In vivo evaluation of blue-light attenuation with tinted and untinted intraocular lenses

Georgios A. Kontadakis, MD, MSc, Sotiris Plainis, PhD, Joanna Moschandreas, PhD, Chrisanthi Tsika, MD, MSc, Ioannis G. Pallikaris, MD, PhD, Miltiadis K. Tsilimbaris, MD, PhD

PURPOSE: To evaluate blue-light attenuation in eyes with a tinted intraocular lens (IOL) or an untinted IOL.

SETTING: Department of Ophthalmology, University Hospital of Crete, Crete, Greece.

DESIGN: Comparative case series.

METHODS: Patients had lens extraction and implantation of an Acrysof Natural tinted or Tecnis ZA9003 or Softec III untinted acrylic IOL. The luminance ratio of green (530 nm) and blue (465 nm) light (green:blue ratio) required for isoluminant perception was determined by heterochromatic flicker photometry. Patients were tested preoperatively and 20 days postoperatively. The parafoveal measure of the green:blue ratio, expressed in decibels, is proportional to the blue-light attenuation by the lens.

RESULTS: Twenty-two patients received the tinted IOL and 21 the untinted IOL. Preoperatively, age was strongly linearly correlated with the green:blue ratio ($r = 0.59$, $P<.001$). The mean postoperative decrease in the green:blue ratio was greater in the untinted IOL group ($P = .003$). Postoperatively, the tinted IOL group had a significantly higher green:blue ratio than the untinted IOL group ($P<.001$). In the tinted IOL group, the green:blue ratio was linearly related to IOL dioptric power.

CONCLUSION: Less blue light reached the retina with tinted IOLs than with untinted IOLs. The absorption properties of tinted IOLs seemed to resemble those of the aging human crystalline lens, while untinted IOLs resembled the lower levels of blue-light attenuation of younger lenses. Thus, tinted IOLs may protect against the presumed blue-light hazard.

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Until recently, most intraocular lenses (IOLs) were designed to provide protection to the retina by absorbing ultraviolet (UV) radiation only; they were transparent in the visible spectrum. Since the early 1990s, a yellow filter has been incorporated into several IOLs. The yellow filter is intended to mimic the spectral properties of the natural crystalline lens in blue-light (short-wavelength) absorption, thus reducing the amount of blue light reaching the retina.

Blue radiation is considered to be primarily responsible for light damage to the retina because of the higher energy of shorter wavelengths, and it is more likely to cause photooxidative damage at lower thresholds.[1–3] Normally, the retina is protected from short-wavelength visible radiation by the crystalline lens, which absorbs all UV-A radiation and a fraction of blue radiation, which increases with age.[4–6] Lens extraction and implantation of a clear (untinted) IOL eliminates the blue light–filtering properties of the crystalline lens and presumably increases the danger of light-induced retinal damage. Speculation about the possible pathogenetic role of short wavelengths has led to increasing use of tinted IOLs in cataract surgery.

At present, psychophysical methods, such as heterochromatic flicker photometry (HFP),[7–9] are used to measure retinal sensitivity in blue light to assess the optical density of the macular pigment. The same techniques could be used to estimate lens optical density[10] by assessing blue-light sensitivity extrafoveally, bypassing macular pigment absorption. The purpose of our study was to evaluate blue-light attenuation in eyes with a commercially available tinted IOL or untinted IOL. The measurements were performed with a new instrument that uses HFP to determine isoluminant perception of blue and green radiation parafoveally before and after cataract surgery.

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PATIENTS AND METHODS

This prospective case series with intraindividual and cross-sectional comparisons enrolled patients between July 2007 and April 2008. The patients were from a continuous cohort presenting to University Hospital of Heraklion or Institute of Vision and Optics, University of Crete, reporting vision deterioration or seeking surgical correction of their refractive error. The Institutional Review Board, University of Crete, approved the study. Patients were informed about the study and gave their consent according to institutional guidelines and the tenets of the Declaration of Helsinki. Patients were assigned to receive an untinted IOL (Tecnis ZA9003, Advanced Medical Optics, Inc., or Softec III, Lenstec, Inc.) or an IOL that contains blue light–filtering tint (Acrysof Natural, Alcon Laboratories, Inc.).

Preoperative inclusion criteria were absence of ocular pathology other than cataract, corrected distance visual acuity (CDVA) no worse than 20/200, and normal retinal evaluation findings. Patients who had an uneventful cataract extraction by phacoemulsification and achieved a postoperative CDVA of 20/35 or better at 20 days were included in the final analysis.

Preoperative evaluation consisted of refractive error estimation by autorefractometry (RK-F1 Full Auto Autorefractor Keratometer, Canon, Inc.), corneal topography (EyeSys System 2000, EyeSys Vision, Inc.), uncorrected distance visual acuity (UDVA), CDVA, manifest refraction, applanation tonometry, and slitlamp inspection of the anterior and posterior segments of the eyes. The density of the nuclear sclerosis was evaluated by a clinician masked to the grading. Grading was performed using the method of Pirie,[11] which ranged from grade 1.0 (pale lens) to grade 4.0 (brunescent cataract) in 0.5 steps.

Measurement Technique

Blue light-attenuation was assessed with an MPS 9000 QuantifEye Macular Pigment Screener (Tinsley Ophthalmic Instruments), a desktop device used to assess macular pigment optical density.[12,13] The device uses the principles of HFP, a common method for assessing macular pigment optical density.[8,9,12–15] In addition, HFP has been used to evaluate the optical density of the crystalline lens.[16,17] In traditional HFP for determining macular pigment optical density, the measurement is based on the perceived intensity of 2 superimposed flickering light sources of different wavelengths, 1 of which is blue and is absorbed by the macular pigment and the other of which is green and is absorbed negligibly by the macular pigment.

When using the pigment screener, the patient fixates on a circular target of 1-degree diameter composed of 2 superimposed light-emitting diodes (LEDs) (peak wavelengths: 465 nm for blue, 530 nm for the green; luminance up to 200 candelas [cd]/m^2 for both LEDs) flickering in counterphase on a white-light pedestal. The target is surrounded by a 30-degree white area (color temperature 5500 K) with a luminance of 250 cd/m^2; this provides control over adaptation in the photopic range. Initially, the luminance of the green light (L_g) is higher than that of the blue (L_b) and the flicker is set at 60 Hz, reducing at a rate of 6 Hz/sec. The patient is instructed to press a button as soon as a flicker is detected. Then, the luminance ratio of blue to green is changed by 0.2 dB, increasing blue luminance (L_b) and decreasing green luminance (L_g), keeping the mean luminance constant. This continues for a series of green:blue luminance ratios, with the minimum corresponding to the equalization of blue and green luminance. To determine macular pigment optical density, the green:blue luminance ratio for isoluminance (green:blue ratio) is determined for central viewing and peripheral viewing with the patient fixating on a 2-degree red spot located at 8 degrees horizontal eccentricity. In this study, evaluation of blue-light absorption by the lens required determination of peripheral data only because any change in the peripheral green:blue ratio (L_{bg}/L_{gb}) would depend on the optical density of the lens (at 465 to 535 nm) and the ratio of retinal sensitivities (at those wavelengths), which is assumed not to alter between preoperative and postoperative measurements. Moreover, the 465 nm (blue) wavelength is absorbed by the IOL or the pigmented crystalline lens, while both the IOL and the crystalline lens show minimal absorption at the 530 nm (green) wavelength.[6,18] The green:blue ratio is effectively measured by the decrease in the green (L_g) component of the green:blue ratio (ie, increase in blue component [L_b] in decibels). Because of preset calibrations, a zero attenuation of blue light corresponds to 4 dB. For example, if the cataractous lens is exchanged with an IOL of zero absorption in blue, a green:blue ratio (corresponding to an increase in the blue component) equal to 4 dB would be expected. For ratios over 4 dB, an increase in the luminance of the blue component would be required because of the attenuation of blue light by the IOL.

For each patient, the measurements were repeated 3 times during 2 sessions; the mean value was calculated. The first session occurred preoperatively, with the measurements corresponding to the green:blue ratio of the crystalline lens. The second session occurred postoperatively, with the measurements corresponding to the green:blue ratio of the IOL (tinted or untinted). Because the green:blue ratio has a linear positive correlation with age in healthy eyes,[13] a reduced green:blue ratio after IOL implantation would correspond to the lower levels of blue-light absorption in a younger crystalline lens.

Preliminary Data

A pilot study was performed with 10 patients to estimate the standard deviation (SD) of the outcome measure and thus calculate an appropriate sample size. Using Altman's

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Corresponding author: Miltiadis K. Tsilimbaris, MD, PhD, Department of Ophthalmology, University Hospital of Heraklion, GR71003 Voutes, Heraklion, Crete, Greece. E-mail: tsilimb@med.uoc.gr.

nomogram,[19] it was calculated, that 18 patients would be required in each group to have an 85% power of detecting a 1 SD difference between means. It was assumed that 15% of patients would not fulfill the postoperative inclusion criteria. Therefore a sample size of 46 was chosen.

Statistical Analysis

Linear correlation between pairs of quantitative variables was assessed using the Pearson correlation coefficient (r). Spearman rank correlation (ρ) techniques were used to assess the correlation of the ordinal variable representing the nuclear sclerosis density with the green:blue ratio. The independent-samples t test was used to compare postoperative results and the mean change in green:blue ratio in the 2 IOL groups. Preoperative to postoperative mean changes were assessed using the paired-samples t test in each group separately. Subsequently, multiple linear regression was used to assess IOL type (tinted or untinted), preoperative green:blue ratio measurements, and nuclear sclerosis density as a binary variable (0 to 1 versus >1) as possible predictors of the postoperative green:blue ratio. Age was not included in the model because it was strongly correlated with the preoperative green:blue ratio. Forward and backward stepwise selection procedures were applied to determine the statistically significant predictors. Postoperatively, the interaction between the implanted IOL's dioptric power and IOL type was assessed in a generalized linear model (identity link), with green:blue ratio as the dependent variable. A 5% significance level was selected. Statistical analysis was performed using SPSS software (version 15.0, SPSS, Inc.).

RESULTS

Of the 46 patients enrolled in the study, 1 had a posterior capsule tear intraoperatively and had anterior vitrectomy and IOL implantation in the sulcus. Two patients had a postoperative CDVA worse than 20/35 at 20 days as a result of persistent corneal edema. These 3 patients were excluded from the final analysis. After the exclusions, the tinted IOL group comprised 22 patients (51%) and the untinted IOL group, 21 patients (49%). Table 1 shows the patients' characteristics overall and by IOL group.

Preoperatively, the green:blue ratio and age were positively linearly correlated (Pearson $r = 0.59$, $P<.001$) (Figure 1). The equation that best fit the data was

$$\text{Green : blue ratio(dB)} = 3.89 + 0.026 \times \text{age} \qquad (1)$$

A significant positive correlation was also found between the preoperative green:blue ratio and the density of nuclear sclerosis ($\rho = 0.53$, $P<.0001$). The mean preoperative green:blue ratio was 5.64 $\pm$ 0.09 (SE) in the tinted IOL group and 5.57 $\pm$ 0.13 in the untinted IOL group (95% confidence interval [CI] for difference between mean values, -0.39 to 0.24; $P=.65$, independent-samples t test).

Postoperatively, the mean green:blue ratio was 5.49 $\pm$ 0.07 dB in the tinted IOL group and 4.92 $\pm$ 0.07 dB in the untinted IOL group (95% CI for difference between mean values, 0.37 to 0.76; $P<.001$, independent-samples t test) (Figure 2, *A*). The preoperative to postoperative difference in the green:blue ratio was higher in the untinted IOL group than in the tinted IOL group, corresponding to a mean decrease of 0.64 $\pm$ 0.11 dB versus 0.15 $\pm$ 0.11 dB, respectively (difference in mean values, 0.49 dB; 95% CI, 0.18-0.81; $P=.003$) (Figure 2, *B*).

The green:blue ratio after IOL implantation was not highly correlated with patient age ($r = 0.28$, $P=.07$). Regression analysis showed that the untinted IOL group had a postoperative green:blue ratio that was a mean of 0.55 dB lower (95% CI, 0.36-0.74) than in the tinted IOL group ($P<.0001$) after adjusting for the preoperative green:blue ratio ($R^2 = 0.49$). The preoperative green:blue ratio was also a significant predictor of the postoperative green:blue ratio in this model (regression coefficient, 0.21; 95% CI, 0.02-0.40; $P=.03$). The postoperative green:blue ratio was not affected by nuclear sclerosis density to a statistically significant extent.

The untinted IOL group had a decrease in the green:blue ratio that was a mean of 0.54 dB greater (95% CI, 0.24-0.83) than in the tinted IOL group ($P=.001$) after adjusting for nuclear sclerosis density; the ratio in eyes with nuclear sclerosis density greater than 1 was a mean of 0.38 dB higher than in eyes with nuclear sclerosis density of 1 or higher (95% CI, 0.08-0.68; $P=.015$; adjusted $R^2 = 28\%$).

Postoperatively, the mean green:blue ratio was linearly related to dioptric power in the tinted IOL group through an interaction of IOL type and IOL dioptric power (Figure 3), with the tinted IOL group having an increase in the green:blue ratio that was 0.05 times the dioptric power for each given IOL dioptric power measurement (95% CI, 0.00-0.10; $P=.052$). The dioptric power main effect was not significant (-0.08 with 95% CI, -0.047 to 0.032; $P=.702$). Therefore, there was no evidence of a relationship between the green:blue ratio and the untinted IOL and dioptric power.

DISCUSSION

Since Ridley introduced IOLs in cataract surgery, progression of their materials and design has been a main area in ophthalmology research. The realization that the spectral characteristics of the human lens play an important role in protecting the retina led to the implementation of UV filters in IOLs, and these IOLs are almost universally used today. In addition to filtering UV light, several IOLs that further filter blue wavelengths have been available since the early 1990s; these IOLs mimic the absorption of short-wavelength radiation offered by the aging crystalline lens.[20,21] The

Table 1. Patient characteristics and UDVA by IOL group.

Parameter	Tinted IOL Group (n= 22)	Untinted IOL Group (n= 21)	All Patients (N = 43)
Sex, n (%)			
Male	10 (45)	14 (67)	24 (56)
Female	12 (55)	7 (33)	19 (44)
Nuclear sclerosis, n (%)			
0 to ≤1	8 (36)	10 (47)	18 (41)
>1 to ≤2	8 (36)	8 (38)	16 (37)
>2 to ≤3	6 (27)	3 (14)	9 (21)
Mean age (y) ±SD	65 ± 10.4	64 ± 12.7	65 ± 11.7
Mean UDVA (decimal) ± SD			
Preoperative	0.35 ± 0.28	0.43 ± 0.32	0.39 ± 0.30
Postoperative	0.67 ± 0.21	0.76 ± 0.26	0.71 ± 0.24

IOL = intraocular lens; ns = nuclear sclerosis; UDVA = uncorrected distance visual acuity

consequences of short-wavelength radiation on the retina, usually referred as the blue-light hazard, seem to be mediated by several retinal substances, such as lipofuscin, which accumulates during aging in the retinal pigment epithelium (RPE).[1–3,22–26] Studies[27,28] have found that cultured human RPE cells and animal retinas in vivo are protected by blue-light filters. In addition, epidemiologic studies imply that cataract surgery and clear IOL implantation may lead to an increased risk for age-related macular degeneration which, except for other reasons, could also be due to increased exposure to light, although data in the literature are conflicting.[29–31] The crystalline lens absorbs all UV-A radiation and a fraction of blue radiation, which is more pronounced as age increases; some consider this a protective factor against retinal damage.[5,22]

Tinted IOLs have been increasingly used during the past few years based on the assumptions related to the protective role of blue-light absorption. At present, the Acrysof Natural is one of the most commonly used yellow-tinted (blue light–filtering) IOLs. Until the present study, the effect of this IOL in filtering blue light has been measured in laboratory settings only.[18,32] In our study, we used a commercially available instrument that applies HFP to evaluate blue-light attenuation in eyes with the tinted IOL and compared it with the eye's preoperative status and with the attenuation by untinted IOLs. Heterochromatic flicker photometry has been used to estimate the optical density of the crystalline lens in several studies,[10,16,17] which found results comparable to those with other in vivo methods. In the present study, the parafoveal measurement of the green:blue luminance ratio for isoluminance was determined for each patient. This ratio is significantly affected by light attenuation in the eye's optical media and with the tested wavelengths, it depends mainly on blue-light attenuation by the lens.[6,18] As a consequence, a higher green:blue ratio value corresponds to increased optical density of the lens.

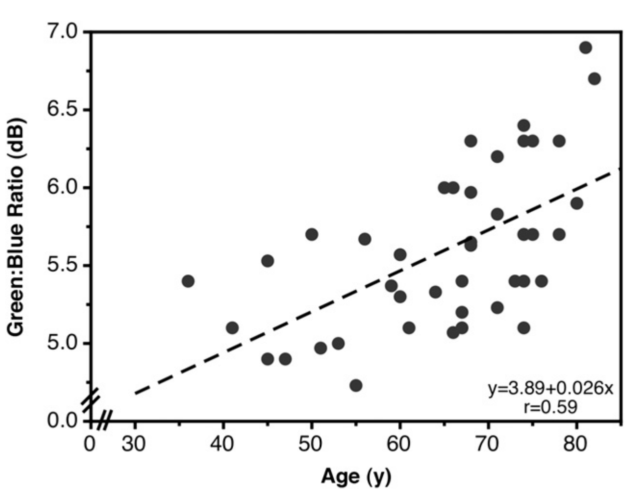

Figure 1. Scatterplot of preoperative green:blue luminance ratio as a function of patient age. The dashed line and the equation correspond to the least-square regression fit.

In our study, the preoperative green:blue ratio measurements were highly correlated with the age of the patient; this is in close agreement with the results in a previous study of healthy eyes[13] and with the well-established observation that absorption of blue light by the crystalline lens increases with age.[4–6,33,34] Postoperatively, the green:blue ratio and age were not highly correlated. A significant correlation would indicate that the patient's flicker sensitivity was affected by age through factors other than the crystalline lens's absorption, which was not the case in our group of patients. Although loss of retinal sensitivity in short wavelengths with age has been reported,[35] the outcome in patients is consistent with the results of Nguyen-Tri et al.,[36] who tested isoluminance in phakic and pseudophakic eyes and found that the loss of relative sensitivity in short wavelengths is the result of lenticular absorption. Furthermore, macular pigment

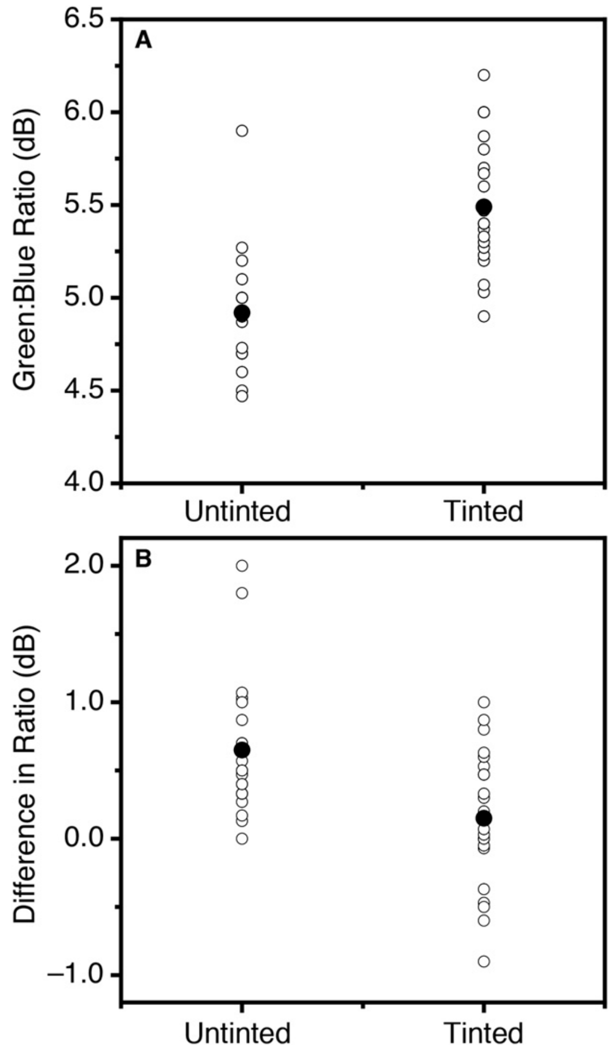

Figure 2. *A*: Postoperative green:blue luminance ratio. *B*: Difference in the green:blue luminance ratio between preoperative and postoperative measurements by IOL group. The filled circles represent mean values.

did not likely interfere with the results of our method because the measurements were performed 8 degrees extrafoveally.

The main outcome in the current study was the significant difference in the measured lens relative green:blue ratio between the tinted IOLs and the untinted IOLs. We found that the relative sensitivity to blue light was less in the group with the tinted IOLs than in the group with an untinted IOL, and this could be attributed to the IOL's absorbance characteristics. Our results suggest that the Acrysof Natural IOL retains the blue light–filtering properties of the aging crystalline lens, while the average green:blue ratio in the untinted group corresponded (according to equation 1) to that measured in a healthy 39.6-year-old lens.

To further evaluate the similarity in absorbance properties between the tinted IOLs and the

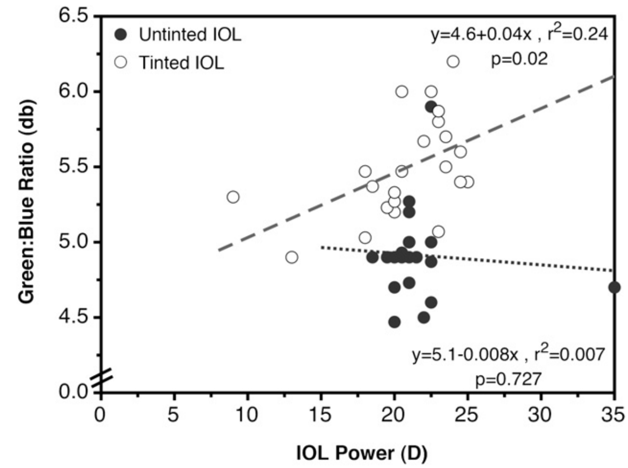

Figure 3. The measured green:blue luminance ratio in the 2 IOL groups as a function of IOL dioptric power. The dashed and the dotted lines and the equations corresponding to the least-square regression fits (IOL = intraocular lens).

crystalline lens, the green:blue ratio was analyzed in a subgroup of patients having surgery for refractive reasons who had nuclear senile cataract of grade 1 or less. The subgroup comprised 18 patients (mean age 58 $\pm$ 9.7 [SD] years) Eight patients (mean age 56 $\pm$ 11.4 years) received an Acrysof Natural IOL and 10 (mean age 57 $\pm$ 9.7 years), an untinted IOL. In the tinted IOL group, the mean preoperative green:blue ratio was 5.39 $\pm$ 0.14 (SE) dB and the mean postoperative green:blue ratio was 5.40 $\pm$ 0.09 dB (mean difference, 0.012 dB; 95% CI, −0.40 to 0.37, $P = .941$). In untinted IOL group, the mean preoperative green:blue ratio was 5.19 $\pm$ 0.09 dB and the mean postoperative green:blue ratio was 4.80 $\pm$ 0.08 dB (mean difference, 0.39 dB; 95% CI, 0.21-0.55; $P = .001$, paired-samples *t* test). Therefore, the postoperative performance of the yellow-tinted IOLs was similar to that of the preoperative performance in patients with mean age of 57 years. Also, the there was a significant reduction in blue-light attenuation in patients of similar age with untinted IOLs.

Furthermore, we found a relationship between the dioptric power of the tinted IOL and the measured green:blue ratio; this was not found in the untinted IOL group. This appears to confirm the assumption that the absorption is related to lens thickness.[37] As can be seen in Figure 3, the difference in dioptric power, such as in high myopia and hyperopia, may result in significant differences in the green:blue ratio. We propose that dioptric power may be incorporated in the manufacturing algorithms of these IOLs.

Several studies have evaluated the implications of blue light–filtering by tinted IOLs, with the main goal of determining the effect of the IOLs on color perception.[38] Color vision in patients with the Acrysof

Natural has been tested with the HMC anomaloscope, the Farnsworth D-15 color perception test, and the Farnsworth-Munsell 100-hue test; these studies found no significant effect of blue light–filtering IOLs on color perception.[39–41] This could be attributed to color-adaptation mechanisms.[42] In a study by Pierre et al.,[43] luminance contrast sensitivity to a blue–red drifting grating was compared between patients with an Acrysof Natural IOL and patient with an untinted IOL. Although the patients were tested with central viewing of the stimulus and the result cannot be attributed to lens absorption alone, Pierre et al. found that more blue light was required to make luminance judgments with the yellow-tinted IOL than with the clear IOL. The results in this study support the assumption that tinted IOLs attenuate blue-light luminance to the same amount as the aging crystalline lens but significantly more than untinted IOLs.

In conclusion, results in the current in vivo study indicate that implantation of blue light–filtering IOLs provides significantly greater blue-light attenuation than implantation of untinted IOLs and that the attenuation is similar to that of the aging crystalline lens. This effect may protect the retina from the blue-light hazard, although this must be further evaluated in future studies.

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First author:
Georgios A. Kontadakis, MD, MSc

Institute of Vision and Optics,
School of Health Sciences,
University of Crete, Crete, Greece