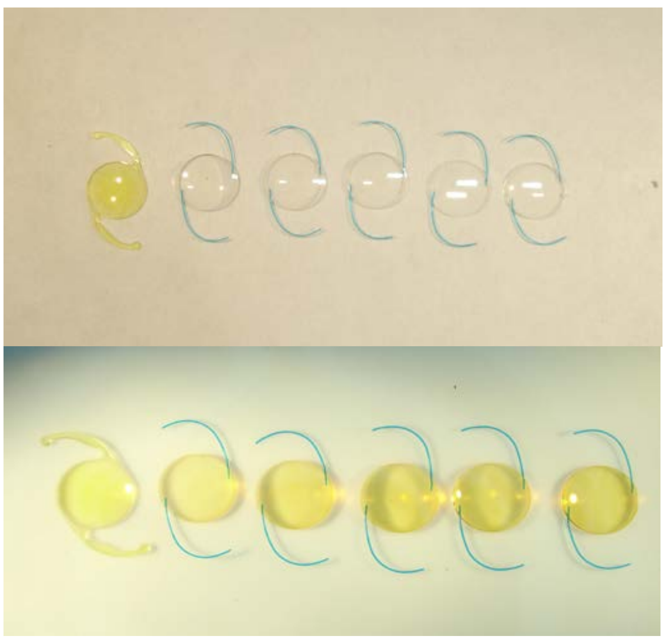

Figure 1. In-vitro study yellow IOL vs. Photochromic IOL (courtesy of Medennium Inc.)

A recent (2006) publication by Drs. Werner and Mamalis[14] et al (University of Utah) indicates that this repeated switch-on and switch-off, the photochromic property, has been successfully observed inside rabbit eyes. While exposed to a UV light source, the IOL inside the rabbit's eye was observed to change to yellow under slitlamp examination. At the end of the study, the explanted photochromic lenses did not show any detectable deterioration in their photochromic property. According to Medennium Inc., the photochromic property of the photochromatic lens has been demonstrated to be stable for up to 23 years in a solar exposure simulation experiment, exceeding the ISO requirement a photostability of 20 years for intraocular lens materials. This experiment has been verified in vivo as recently published (2011) by Werner et al[19]. A key reason for the durability of the Eclipse photochromic property is the intraocular environment. The switching kinetics are enhanced at body temperature and, unlike photochromic eyeglasses, the Eclipse lens is protected from direct exposure to sunlight and high concentrations of oxygen and free radicals. The UV-Visible curve of Focus Acrylic® eclipse with and without the presence of UV light is shown in Figure 2.

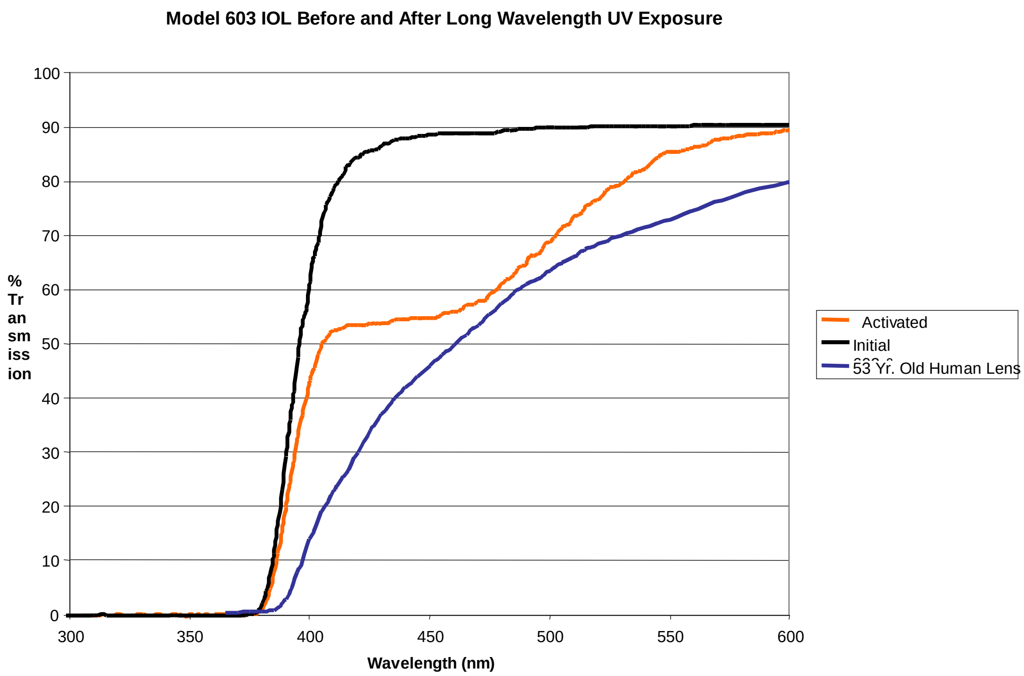

Figure 2. Light Transmission of Focus Acylic® eclipse in its Clear and Activated States (Courtesy of eyePx LLC.)

MATERIALS AND METHODS

The Focus Acrylic® eclipse Model 603 is a single-piece lens with aspherical biconvex optics which correct 0.17ųm aberration. The overall diameter of the lens is 13.0 mm, with a 6.0 mm biconvex optic. The lens has a 0-degree posterior optic-haptic angulation, a frontal 2 degree draft on the haptics and it has square edges. The lens is photochromatic in nature. The control lens identified as Focus Acrylic Yellow Model 602 has the same exact construction with the exception of being yellow all the time.

Of 35 subjects, 20 are female and 15 male with ages ranging from 51 to 80 years old. Two subjects have pre-existing rheumatoid arthritis controlled with medicine. Two subjects have pre-existing Type II diabetes with low non-proliferative diabetic retinopathy. Five subjects have controlled systemic high blood pressure and 26 subjects have no systemic diseases. All subjects underwent phacoemulsification for senile cataract removal followed by bilateral implantation. One eye of each subject was randomly selected for receiving a Focus Acrylic® eclipse (Model 603) and Focus Acrylic® Yellow (Model 602) in the fellow eye. All surgeries and subsequent tests were performed by Dr. David Mendez. The surgeries were uneventful. All lenses were implanted with the Epsilon Model EL22 injector and Ophtec cartridge type “501” through a clear corneal incision of about 2.8 mm.

All 35 subjects were then followed at day 1. However, 3 subjects did not comeback for the 1 month and 12 month follow-up examinations; they were excluded from the study. The other 32 subjects completed the 1 month and 12 month follow-up examinations. At month 1 and month 12, BCVA of 32 subjects was measured at scotopic conditions with light intensity starting at 11 Lux and gradually increasing to 1200 Lux. At month 12, a subset of 15 subjects were asked to move outdoors for measurements under a full sun photopic environment. BCVA of each eye was evaluated while the subject wore UV blocking sunglasses as well as without wearing the sunglasses. This evaluation was a measure of real life conditions, particularly because it is standard practice for people to wear UV blocking sunglasses outdoors after cataract surgery.

BCVA was measured using standard Snellen charts and the Snellen data were converted into LogMar for data analysis. The Snellen chart with various lighting levels is shown in Figure 3. Standard dim lighting conditions were achieved by blocking the day light in the examination room. The illumination light was turned on from a low level and increased gradually. Illumination levels were measured with a standard Lux meter (VWR Scientific 62344-944 Dual Range Light Meter). All subjects were corrected to his/her best corrected visual acuity using trial frames at normal test room illumination levels, then all room lights were turned off for about 5 minutes for the subject to become dark adapted. The subject was asked to cover one eye for testing at the lowest lighting level (11 Lux for example). Once the first eye was tested, the subject was asked to cover the first eye to test the second eye at the same light level. Technicians increased the light intensity to the next level. Both the first eye and the second eye were tested and results recorded. BCVA for the first and second eye were obtained separately for all 32 subjects at all light levels.

A (40 Lux) B (80Lux) C(200 Lux) D (300 LUX) E (400 Lux)

Figure 3. The Snellen Test Illustration of Lighting Conditions at Various Illumination Levels (in Lux)

RESULTS

At month 1, for all 32 subjects, BCVA was measured with the eye implanted with Focus Acrylic® eclipse and with Focus Acrylic® Yellow respectively at various levels of light illumination intensities. The average BCVA (in Log MAR) of all 32 eyes with Focus Acrylic® eclipse was calculated at each of illumination level. Similarly, the average BCVA (in Log MAR) of all 32 eyes Focus Acrylic® Yellow was also calculated. The results of these two averages are listed in Table 1 and plotted vs. various illumination levels (Lux) in Figure 4. For comparison reasons, 4 healthy subjects (no cataract) were tested for their BCVA under the same illumination levels and their average BCVA was calculated and plotted against various illumination levels (Figure 4).

Table 1. BCVA (Log MAR) at Various Illumination Levels (Month 1). Focus Acrylic® eclipse in Comparison with Focus Acrylic® Yellow and Healthy Subjects (Control)

BCVA with Focus Acrylic® Eclipse	BCVA with Focus Acrylic® Yellow	BCVA of Healthy Subject (Control)	Illumination Level (in Lux)
0.27	0.37	0.18	11
0.21	0.29	0.10	19
0.17	0.21	0.10	34
0.15	0.20	0	66
0.11	0.17	0	105
0.12	0.16	0	150
0.07	0.13	0	206
0.06	0.13	-0.12	275
0.04	0.13	-0.12	366
0.04	0.11	-0.12	495
0.04	0.11	-0.12	600
0.04	0.11	-0.20	700
0.04	0.08	-0.20	875
0.04	0.08	-0.20	1200

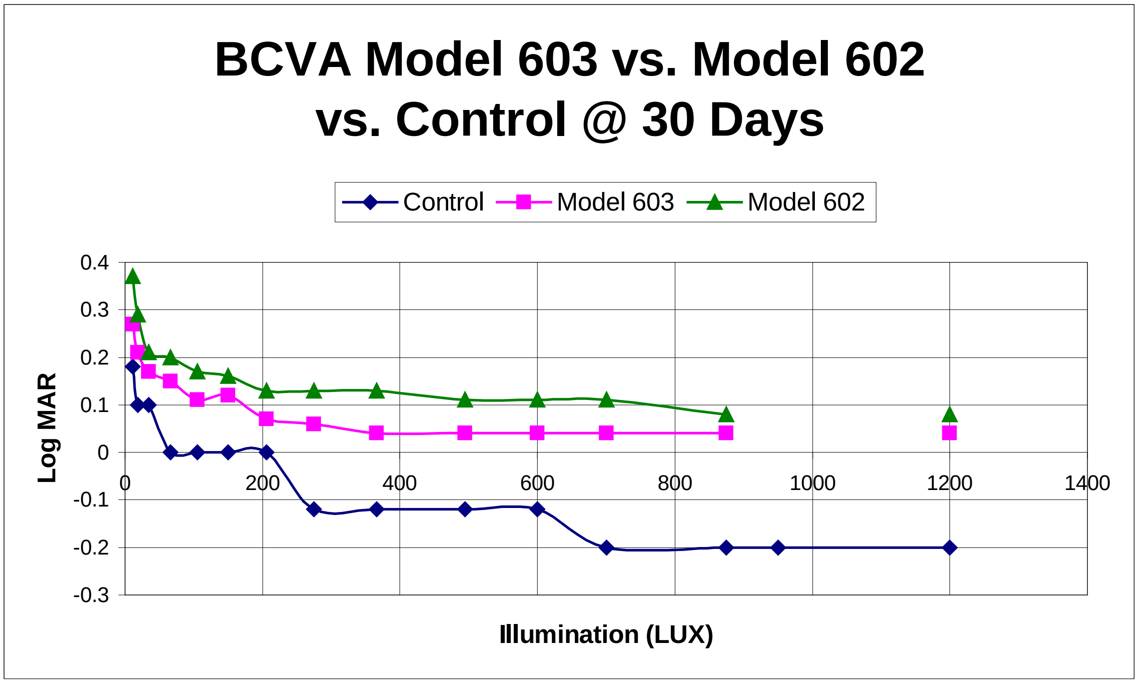

Figure 4. BCVA (Log MAR) at Various Illumination Levels at Month 1. Focus Acrylic® eclipse (model 603) in Comparison with Focus Acrylic® Yellow (Model 602) and Healthy Subjects (Control)

At month 12, all 32 subjects were examined again and their BCVA measured. The average of 32 patients' BCVA for Focus Acrylic® eclipse and for Focus Acrylic® Yellow was calculated respectively at each illumination level. The results are listed in Table 2 and plotted in Figure 5.

Table 2. BCVA (Log MAR) at Various Illumination Levels (Month 12). Focus Acrylic® eclipse in Comparison with Focus Acrylic® Yellow and Healthy Subjects

BCVA of Focus Acrylic® Eclipse	BCVA of Focus Acrylic® Yellow	BCVA of Healthy Subject (Control)	Illumination Level (Lux)
0.34	0.39	0.18	11
0.26	0.31	0.10	19
0.22	0.25	0.10	34
0.18	0.22	0	66
0.16	0.18	0	105
0.13	0.17	0	150
0.07	0.15	0	206
0.07	0.13	-0.12	275
0.06	0.12	-0.12	366
0.05	0.11	-0.12	495
0.04	0.09	-0.12	600
0.04	0.08	-0.20	700
0.03	0.06	-0.20	875
0.02	0.06	-0.20	950
0.02	0.05	-0.20	1200

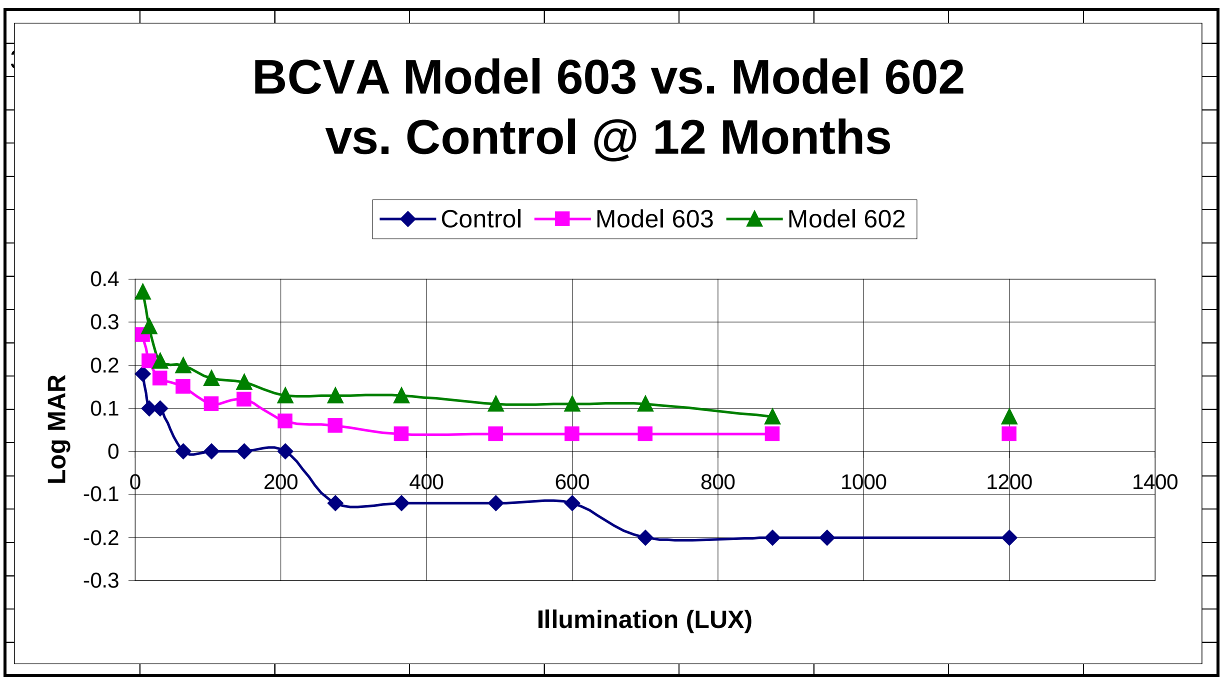

Figure 5. BCVA (Log MAR) at Various Illumination Levels at Month 12. Focus Acrylic® eclipse (603) in Comparison with Focus Acrylic® Yellow (602) and Healthy Subjects (Control).

The results for measurements in outdoor full sun environment are illustrated in Figure 6 for eyes with Focus Acrylic® eclipse IOLs and Figure 7 for eyes with Focus Acrylic® Yellow IOLs.

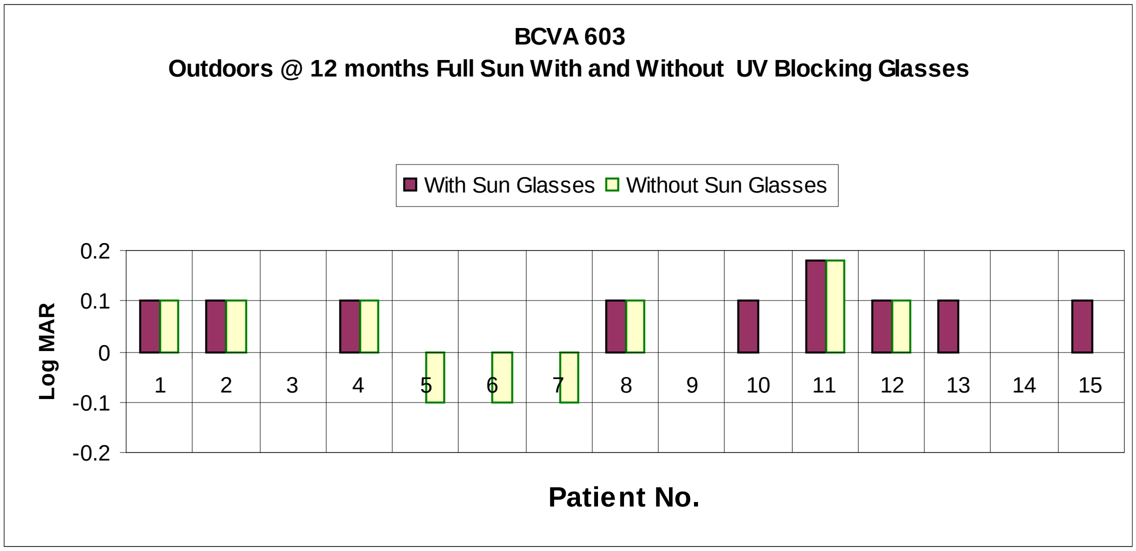

Figure 6. BCVA (Log MAR) of Eyes with Focus Acrylic® eclipse IOLs for 15 Subjects Measured Outdoors. Comparison with and without UV Blocking Sunglasses

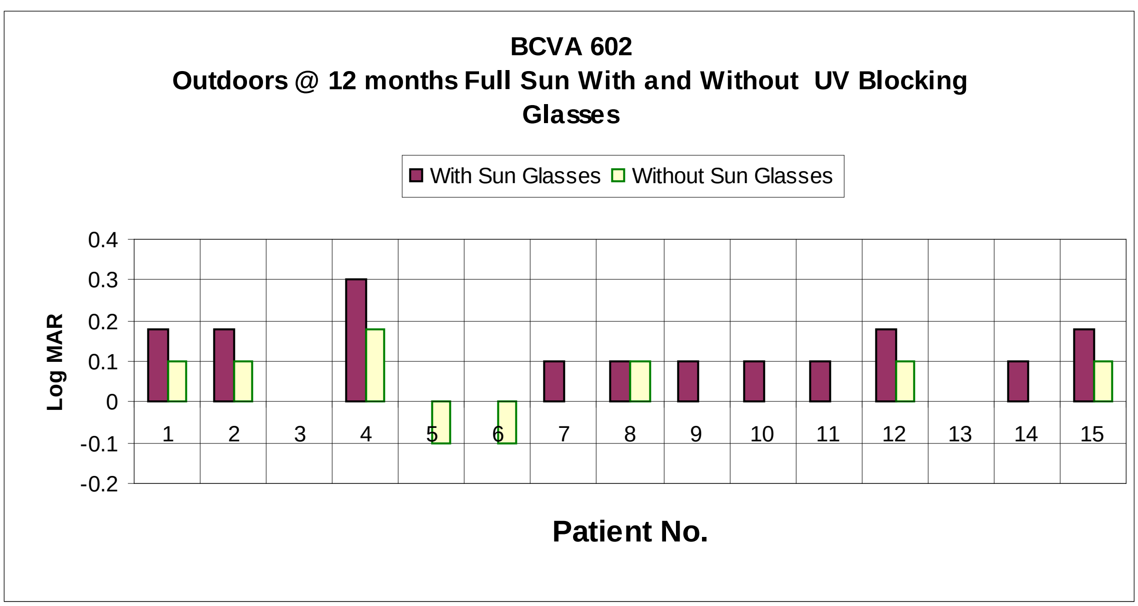

Figure 7. BCVA (Log MAR) of Eyes with Focus Acrylic® Yellow IOL for 15 Subjects in Outdoor Full Sun. Comparison with and without UV Blocking Sunglasses

DISCUSSION

Recent studies suggest that blue light may present a hazard to the retina, especially for the post cataract population. Lipofucsin-containing retinal pigment epithelial cells may be damaged by blue-light, indirect evidence that a blue-light absorbing IOL may reduce the risk for macular degeneration or its progression.[7-9,17] Yellow IOLs, which absorb blue-light, are thought to mimic the transmission characteristics of an aged human crystalline lens and may offer protection from blue-light damage. On the other hand, yellow IOLs have been reported to compromise scotopic (or dim light) vision important for common evening activities such as driving at night.[11,12]

In this report of human clinical experience with a new photochromic IOL designed to overcome the yellow IOL low light compromise, it was found that visual acuity (BCVA in Log MAR) of eyes with both the study lens and the control lens increases as the illumination level increases in the low Lux environment and then remains constant once the illumination level reaches about 500 Lux or higher. Eyes with Focus Acrylic® eclipse consistently outperform eyes with Focus Acrylic® Yellow, a yellow aspheric IOL, in BCVA at both month 1 and month 12 postoperative examinations. The differences in BCVA between these two groups of IOLs are particularly significant under low illumination levels. The increased difference in BCVA between the study IOL and the control IOL under low illuminance levels can be explained by the fact that the control IOL is a yellow lens that blocks blue light from reaching the rod cells in the retina. This reduced light intensity received by the retina of subjects with a yellow IOL is equivalent to an environment with a lower lighting level for patients with a clear IOL (such as an unactivated photochromic IOL). For example, BCVA of subjects with Focus Acrylic® eclipse under 19 Lux (0.21 log MAR) illuminance is equivalent to the BCVA of subjects with Focus Acrylic® Yellow under 34 Lux (also 0.21 log MAR). A yellow IOL blocks blue light, the spectral region that rod cells of the retina respond to most strongly under mesopic conditions. Eyes with a yellow (or violet) IOL require more light to achieve a response equal to an eye with a clear IOL. Therefore, BCVA with a yellow IOL will be poorer than that with a clear IOL under low illuminance levels. Once the amount of available light becomes sufficiently strong (for example 800 Lux or higher), the negative blue-light blocking effect on the visual acuity by a yellow IOL becomes insignificant.

In addition, evaluation of subjects wearing sunglasses outdoors indicated that the photochromic Eclipse lens performed better than the yellow IOLs. Most eyes with Focus Acrylic® eclipse IOLs did not show a reduction in BCVA when available light levels were reduced by the sunglasses. In contrast, most eyes with Focus Acrylic® Yellow IOLs showed a significant reduction in BCVA when UV blocking sunglasses were used. The sunglasses significantly reduced the amount of light entering the eye (as they are designed to do), creating an outdoor low light situation equivalent to the indoor low light environment described in the previous paragraph. The Eclipse IOL quickly becomes clear when the UV component of the sunlight is blocked by the sunglasses and provides the eye with the benefit of a clear, unobstructed lens. The yellow IOL further reduces the light incident on the retina, giving the optical nerve cells less light and thus, poor visual acuity in most cases.

Under mesopic conditions, BCVA of healthy human eyes should increase as the illumination levels increase from low Lux to high Lux. To verify this and provide a reference point for natural vision, we measured the best corrected visual acuity of four healthy subjects (without cataract) as a control group. The trend for BCVA to increase as the illuminance level increases was confirmed by test results for the four healthy subjects (Figures 4 and 5). The control group confirms the commonsense notion that in low lighting conditions, providing the eye with more light (from 11 Lux to about 400 Lux) improves its visual acuity.

Table 3 lists various environments we experience in our daily lives and their respective illumination levels.

Table 3. Examples of Various Illumination Levels[18]

Illuminance	Abbr.	Example
0.00005 lux	50 µlx	Starlight
<1 lux		Moonlight
10 lux		Candle at a distance of 30 cm (1 ft)
400 lux		A brightly lit office
400 lux		Sunrise or sunset on a clear day.
1000 lux	1 klx	Typical TV studio lighting
32000 lux	32 klx	Sunlight on an average day (min.)
100000 lux	100 klx	Sunlight on an average day (max.)

As we can see from Table 3, normal indoor environments basically have a light illumination level of 400 Lux or less. We often find ourselves in situations with an illuminance of about 10 Lux, such as romantic lighting in an upscale restaurant or in a seminar room where the speaker is using a projector or slide show. On other occasions, such as a darkened movie theatre or night driving, light levels are at or below 1 Lux. Our preliminary data suggests that patients with a yellow IOL will likely suffer some degree of loss of visual acuity in these low illumination environments as compared to patients with a clear IOL.

Because the sample size is relatively small in the study group, one should be cautious in drawing conclusions. Nevertheless, it appears that Focus Acrylic® eclipse IOLs are safe and effective in comparison with control IOLs in our study population. In the indoor environment, BCVA of both Focus Acrylic® Eclipse and Focus Acrylic® Yellow as well as the healthy subjects increases as the illumination level increases from low illuminance to moderate illuminance (from 11 Lux to about 500 Lux) and then flattens out at high levels of illumination (about 500 Lux or higher). Focus Acrylic® eclipse outperforms Focus Acrylic® Yellow in postoperative scotopic vision (BCVA in Log MAR), especially under low level illumination. A yellow IOL blocks blue light which is the most sensitive to the rod cells at mesopic conditions. Consequently, patients with a yellow IOL require stronger lighting to receive the same amount of light at the retina equivalent to a clear lens under weaker lighting conditions. Therefore, patients with a yellow IOL suffer some degree of loss in visual acuity in comparison with a clear IOL under the same low lighting conditions.

REFERENCES

1. Gaillard ER, Zheng L, Merriam JC, Dillon J. Age-related changes in the absorption characteristics of the primate lens. Invest Ophthalmol Vis Sci 2000; 41:1454-1459.

2. Mellerio J. Yellowing of the human lens: nuclear and cortical contributions. Vis Res 1987; 27:1581-1587.

3. Chylack LT Jr. Aging changes in the crystalline lens and zonules. In: Albert DM, Jakobiec FA, eds, Principles and Practice of Ophthalmology. Basic Sciences. Philadelphia, PA, WB Saunders Co, 1994; 702-710.

4. Yanagi, Y, Inoue Y, Iriyama A, Jang WD. Effects of yellow intraocular lenses on light-induced upregulation of vascular endothelial growth factor. J. Cataract Refract. Surg. 2006; 32:1540-1544.

5. Sparrow JR, Miller AS, Zhou J. Blue light-absorbing intraocular lens and retinal pigment epithelium protection in vitro. J Cataract Refract Surg 2004; 30:873-878.

6. Sparrow JR, Nakanishi K, Parish CA. The lipofucsin fluorophore A2E mediates blue light-induced damage to retinal pigmented epithelial cells. Invest Ophthalmol Vis Sci 2000; 41:1981-1989.

7. Age-Related Eye Disease Study Group. Risk factors associated with age-related macular degeneration. A case-control study in the age-related eye disease study: Age-related eye disease study report number 3. Ophthalmology 2000; 107:2224-2232.

8. Pollack A, Marcovich A, Bukelman A, Oliver M. Age-related macular degeneration after extracapsular cataract extraction with intraocular lens implantation. Ophthalmology 1996; 103:1546-1554.

9. Van der Schaft TL, Mooy CM, de Bruijn WC, et al. Increased prevalence of disciform macular degeneration after cataract extraction with implantation of an intraocular lens. Br J Ophthalmol 1994; 78:441-445.

10. Werner L, Apple DJ, Schmidbauer JM. Ideal IOL (PMMA and foldable) for year 2002. In: Buratto L, Werner L, Zanini M, Apple DJ, eds, Phacoemulsification: Principles and Techniques, Thorofare, NJ, Slack Inc, 2003; 435-451.

11. Mainster MA. Intraocular lenses should block UV radiation and violet but not blue light. Arch Ophthalmol 2005; 123:550-555.

12. Mainster MA, Sparrow JR. How much blue light should an IOL transmit? Br J Ophthalmol 2003; 87:1523-1529.

13. Olson RJ, Werner L, Mamalis N, Cionni R. New IOL technology. Am J Ophthalmol 2005; 140:709-716.

14. Werner L, Mamalis N, et al, New Photochromic foldable Intraocular Lens: Preliminary Study of Feasibility and Biocompatibility. Journal of Cataract and Refractive Surgery 2006; 32: 1214-1221.

15. Curcio CA, Millican CL, Allen KA, Kalina RE. Aging of the human photoreceptor mosaic: evidence for selective vulnerability of rods in central retina. Invest Ophthalmol Vis Sci 1993; 34:3278-3296.

16. Jackson GR, Owsley C. Scotopic sensitivity during adulthood. Vision Res 2000; 40:2467-2473.

17. Ham WT Jr, Ruffolo JJ Jr, Mueller HA, Clarke AM, Moon ME. Histologic analysis of photochemical lesions produced in rhesus retina by short-wave-length light. Invest Ophthalmol Vis Sci 1978; 17:1029-1035.

18. Wikipedia, the free encyclopedia, Website: http//en.wikipedia.org/wiki/Lux

19. Werner L, et al, Accel;eratyed 20-year sunlight exposure simulation of a photochriomatic foldable intraocular lens in a rabbit model. Journal of Cataract and Refractive Surgery 2011; 37: 378-385.

FIGURE LEGENDS

Figure 2. Transmission spectra of the Focus Acryli eclipse. The spectra were collected with a Varian Cary 3 UV-Visible spectrophotometer, scanning from 600 to 300 nm at a slit width of 2 nm and a scan speed of 1000 nm/minute. The lens was placed in a special cuvette with a 3 mm aperture, centered on its optical axis. After spectra at the "initial" state were collected, a 365 nm wavelength UV light was shined through the aperture for 30 seconds and spectra at the "activated" state were collected. The spectrum of a 53-year-old human crystalline lens was also included in the Figure, for comparison.