Glistenings on Intraocular Lenses

To the Editor:

I read the recent article by Colin and Orignac, which appeared in the December 2011 issue of the Journal of Refractive Surgery, with great interest. Of particular note were the data presented on the effect of glistenings on straylight as measured by the C-Quant device (Oculus Optikgeräte GmbH, Wetzlar, Germany). The data presented vary with data previously presented by the author at a 2010 lecture given at the annual meeting of the American Academy of Ophthalmology (AAO) in Chicago and probably involves the same cohort of patients. I believe it to be the same cohort, as the other values reported (corrected distance visual acuity and contrast sensitivity) are the same in the paper and presentation. However, in the AAO presentation, the C-Quant log values were significantly higher, 1.45 (grade 0), 1.70 (grade 1), and 1.89 (grade 2). The values reported at the presentation would make the results clinically significant as those of young individuals and in a range expected to adversely affect nighttime driving (“danger zone for driving at night”).

The authors also stated that “This study of AcrySof IOls in 97 healthy eyes...indicated that the intensity of glistenings was stable with postoperative duration, was not associated with increased intraocular light scattering...” Light scattering testing was reported only in 53 eyes, so this statement is misleading. Numerous studies show that intraocular straylight is the origin of disability glare. The authors’ data are interesting, but online Food and Drug Administration (FDA) resources document adverse clinical problems associated with glistenings.

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The author has no financial or proprietary interests in the materials presented herein.

REFERENCES


Reply:

We appreciate Dr Beiko taking the time to read and comment on our article, and are pleased to take this opportunity to discuss our work.

The nature of our study was retrospective and exploratory. For many of the outcomes, we tried to analyze the data several ways, looking for any possible effects and associations between glistenings and other variables. For the outcome of intraocular scatter (straylight) in particular, we performed many different analyses (Table); none of the analyses revealed significant associations between glistenings and intraocular scatter.

At the American Academy of Ophthalmology (AAO) meeting in 2010, we presented several different straylight analyses; the conclusion for all was that no significant differences in straylight were associated with density of glistenings. The simplest and most preliminary analysis that we presented was mean log (straylight) data for all 97 eyes in the study, grouped by glistenings grade. These are the values cited by Dr Beiko in his letter. Beyond just the mean values that were given in the letter, other important values are the standard deviations and statistical nonsignificance to those means. The mean log (straylight) values were 1.45±0.82 for grade 0 glistenings (n=39), 1.70±1.26 for grade 1 (n=31), and 1.89±1.55 for grade 2 (n=27), with P=.34 among groups by general linear model analysis (analysis of variance).

In the article, our refined method was to analyze the straylight data that were the most reliable. The criteria were described in the Methods section of the manuscript: “Criteria for reliable measurements were as follows: ‘log (straylight parameter)’ value <6, standard deviation (ESD) <0.10, and reliability index (Q value) >1.0.” These criteria were in accordance with an instruction sheet for the C-Quant (Oculus Optikgeräte GmbH, Wetzlar, Germany). This manual states that “log(s)=6.00 is a meaningless value” and “the measurement is considered reliable when ESD ≤0.08 and Q ≥1.0,” but “in most clinical cases, measurements with ESD ≤0.1 or even ESD ≤0.12 are sufficiently reliable.” As stated in the Results section of our article, “Intraocular straylight data that met the reliability criteria were available for 53 of 97 eyes. The straylight subgroups were evenly sampled from the parent groups of glistenings grades: straylight data were provided for 53.8% of eyes with grade 0 (21/39), for 54.8% of eyes with grade 1 (17/31), and 55.6% of eyes with grade 2 (15/27).” The results of the “reliable criteria” analysis were as stated in the article: The mean log (straylight) values were 1.2±0.2 for grade 0 eyes (n=21), 1.2±0.2 for grade 1 eyes (n=17), and 1.3±0.2 for grade 2 eyes (n=15), with P=.31 among groups. Because informa-
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Explanatory Analyses of Intraocular Straylight With Respect to Glistening Grade (Subjective) or Glistening Density (Objective)

<table>
<thead>
<tr>
<th>No. of Eyes</th>
<th>Glistenings Groups or Scoring</th>
<th>Significance or Correlation</th>
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</thead>
<tbody>
<tr>
<td>Raw mean C-Quant values by grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>log (straylight)</td>
<td>97</td>
<td>Subjective: Grade 0, Grade 1, Grade 2</td>
</tr>
<tr>
<td>Standard deviation (ESD)</td>
<td>97</td>
<td>Subjective: Grade 0, Grade 1, Grade 2</td>
</tr>
<tr>
<td>Reliability index (Q value)</td>
<td>97</td>
<td>Subjective: Grade 0, Grade 1, Grade 2</td>
</tr>
<tr>
<td>Raw mean C- Quant values by density</td>
<td></td>
<td></td>
</tr>
<tr>
<td>log (straylight)</td>
<td>62*</td>
<td>Objective, vacuoles/mm²: &lt;150, ≥150 to ≤280, &gt;280</td>
</tr>
<tr>
<td>Standard deviation (ESD)</td>
<td>62*</td>
<td>Objective, vacuoles/mm²: &lt;150, ≥150 to ≤280, &gt;280</td>
</tr>
<tr>
<td>Reliability index (Q value)</td>
<td>62*</td>
<td>Objective, vacuoles/mm²: &lt;150, ≥150 to ≤280, &gt;280</td>
</tr>
<tr>
<td>Reliable† mean C-Quant values by grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>log (straylight)</td>
<td>53‡</td>
<td>Subjective: Grade 0, Grade 1, Grade 2</td>
</tr>
<tr>
<td>Scatter plot</td>
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<td></td>
</tr>
<tr>
<td>log (straylight) vs glistenings</td>
<td>48§</td>
<td>Objective, vacuoles/mm² (individual values)</td>
</tr>
</tbody>
</table>

*Number limited by image quality for vacuole density analysis.
†Reliable = log (straylight parameter) value <6, standard deviation (ESD) <0.10, and reliability index (Q value) >1.0.
‡Number limited by reliable C-Quant values.
§Number limited by both criteria: Image quality and C-Quant values.

The authors have no financial or proprietary interests in the materials presented herein. Writing assistance provided by Alcon Research Ltd (Ft Worth, Texas).
Absorption of UV-light by Riboflavin Solutions With Different Concentration

To the Editor:

In previous articles,\textsuperscript{1-3} it was concluded that the ultraviolet (UV) light (365 nm) absorption of riboflavin depends at first linear (0.0% to 0.2%) on the concentration. The linear coefficient $\beta$, which couples the absorption coefficient $\mu(c) = \beta \cdot c$ with the concentration $c$ (in mg/mL, or %) of the riboflavin, was found to be nearly the same.\textsuperscript{1-3} However, at a specific concentration, depending on the measurement method, the linear relation turned into a constant value. This fact initiated a systematic error within the measurement methods that is present in all data sets. We describe the underlying problem and provide corrective data for the absorption of UV light depending on riboflavin concentration.

The error is caused by the dynamic range of the UV light. The light intensity that is transmitted through the absorbing layers of riboflavin (cuvette filled with riboflavin solution or tissue samples soaked with riboflavin) is, at a certain level, too small to be detected by the sensors mentioned in previous publications. The transmitted light intensity thereby depends solely on the Lambert-Beer-Law:

$$ I(c,z) = I_0 \exp(-\mu(c) \cdot z). $$

Considering a linear dependence of the absorption coefficient $\mu(c)$ for all concentrations of riboflavin, one can estimate the light intensity behind the tissue sample using the linear coefficient $\beta=560$ (mL/mg) cm$^{-1}$ ($\beta=560$ (%) cm$^{-1}$) obtained from the data of Spoerl et al.\textsuperscript{1}

For a sample saturated with riboflavin solution of 0.02%, the absorption coefficient would be $\mu(0.02%) = 11.2$ cm$^{-1}$ and for a solution concentration of 0.2% $\mu(0.2%) = 112$ cm$^{-1}$. Assuming a UV-light source of $I_0=3$ mW/cm$^2$ is used for cross-linking of the cornea and an absorbing riboflavin layer of 1 mm, the resulting transmitted intensities are $I(0.02\%, 1\text{mm}) = 0.33 \cdot I_0$ and $I(0.2\%, 1\text{mm}) = 0.000014 \cdot I_0$. In the second case, the resulting intensity $42 \cdot 10^{-6}$ mW/cm$^2$ cannot be detected with the light detectors used in previously published experimental setups. It may be that the ambient light, even in a dark room (1 to 10 $\mu$W/cm$^2$), is detected and causes the constant absorption coefficient. Considering the lowest intensity that can be detected is 5 $\mu$W/cm$^2$ and an incident light intensity of 3 mW/cm$^2$ ($I/I_0 = (5/3) \cdot 10^{-3}$), the maximal detectable concentration is 0.11%. Investigating higher concentrations, the light detector finds ambient light or noise, because the transmitted light is too small to be detected.

To detect transmitted light for higher concentrations (eg, 0.5% of riboflavin), one must change the experimental setup. Using a high intensity light source (365 nm, up to 90 mW/cm$^2$) and a special designed cuvette, which allows only a fluid thickness of 100 $\mu$m of riboflavin solution, we repeated the measurements and obtained a linear relationship of concentration and absorption coefficient over the whole concentration range from 0.0% to 0.5% riboflavin with a linear coefficient of $\beta=469$ (mL/mg) cm$^{-1}$ ($\beta=469$ (%) cm$^{-1}$) (Fig).

\textbf{Figure.} A) Normalized ultraviolet light transmission for different riboflavin concentrations and B) the resulting absorption coefficient.

\begin{center}
\includegraphics[width=\textwidth]{fig.png}
\end{center}
Letters to the Editor

These results demonstrate that the absorption coefficient depends linearly on the concentration up to 0.5% riboflavin. Previous publications may suffer from the described systematic error.

We apologize for the initial errors in our experimental setups.

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REFERENCES


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