Ocular Straylight and Artificial Lenses

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Oculair strooilicht en artificiële lenzen

Thesis

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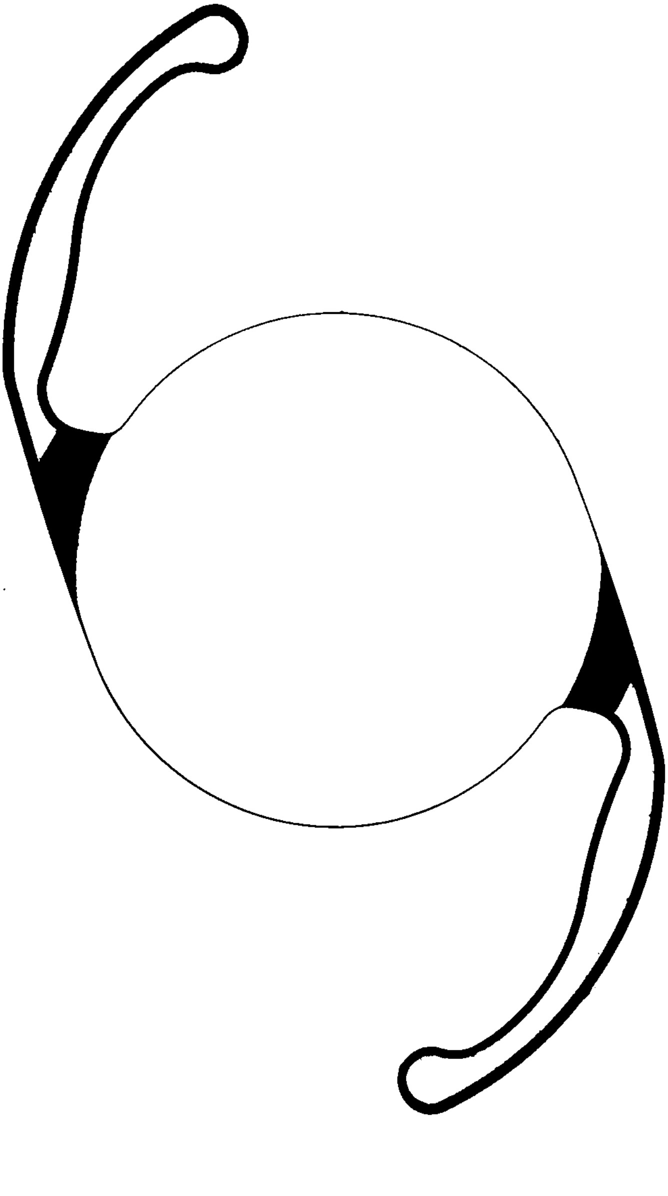

Chapter 1

Aim and scope of the thesis

Cataract is an opacification of the crystalline lens that progressively impairs vision. Cataract development can cause a perceived decrease of function of the affected eye. This perceived decrease of function is generally expressed as a loss of distance visual acuity (VA). Although early cataract most often does not cause VA symptoms,[1-3] patients may still report visual problems, which indicates that high contrast VA charts may not be a good representation of real-life situations,[4-6] To address this issue, the contrast sensitivity (CS) test has been adopted in the evaluation of cataractous patients.[1-4] CS measures the ability of the eye to detect small differences in luminance between a test object and its background. Although very important, VA and CS are limited to the central part (from 0.02 to 0.33°) of a functional point spread function (PSF).[7] But the outer part of the PSF (over approx. 1°) is also very important, and can be assessed by means of straylight measurements.[7] Development of (early) cataract is associated with increased straylight due to light scattering from lens opacification, and that may cause different visual symptoms, such as a loss of contrast, decreased color vision, and higher sensitivity to glare sources.[7-14] To restore good visual quality and to prevent loss of VA, a cataractous lens is removed, and replaced with an intraocular lens (IOL), in the course of cataract surgery. Although on average a substantial straylight decrease has been found following surgery, a recent clinical study has shown that in 15% of pseudophakic patients straylight remains at the preoperative level or increases after surgery.[15] A large population study on European drivers has reported that straylight of 10% of the pseudophakic patients was above the norm for phakic patients. Although in another 46% straylight was within the norm, a lower straylight level would be expected as the crystalline lens is an important source of straylight in the eye.[7, 10, 13] Based on the CIE standard, a value of 0.69 would be expected that is a straylight level of the young eye without contribution of the crystalline lens.[10, 13, 16] Clinical studies have shown, however, that even in the absence of postoperative complications the average straylight level ranges from 1.10 to 1.47 log(s).[15, 17-32] Therefore, the goal of this thesis was (1) to study *in vivo* the contribution to straylight of artificial eye lenses (with a focus on IOLs), (2) to determine the source of straylight elevation in pseudophakic eyes, and (3) to establish a new method for *in vitro* straylight assessment of IOLs.

To address the problem of increased straylight in pseudophakic patients, a literature review on straylight in pseudophakia was performed and is presented in **Chapter 3**. As it has also been realized that straylight–age dependence differs between phakic and pseudophakic patients, a new straylight norm for the pseudophakic patients was proposed. To minimize the potential for straylight increase following lens extraction, a model for predicting postoperative straylight improvement was created.

Several clinical studies have been conducted that investigate differences in straylight between different types of IOLs.[18-25, 29, 30, 32] Most often, monofocal and multifocal IOLs have been compared.[18-20, 25, 29] However, differences in multifocal designs and/or material properties must also be considered as potential reasons for straylight elevation. Straylight can be expected to be increased in patients with multifocal diffractive lenses, as only part of the light is focused while up to 18% is spread to higher-order foci, and might contribute to the straylight level.[33] In **Chapter 4**, postoperative straylight values were studied in 2 types of multifocal diffractive IOLs with different apodization patterns. To delineate other parameters (*e.g.* material properties) and to study the effect of different optical designs a literature review on multifocal IOLs was performed and is presented in **Chapter 5**.

Another reason for light scattering by IOLs may be "glistenings". Glistenings are fluid-filled microvacuoles of 1 to 20 μm size, which have most often been associated with hydrophobic acrylic material.[34-39] Postoperative glistenings formation in the IOL bulk is considered as an IOL-related complication, but it has not yet been well understood how they affect visual performance.[40-56] Although it is expected that the presence of glistenings must have adverse implications on visual quality, the scientific literature has shown rather inconsistent results. Most often, VA and CS have been used to assess glistenings effects.[40-56] However, as the difference in the refractive index of the fluid (glistenings) and of the surrounding medium (the IOL material) causes light scattering, one would expect to find these effects on straylight, instead of VA or CS. To better understand this problem, in **Chapter 6** straylight from glistenings is studied and discussed in relation to a general scattering theory.

In several studies IOL opacification following uneventful crystalline lens replacement has been reported.[57-63] The form of opacification depends on the type of material for IOLs.[57-63] Snowflake degeneration has been found in Poly(methyl methacrylate) (PMMA) lenses, in some patients ten (or more) years after implantation.[57] It has been suggested that a snowflake lesion may be triggered by UV light exposure, as it has frequently been found in the central and midperipheral areas of the lens.[57] Hydrophilic acrylic lenses have been associated with calcium and phosphate precipitations.[58, 60] However, studies have reported calcium deposits on hydrophilic lenses with hydrophobic coating,[62] and on PMMA lenses as well.[63] As opposed to snowflake degeneration, calcium-induced opacification appears relatively early postoperatively, in the second year following implantation.[57, 58, 60] It has been reported that calcification of hydrophilic lenses has a multifactorial etiology, and can be related to lens packaging, ophthalmic viscosurgical device or surgical technique.[58, 59] Calcification of silicone IOLs has been associated with asteroid hyalosis.[58, 61] Glistenings formation may occur in hydrophobic acrylic IOLs, as mentioned in the preceding paragraph.[39] The incidence rate of IOL degeneration/alteration and its effect on straylight were studied and are presented in **Chapter 7**. To this end, a random sample of 74 IOLs extracted from donor eyes were analyzed with a straylight meter, and with a slit lamp and light microscopy.

Straylight resulting from the use of contact lenses has been studied for soft as well as rigid gas permeable (RGP) materials.[64-70] A recent clinical study has shown that wearing RGP contact lenses is associated with increased straylight part of which persists after removal of the contact lenses.[70] That study also reported that soft contact lenses do not affect straylight.[70] Straylight of multifocal contact lenses has never been studied, but it might be that multi-zonal designs can increase straylight,[71] especially since it has been reported that multifocal contact lenses wearers are more prone to experience glare related symptoms (*e.g.* while driving at night).[72] To address this problem, straylight of 4 types of multifocal contact lenses was measured clinically with a commercial straylight meter. Results of this study are presented in **Chapter 8**.

To study light scattering from IOLs directly, *in vitro* methods are needed. Two such methods have been reported.[73, 74] These methods provide reliable and precise measurements, but require several specialized optical tools (*e.g.* an optical bench, a high-dynamic range camera). Therefore, they are not easily available for many researchers and clinicians. As discussed in the introduction, the C-Quant straylight meter is widely used in clinics. Although the C-Quant was designed to assess the functional *in vivo* straylight value,[75] it has been shown that this device can also be used for straylight measurements of, *e.g.* scattering filters.[76] Another potential application could be to evaluate (*in vitro*) straylight from IOLs. IOLs are, however, very different from standard scattering filters in terms of size and refractive power, as they are designed to have their refractive effect in the eye. Moreover, IOLs must be tested in solution. Therefore, an adaptation to the C-Quant was designed for straylight assessment of IOLs, and that is presented in **Chapter 9**. Since the straylight parameter refers to what is "seen" by the patient, the C-Quant adaptation is advantageous to clinical practice, as it allows a direct comparison between *in vivo* and *in vitro* straylight values.

In vitro straylight of IOLs has most often been assessed in case of the presence of large particles,[77-79] such as glistenings or surface deposits, but small (< λ) particles have also been found in implanted IOLs, *e.g.* nanoglistenings.[80-83] In **Chapter 10** a new method for detection and assessment of small particles is proposed and validated.

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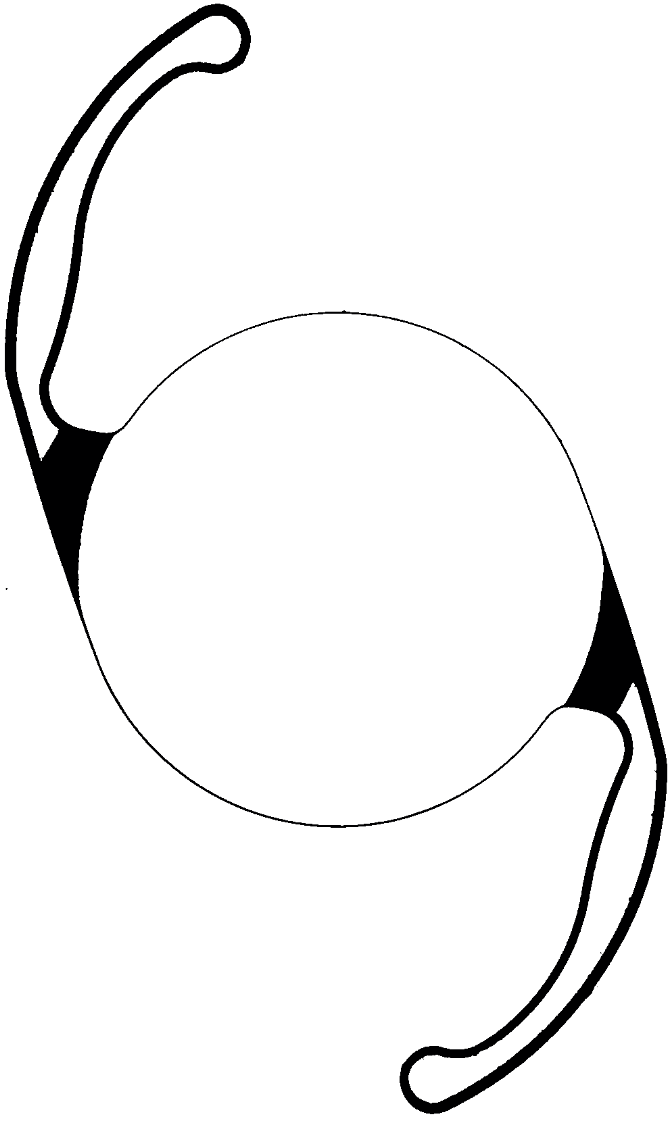

Chapter 2

Introduction to straylight

In an optical system, straylight refers to the light redirected by the process of light scattering out of an intended path defined by the optical design. Scattering originates from material inhomogeneities, *e.g.* particles, or surface roughness.[1] Scattering also takes place in the human eye.[2, 3] It results from optical imperfection of the eye optical media and creates a veil of light, which falls onto the retina and degrades contrast of the in-focus image.[2, 3] The CIE (Commission Internationale d'Éclairage) defined straylight as the means of proper quantification of disability glare.[4] It corresponds to the outer (>1°) part of the functional Point Spread Function (PSF) (**Figure 1**) and is expressed by means of the straylight parameter (s):

$$s = \theta^2 \times PSF(\theta) \quad [deg^2/sr]$$

at a θ distance from the straylight source.[4] In a clinic, however, most often straylight is presented logarithmically as log(s).

Straylight is a separate, from visual acuity (VA) and contrast sensitivity (CS), domain of the functional PSF (**Figure 1**), thus standard ophthalmic tests cannot be used for its assessment in the eye.[3] In response to the need of a clinical instrument, new devices have been proposed that are designed based on the PSF approach.[3, 5-7] One such a device is the C-Quant straylight meter (Oculus Optikgeräte GmbH, Germany), which follows the CIE standard, using a psychophysical approach to directly assess the functional PSF at 7-degree scatter angle,[3, 6] and is the subject of this thesis. The HD Analyzer (Visiometrics SL, Terrassa, Spain) is an instrument that uses a double-pass method for the PSF assessment of the eye.[5, 7] This apparatus, however, measures the PSF in an angular range of minutes of arc.[5, 7] Its validity for scatter assessment has been seriously criticized.[7] A new double-pass approach has been proposed that may be free of some of those limitations,[8] but a clinical instrument is yet to be introduced.

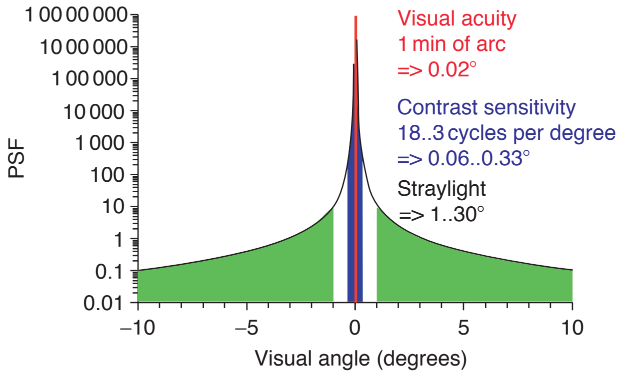

Figure 1. Functional Point Spread Function (PSF) of a normal eye. The PSF can be used to quantify visual performance in terms of: visual acuity (red peak), contrast sensitivity (blue area) and straylight (green area) *(Encyclopedia of the Eye, 2010).*

C-Quant straylight meter

The PSF approach, as defined by the CIE standard, is applied in the C-Quant straylight meter (**Figure 2**).[2, 3, 6, 9]

The C-Quant assesses the straylight parameter (presented as log[s]) by means of the psychophysical compensation comparison method.[6, 9, 10] This methods works as follows. A C-Quant test screen (**Figure 3**) consists of a flickering (in black and white) ring that surrounds the test field and serves as a straylight source.

Figure 2. C-Quant straylight meter.

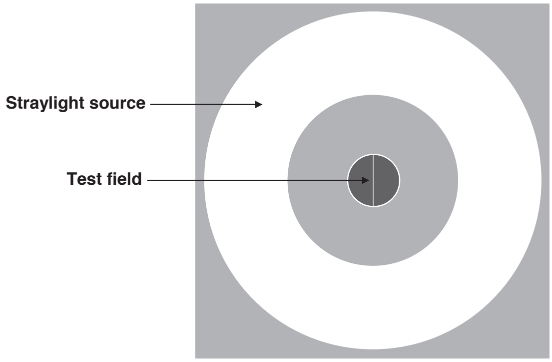

Figure 3. C-Quant test screen.

The test field is divided into 2 halves. In both halves flickering results from light scattering in the eye (part of the straylight source is scattered towards the fovea). But in one, randomly chosen half, counter-phase light (called compensation light) with different modulation depths is added. In the course of the C-Quant test, a patient decides which of the 2 halves flickers stronger and presses a respective push button (the left/right button correspond to the left/right half) to provide a response. The difference between the 2 halves is compensated by compensation light of a known value. After pressing the button, another amount of compensation light is added and at a certain moment both halves flicker at more or less the same intensities. This point defines the straylight value, by the equivalence principle. Although, at this point a difference may be difficult to see, the subject must guess and press one push button. This is a well-established psychophysical principle, called a 2-alternative forced choice method. Based on the subject's responses a psychometric curve is fitted with the minimum giving the sought straylight value.[6, 9, 10]

The C-Quant has proved repeatable and reliable in clinical studies.[11, 12] This instrument provides a functional straylight parameter that is subjectively almost as important as VA for overall appreciation of visual quality. It has been shown that a 0.1 increase in log(s) is close in subjective importance to a loss of 1 line on the logMAR scale.[13]

Straylight in the phakic eye

Four major anatomical sources of ocular straylight can be found in a young normal eye (**Figure 4**).[2, 3, 14]

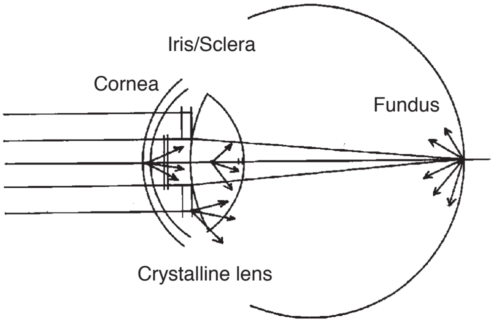

Figure 4. Sources of straylight in a healthy eye *(Encyclopedia of the Eye, 2010).*

The cornea and the crystalline lens account for 2/3 of total scattering (1/3 each), the remaining 1/3 results from fundus reflectance and light transmittance through the ocular wall.[2, 3, 14] This proportion may, however, change due to aging of the crystalline lens.[2, 3, 14-16] It has been shown that ageing is an important factor in straylight of the eye. Most recently, a large population study has assessed straylight in over 2,000 healthy eyes introducing a new norm of straylight in normal phakic eyes (**Figure 5**).[16]

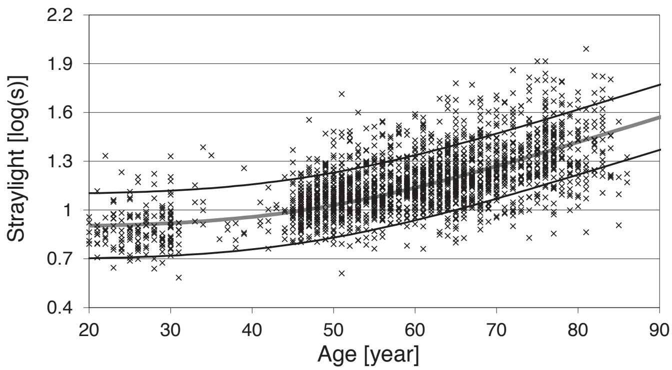

Figure 5. Straylight as a function of age in normal phakic eyes (*Van den Berg et al. Am J Ophthalmol 2007;144*).

Figure 5 shows a clear straylight increase with age in normal eyes, and this relationship was used to formulate a CIE standard for the PSF.[3, 4, 14-16] The CIE standard contains formulas of different levels of complexity. One such formula is:

$$PSF = \frac{10}{\theta^3} + \left(\frac{5}{\theta^2} + 0.1\,\frac{p}{\theta}\right)\left[\,1 + \left(\frac{Age}{62.5}\right)^4\,\right] + 0.0025p$$

where θ is the visual angle and p is a parameter for the degree of pigmentation of the eye.[2, 4, 11, 16, 17] The p parameter depends on iris color (pigmentation) and ranges from 0.00 to 1.21, *e.g.* for an average Caucasian eye p=1.[14] **Figure 5** and the model also show that even a young, healthy eye scatters light at a level of log(s)=0.9, and it accounts for (approx.) 5% of the incoming light.[14] Straylight remains at this level until age 40, then it gradually increases to be doubled at the age of 65 years.[14, 16] A model prediction of straylight for a 35-year-old and 65-year-old eye, and a cataractous eye are presented in **Figure 6**.

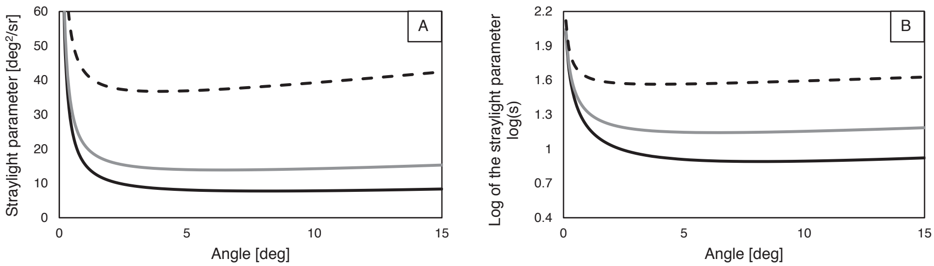

Figure 6. CIE standard for the Caucasian eye presented as the straylight parameter (A), and clinically as log(s) (B). The black and gray solid lines refer to a normal eye at aged 35 and 65, respectively. The black dashed line indicates straylight of a cataractous eye that was calculated as an equivalent to that of a 95 year-old eye.

Several pathological conditions have been associated with straylight elevation.[3, 17-31] Increased straylight results in disability glare, which may be described by patients as difficulties while driving at night (as caused by headlights of approaching cars) or against a low sun.[2, 3, 32] Straylight can also be related to such complaints as hazy vision, problems with face recognition and decreased color sensitivity.[2, 3, 32] **Figure 7** illustrates high and low straylight levels.

Although a young crystalline lens shows very low straylight (*e.g.* for a 20-year-old lens it is 0.39 log[s]),[14] aging process and lens-related disorders, such as (early) cataract, cause ocular straylight to increase.[3, 17, 19, 24] The literature has shown that all cataract types are associated with straylight elevation. However, significant differences between the types exists,[3, 17, 19, 24, 33] as a mean straylight increase of 1.05 log(s), 1.36 log(s) and 1.54 log(s) was found in patients with cortical, nuclear and posterior subcapsular cataract, respectively.[33] Although the CIE standard is mostly used for age-based prediction of straylight of the normal eye, the same formula can also be used to model cataract (**Figure 6**). This can be understood as early aging of the crystalline lens, *e.g.* straylight of best 95-year-old lenses (log[s]=1.52) is comparable to the average effect of cataract found in a population

Figure 7. Visualization of a (A) low and (B) high (1.47 log[s]) straylight level *(Encyclopedia of the Eye, 2010).*

study.[3, 14, 15, 19] The cornea may become an important source of ocular straylight, as loss of transparency or integrity yields a significant straylight increase. Most of the corneal dystrophies such as crystalline[18, 20] or Fuch's dystrophy[23, 25, 29] result in straylight elevation. For instance, a 20-fold straylight increase, as compared to straylight of the healthy eye, has been reported in most severe cases.[18, 20] Significantly increased straylight (a 2.5-fold increase) has also been found in patients with keratoconus as compared to normal (control) subjects.[30] Although the effect of the vitreous of a healthy eye on straylight is minute, vitreous turbidity (*e.g.* floaters) can give rise to functionally important straylight elevation, and that is 1.54 log(s) on average.[28]

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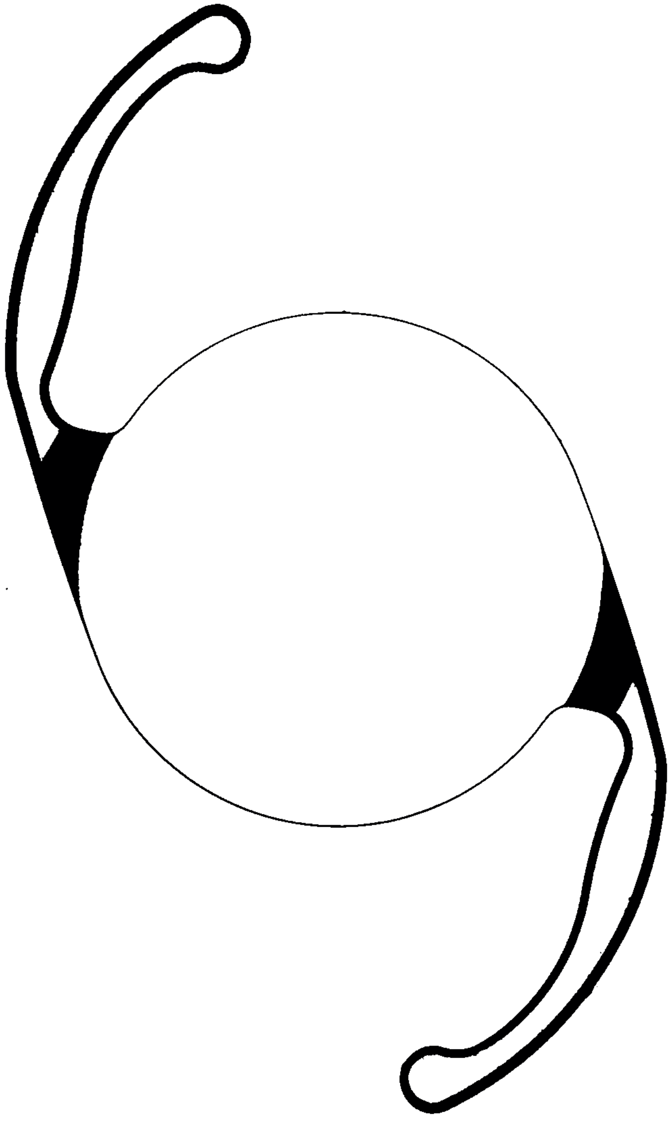

Chapter 3

Ocular straylight in the normal pseudophakic eye

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J Cataract Refract Surg. 2015 Jul;41(7):1406-15

ABSTRACT

Purpose

To assess normal values for straylight in the pseudophakic eye as a function of age and to develop a model to predict the improvement in straylight after lens extraction based on preoperative straylight levels.

Methods

A literature review was performed to identify relevant papers on straylight and pseudophakia with no patient comorbidities. Sixteen papers met the eligibility criteria and were included in the analysis. The postoperative results were used to define the norm for straylight in pseudophakia. Straylight improvement after lens replacement was assessed by evaluation of preoperative and postoperative values. The age effect was incorporated to determine a model for straylight improvement.

Results

The mean postoperative straylight value derived from 16 studies (1869 eyes) was 1.21 log units ±0.21 (SD). Age dependence could be assessed from 13 studies (1533 eyes), resulting in the straylight age-norm curve in pseudophakic eyes as follows: Straylight value = 0.0044 x age + 0.89 with ±0.42 log units of 95% confidence interval. A strong correlation was observed between preoperative straylight and its improvement after lens extraction, yielding the following relationship: Straylight improvement = 1.04 x preoperative straylight value - 0.006 x age - 0.84.

Conclusion

A norm for straylight in the pseudophakic eye was developed that is considerably different from the previously published norm for the phakic eye. The new pseudophakic norm can be used clinically to predict the straylight value after lens replacement and as a reference criterion for clinical studies.

INTRODUCTION

The influence of light scattering on visual quality has been studied since the beginning of the 20th century. This phenomenon was first described as a veil of light over the retina by Cobb.[1] Light scatter is produced by small inhomogeneities in the eye's optical media due to variations in the refractive index. It results in the visual effect of light radiation around bright sources of light, called straylight. Straylight causes glare and other visual disturbances.[2] Almost 10% of the incoming light is scattered in young normal eyes.[3] Straylight remains stable until the fifth decade of life. Above the age of 50 years, however, a considerable increase is observed. Because of senile processes affecting the crystalline lens, straylight increases 2-fold at 65 years and is tripled by the age of 77 years for eyes with good visual acuity.[4] Increased straylight can lead to severe functional difficulties, such as disability glare, hazy vision, and decreased color sensitivity.[5] Many ophthalmologic conditions have been studied for their effect on straylight.[6] For example, a considerable increase in straylight can be observed as a consequence of corneal dystrophies,[7] cataract,[8] vitreous turbidity,[9] posterior capsule opacification (PCO),[10,11] and intraocular lens (IOL) opacity.[12]

Intraocular straylight is caused by light scattered toward the retina (forward scatter). Some part of the light is scattered backward, as observed with techniques such as biomicroscopy and Scheimpflug imaging; however, the relationship between forward scatter and backscatter is weak.[13] Therefore, these techniques are inadequate to assess straylight. Similarly, visual acuity and contrast sensitivity cannot be used to assess the amount of straylight in the human eye.[4,14] Straylight can be measured with dedicated instrumentation such as the clinically available C-Quant instrument (Oculus).[A] This device delivers a functional parameter, called log(s); a 0.1 increase in the log(s) value has more or less the same importance as loss of 1 line on the logMAR chart. This instrument has been shown to have good reliability and repeatability.[15–17]

In the management of cataract, visual acuity is still considered the primary criterion for quality of vision.[18] However, disability glare has been accepted as a criterion as well.[19,20] Because straylight increases with age, a phakic norm curve has been defined[4] to be used as reference in clinical practice as well as in clinical studies. In cataract cases, straylight can increase far above the norm. Cataract surgery has proved to be effective in reducing straylight even in cases of "clear lenses."[21] However, van der Meulen et al.[22] recently found that almost 15% of healthy cataract patients after uneventful lens replacement had no change or an increase in straylight when decision-making involved only visual acuity. This can result in postoperative dissatisfaction even though visual acuity is good. To avoid disappointment after crystalline lens extraction, it is desirable to know what straylight value can be expected in pseudophakic eyes. Thus, a pseudophakic norm curve is needed in addition to the phakic norm. This norm curve can also serve as reference for clinical studies of pseudophakic eyes.

The objectives of this study were to determine a pseudophakic norm for straylight as a new reference and to study the predictability of straylight improvement after cataract surgery. To achieve this goal, a comprehensive literature review and a cross-study data analysis were performed.

METHODS

This study included 2 parts. First, a comprehensive review was performed to assess normal straylight values as a function of age in pseudophakic eyes. Second, changes in intraocular scatter after crystalline lens replacement were evaluated by analyzing raw data from available studies.

Comprehensive Review

Eligibility Criteria

A literature examination was performed without language restrictions and encompassing all studies reporting straylight values obtained with the natural pupil using the C-Quant instrument after uneventful phacoemulsification and IOL implantation. There were no limitations with regard to age, sex, or race of the participants. Studies were excluded that enrolled patients with PCO, previous laser posterior capsulotomy, visible disturbances of the IOL, ophthalmic comorbidity, or a history of ocular surgery (excluding natural lens extraction). Data with an expected standard deviation of 0.12 log units or less were deemed reliable and used for analysis.[17]

Review Process

The scientific databases PubMed, Proquest, Embase, Medline, and Google Scholar were screened using the following keywords: C-Quant, intraocular lens, and straylight. **Figure 1** shows the results of this screening and further selection of papers.

For studies with overlapping datasets, the article containing the largest population was used. In the case of deficient data concerning the log(s)–age linear regression, the respective authors were contacted. If a response was not obtained, GSYS2.4 software[B] was used to extract missing data from the published plots. Sixteen studies fulfilled the eligibility criteria and were included in the numerical analysis. **Figure 2** shows the details of the data used to determine the pseudophakic norm.

A linear regression equation describing the dependence of straylight on age was published in 2 articles.[11,23] To collect additional information, a request was sent to the corresponding authors of the other papers. In response, raw data were received from 6 authors[4,21,22,24–26]; 3 others[27–29] delivered their linear regression equation that had not been

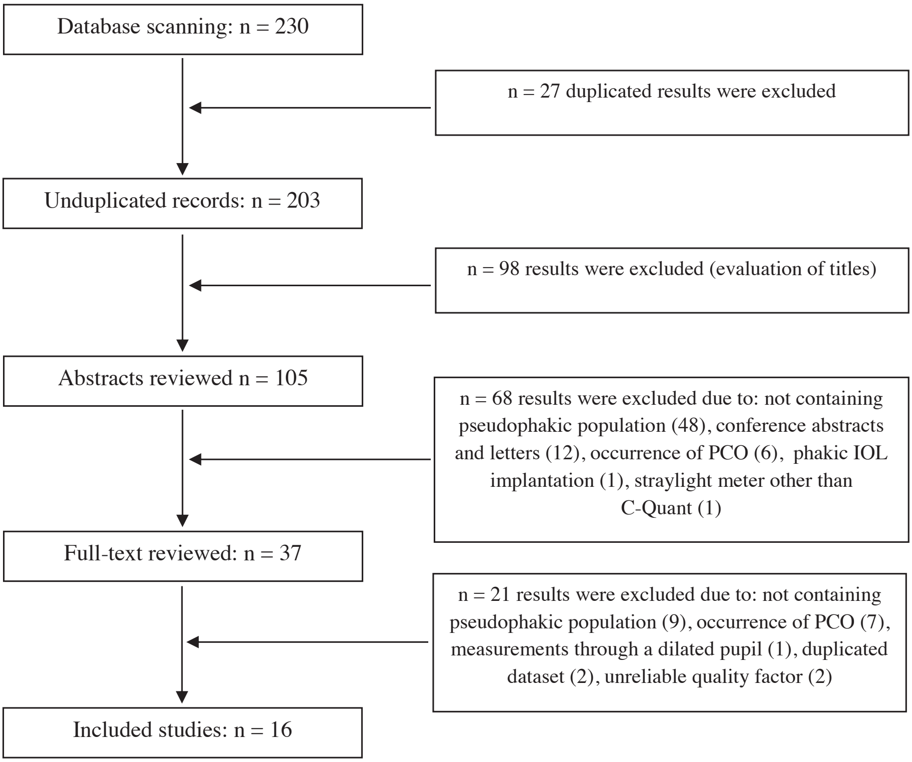

Figure 1. Flow diagram of systematic literature review (IOL=intraocular lens; PCO=posterior capsule opacification).

described in the article. No answer was obtained for 5 studies. The necessary data could be extracted from the published plots of 2 of these papers.[30,31] The remaining articles[32–34] were not used to develop the pseudophakic norm.

Breakeven Point as a Function of Age

To study actual straylight improvement after cataract surgery, both preoperative and postoperative values are needed. For this purpose, raw data were received from the authors of 3 different papers.[21,22,25] Analysis of the complete datasets from these studies led to the development of a computational model of straylight improvement after crystalline lens replacement. Improvement was defined as preoperative log(s) minus postoperative log(s), after which the relationship between preoperative straylight and its improvement was studied. The preoperative log(s) value for which improvement crosses the value zero was called the breakeven point. The breakeven point gives the 50% probability criterion to achieve a postoperative enhancement or deterioration of intraocular scatter. To incorporate the influence of aging, the calculation was performed for different decades of life. The approval for using the raw clinical data was obtained from the original authors.

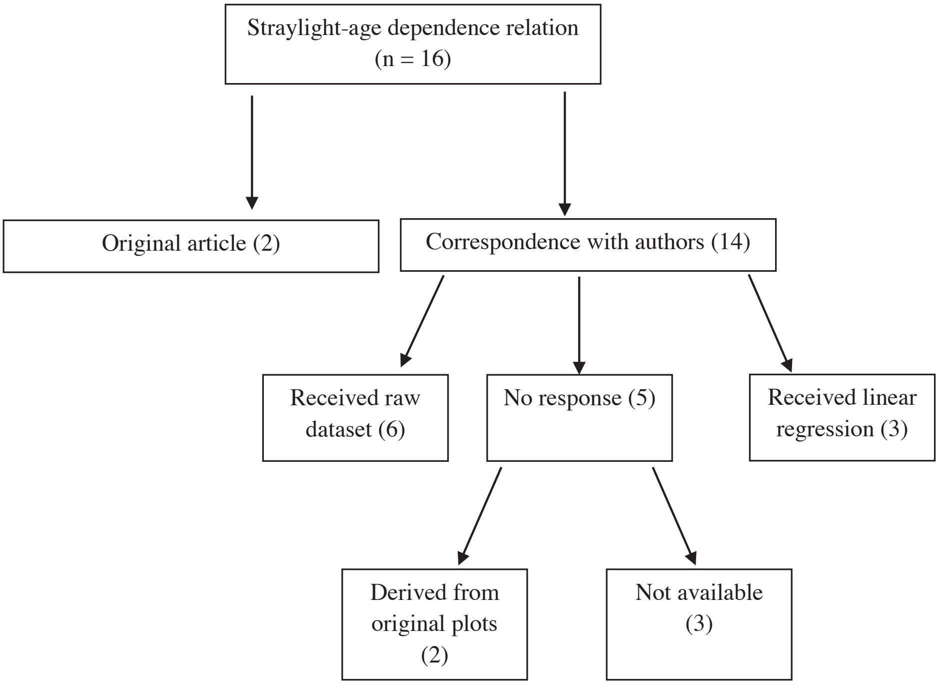

Figure 2. Data-acquisition process.

Statistical Analysis

Simple linear regression analysis describing straylight value log(s) as a function of age was calculated with Excel software (2007, Microsoft Corp.). For articles in which different IOLs were studied, the age dependency was assumed to be the same for all IOLs. To calculate the pseudophakic reference curve, a weighted average of each linear regression equation per study was performed. The raw data supplied by the original authors or the plots analysis was used to determine the 95% confidence interval (CI).[4,11,21–26,28,30,31]

To study the consistency of the new pseudophakic reference curve, it was compared to each of the 16 collected articles. The cross-validation technique was applied to avoid the influence of a particular result. The reference log(s) was calculated based on the mean age of the population in the individual study. The hypothetical control group was used to compare its result with the published log(s) value. To this end, a forest plot was created using Comprehensive Meta-Analysis software (version 2.0, Biostat, Inc.). Homogeneity was assessed by calculating the chi-square value. The difference in means (±95% CI) was used to assess effect size. Because age differences between studies induced heterogeneity, the random-effect model was chosen. The significance level was set at a P value less than 0.05.

Because both preoperative and postoperative straylight values have an uncertainty, Deming regression analysis was used to calculate the breakeven point. To improve accuracy, the slope was derived by analysis of the entire population, whereas constants and R^2 coefficients were calculated for different decades of life separately.

RESULTS

Comprehensive Review

As explained in the Methods, 16 reports fulfilled the eligibility criteria. **Table 1** shows a summary of their outcomes with the time of follow-up visits and information on the implanted IOLs.

The evaluation was of 1869 eyes. The mean age of the patients was 68 years ±9 (SD), and the mean straylight value was 1.21 ±0.21 log units (range 0.58 to 2.13 log units). **Figure 3** shows the log(s)–age linear regression as well as centers of gravity for each study.

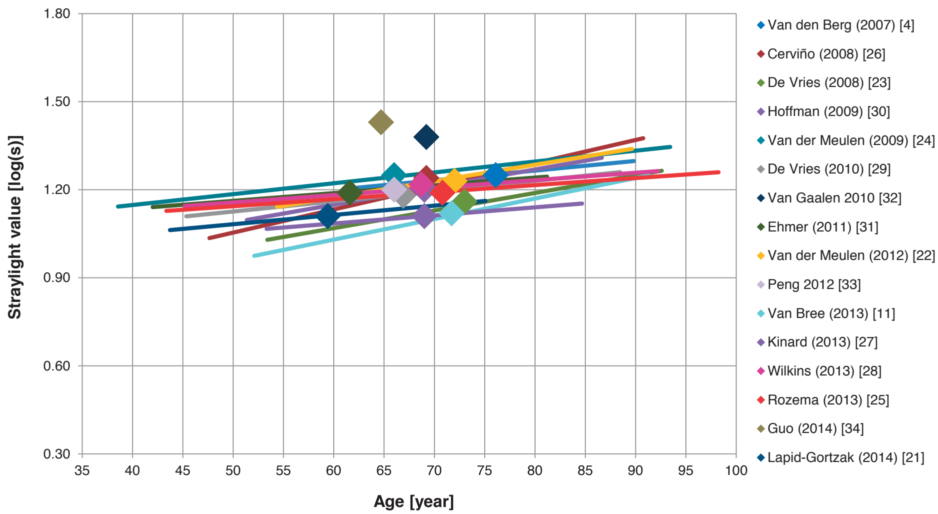

Figure 3. Linear model of log(s)-age dependency for the 13 included articles (solid lines). For each study, the plotted line is centered on the study's mean age and has a length of ±1.96 x SD of the respective age distribution. For 3 studies the regression line was not available. The diamonds represent the centers of gravity of all 16 articles included.

Pseudophakic Norm

The pseudophakic norm curve was based on 13 studies (1533 eyes). It reads:

$$\text{Straylight value} = 0.0044 \times \text{age} + 0.89$$

Table 1. Overview of published data (unless otherwise noted) in the 16 included studies.

		Mean Age	Log(s)				
First Author (Year)	N	(Y) ± SD	Mean ± SD	Range	FU(Mo)	IOL Model*	Log(s)-Age Dependency
Van den Berg[4] (2007)	220	76 ± 7	1.25 ± 0.22	0.61, 1.95	>1	Unknown	log(s) = 0.003 × age + 1.00†
Van Bree[11] (2013)	99	72 ± 10	1.12 ± 0.19	0.58, 1.59	>6	Unknown	log(s) = 0.007 × age + 0.61
Van der Meulen[12] (2009)	56	66 ± 14†	1.25 ± 0.27†	0.68, 2.13	>2	Acrysof SA60AT/SN60WF	log(s) = 0.004 × age + 1.00†
Van der Meulen[12] (2009)	32	73 ± 9	1.24 ± 0.24	0.80, 1.68	>2	Thinoptx IOL/Acri.Smart48	log(s) = 0.008 × age + 0.66†
Cervino[15] (2008)	35	66 ± 12	1.24 ± 0.30	0.93, 1.97	>6	Rezoom/Acrysof Restor SN60D3	log(s) = 0.008 × age + 0.66†
Lapid-Gortzak[21] (2014)	160	59 ± 8	1.11 ± 0.16	0.76, 1.63	>3	SN60WF/AT Lisa 809M/Mplus LS-313/Restor SN6AD1/SeeLens MF	log(s) = 0.003 × age + 0.92†
Van der Meulen[22] (2012)	309	72 ± 9	1.23 ± 0.16	0.64, 1.82†	NA	Acrysof SN60WF	log(s) = 0.006 × age + 0.84†
De Vries[23] (2008)	44	71 ± 9	1.10 ± 0.19	0.78, 1.60	>6	Acrysof SA60AT	log(s) = 0.006 × age + 0.77
De Vries[23] (2008)	60	75 ± 10	1.20 ± 0.16	0.86, 1.61	>6	Acrysof Restor SA60D3	log(s) = 0.006 × age + 0.77
Rozema[25] (2013)	81	71 ± 14	1.19 ± 0.21	0.73, 1.68	>6	89A Morcher	log(s) = 0.002 × age + 1.02†
Kinard[27] (2013)	70	69 ± 8	1.11 ± 0.19	0.78, 1.76	>6	Acrysof SN6WF	log(s) = 0.003 × age + 0.92§
Wilkins[28] (2013)	83	69 ± 12	1.18 ± 0.28§	0.55, 1.92‡	>4	Akreos AO	log(s) = 0.003 × age + 0.89§
Wilkins[28] (2013)	82	67 ± 11	1.21 ± 0.29§	0.62, 2.00‡	>4	Tecnis ZM900	log(s) = 0.003 × age + 0.89§
De Vries[29] (2010)	47	65 ± 10	1.19 ± 0.19	0.85, 1.79‡	>6	Acrysof Restor SN6AD3	log(s) = 0.003 × age + 0.95§
De Vries[29] (2010)	45	68 ± 11	1.16 ± 0.16	0.89, 1.61‡	>6	Acrysof Restor SN60D3	log(s) = 0.003 × age + 0.95§
Hofmann[30] (2009)	40	72 ± 8‡	1.20 ± 0.24‡	0.75, 1.87†	>18	SA60AT	log(s) = 0.006 × age + 0.79‡
Hofmann[30] (2009)	40	68 ± 9‡	1.20 ± 0.20‡	0.84, 1.65†	>18	Acrysof Restor SA60D3	log(s) = 0.006 × age + 0.79‡
Ehmer[31] (2011)	10	60‡ ± 14‡	1.12 ± 0.12‡	0.95, 1.35	>3	ReZoom	log(s) = 0.003 × age + 1.03‡
Ehmer[31] (2011)	10	59‡ ± 10‡	1.32 ± 0.22‡	1.04, 1.76	>3	Tecnis ZM900	log(s) = 0.003 × age + 1.03‡
Ehmer[31] (2011)	10	65‡ ± 7‡	1.14 ± 0.19‡	0.87, 1.51	>3	Mplus LS-313	log(s) = 0.003 × age + 1.03‡
Van Gaalen[32] (2010)	29	69 ± 10	1.38 ± 0.26	NA†	>1.5	Tecnis Z9000	NA
Van Gaalen[32] (2010)	29	69 ± 10	1.38 ± 0.25	NA†	>1.5	Sensar AR40e	NA

Table 1. Overview of published data (unless otherwise noted) in the 16 included studies. (continued)

First Author (Year)	N	Mean Age (Y) ± SD	Log(s) Mean ± SD	Log(s) Range	FU(Mo)	IOL Model*	Log(s)-Age Dependency
Peng[33] (2012)	102	67 ± 9	1.16 ± 0.23	NA†	>6	Acrysof SN60WF	NA
Peng[33] (2012)	100	66 ± 9	1.23 ± 0.21	NA†	>6	Acrysof Restor SN6AD1	NA
Guo[34] (2014)	24	67 ± 7	1.47 ± 0.22	0.93, 1.88	>1	Sensar AR40e	NA
Guo[34] (2014)	28	63 ± 10	1.37 ± 0.24	0.95, 1.82	>1	Hexavision HQ201hep	NA
Guo[34] (2014)	24	65 ± 8	1.45 ± 0.23	0.96, 1.87	>1	Henan PC156C55	NA

FU = follow-up; IOL = intraocular lens; NA = not available

*BIL (Type 89A, Morcher GmbH, Germany); Acri.Smart48 (Carl Zeiss Meditec, Jena, Germany); Acrysof Restor SN60D3 (Alcon Laboratories, Fort Worth, TX, USA); Acrysof Restor SN6AD1 (Alcon Laboratories, Fort Worth, TX, USA); Acrysof Restor SN6AD3 (Alcon Laboratories, Fort Worth, TX, USA); Acrysof SA60AT (Alcon Laboratories, Fort Worth, TX, USA); Acrysof SN60WF (Alcon Laboratories, Fort Worth, TX, USA); Akreos AO (Bausch & Lomb, Rochester, NY, USA); AT Lisa 809M (Carl Zeiss Meditec, Jena, Germany; PC156C55 (Henan Universe Intraocular Lens Research and Manufacture Co, Henan, China); HQ201hep (Hexavision, Paris, France); Mplus LS-313 (Oculentis GmbH, Berlin, Germany); Restor SN60D3 (Alcon Laboratories, Fort Worth, Texas, USA); Rezoom (Advanced Medical Optics, Santa Ana, California, USA); SeeLens MF (Hanita Lenses RCA Ltd., Kibbutz Hanita, Israel); Sensar AR40e (Advanced Medical Optics, Santa Ana, California, USA); Tecnis Z9000 (Advanced Medical Optics, Santa Ana, California, USA);Thinoptx IOL (ThinOptX Inc, Abrindon, Virginia, USA)

†Derived from) analysis of raw records

‡Derived published plots

§Derived correspondence with the authors

The 95% CI derived from 1366 raw records was ±0.42 log units. **Figure 4** shows the new reference curve and the 1366 individual postoperative log(s) values from available studies.

The above norm function recalculated by the cross-validation technique was applied to compare the outcomes of the included papers. Heterogeneity was observed with $I^2 = 85\%$ ($P < .05$); therefore, the random-effect model was used. Eleven of the 16 evaluated studies did not show statistically significant differences in the mean log(s) value compared with the reference curve. **Figure 5** shows the pooled study's distribution as a graph. The mean overall difference was -0.02 ±0.02 log units; however, the effect was not statistically significant (P = .26).

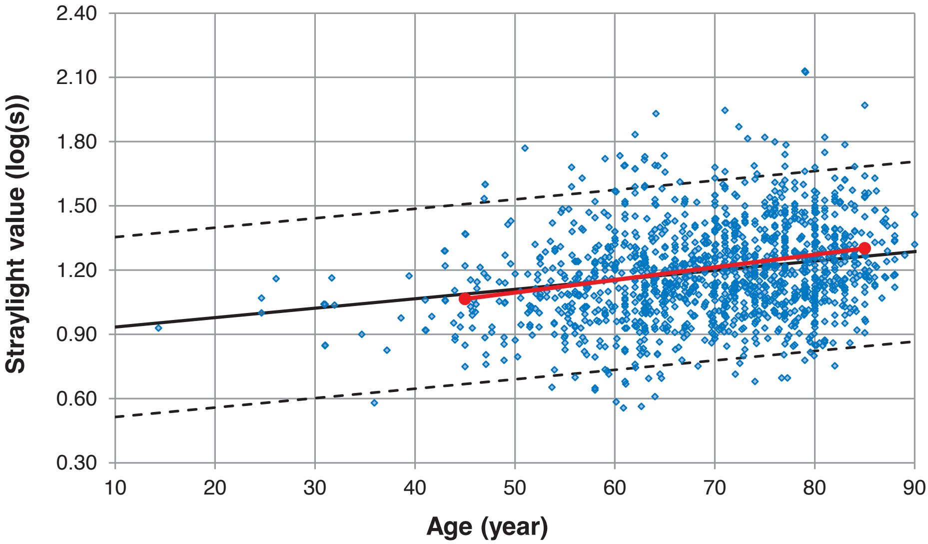

Figure 4. Intraocular scatter as a function of age in pseudophakic eyes (diamonds). The solid blackline represents the straylight pseudophakic norm with 95% CI (dashed lines). The solid red line shows the break-even point for age dependency.

Breakeven Point in Relation to Age

For 558 records, individual postoperative and preoperative straylight values were available. They were partitioned according to patient age in 5 decades of life from 40 to 90 years. Five eyes were excluded from the analysis because they did not fall into any of the age bands. **Figure 6** shows the difference between preoperative and postoperative straylight values as a function of preoperative straylight.

The reference curve reads

Straylight improvement = 1.04 x preoperative straylight value - 0.006 x age - 0.84 (R^2= 0.59, P<.05). **Table 2** shows detailed information on preoperative and postoperative straylight, including breakeven points for different decades of life. **Figure 4** is a graph of the breakeven point increase with patient age.

Study name	Difference in means	Standard error	Lower limit	Upper limit	p value
Van den Berg (2007)	-0.03	0.02	-0.07	0.01	0.14
Cervino (2008)	-0.05	0.04	-0.13	0.03	0.21
De Vries (2008)	0.05	0.03	-0.00	0.10	0.06
Hoffman (2009)	-0.01	0.03	-0.08	0.06	0.77
Van der Meulen (2009)	-0.08	0.05	-0.17	0.01	0.08
De Vries (2010)	0.00	0.03	-0.06	0.06	1.00
Van Gaalen (2010)	-0.18	0.04	-0.27	-0.09	**0.00**
Ehmer (2011)	-0.03	0.05	-0.13	0.07	0.57
Van der Meulen (2012)	-0.03	0.02	-0.06	0.00	0.06
Peng (2012)	-0.02	0.02	-0.06	0.02	0.35
Van Bree (2013)	0.09	0.03	0.03	0.15	**0.00**
Kinard (2013)	0.09	0.03	0.02	0.16	**0.01**
Wilkins (2013)	-0.03	0.03	-0.08	0.03	0.31
Rozema (2013)	0.01	0.03	-0.05	0.07	0.76
Guo (2014)	-0.25	0.04	-0.32	-0.18	**0.00**
Lapid (2014)	0.05	0.02	0.01	0.09	**0.02**

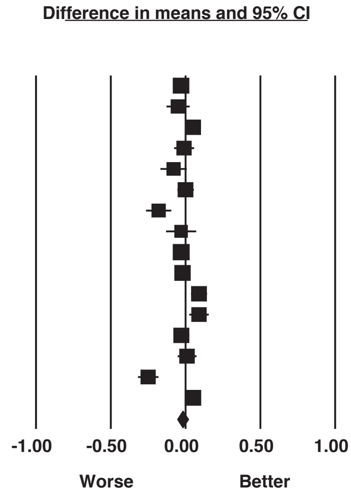

Figure 5. Forest plot characterizing differences between studies and computational age-matched control groups. The hypothetical straylight value was calculated based on the mean age in each article. Of 16 studies, 11 did not show a statistically significant difference in means, whereas 5 indicated abnormal results. Boldfaced P values indicate statistical significance. For more details about the computational technique and the discussion of the outcomes, please refer to the Discussion section (CI = confidence interval).

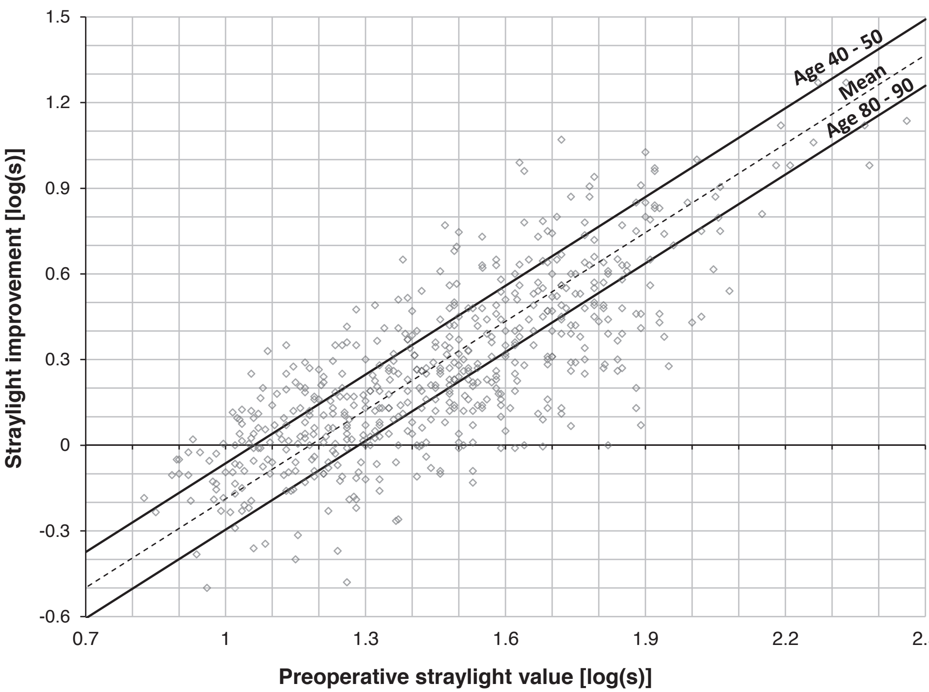

Figure 6. Improvement in straylight after crystalline lens exchange. The dashed line represents the mean rate, while the solid lines indicate the age effect. The upper line corresponds with the age range 40 to 50 years and the lowest line with the age range 80 to 90 years.

Table 2. Preoperative and postoperative straylight values and postoperative improvement for 553 eyes stratified over 5 decades of age.

	Age (Y)				
Parameter	40 to 50 (n = 23)	50 to 60 (n = 90)	60 to 70 (n = 160)	70 to 80 (n = 193)	80 to 90 (n = 87)
Preoperative straylight value					
Mean ± SD	1.21 ± 0.34	1.29 ± 0.32	1.41 ± 0.27	1.57 ± 0.25	1.57 ± 0.25
Range	0.89, 2.33	0.83, 2.26	0.93, 2.06	0.96, 2.46	0.94, 2.38
Postoperative straylight value					
Mean ± SD	1.06 ± 0.16	1.12 ± 0.20	1.17 ± 0.17	1.24 ± 0.20	1.27 ± 0.21
Range	0.76, 1.43	0.64, 1.68	0.78, 1.67	0.68, 1.82	0.75, 1.82
Straylight improvement					
Mean ± SD	0.16 ± 0.37	0.17 ± 0.33	0.24 ± 0.27	0.33 ± 0.31	0.29 ± 0.28
Range	–0.35, 1.27	–0.32, 1.12	–0.36, 1.03	–0.50, 1.27	–0.38, 0.98
Improvement rate* (%)	61	63	81	86	81
Breakeven point					
Log(s)	1.06	1.13	1.18	1.26	1.29
R^2	0.81	0.64	0.56	0.58	0.42
P value	<.05	<.05	<.05	<.05	<.05

*Frequency of values above zero (no change)

DISCUSSION

In the present study, a normative reference curve for straylight in pseudophakic eyes was established. This was based on data from 13 publications. We believe that the creation of the straylight pseudophakic norm is advantageous to the ophthalmic practice as well as to clinical studies. Several authors have used the phakic straylight reference curve in their research to compare the straylight value in pseudophakic eyes.[10,21,24,26,29,30] However, when comparing the pseudophakic curve with the phakic curve, there are important differences. Straylight levels are stable in young phakic eyes and increase considerably above the age of 50 years; thus, the phakic reference is approximated by a logarithmic function. The present study shows that in pseudophakic eyes, the relationship between straylight and age is linear. In addition, the phakic reference shows a mean increase in straylight of 0.15 log units per decade,[4] whereas our current findings show a 0.044 log unit increase per decade after crystalline lens replacement. Therefore, evaluating postoperative results using age matched noncataractous phakic subjects could lead to misjudgment.

The new reference norm was compared with the published log(s) values in the studies included in the analysis. The pseudophakic normative curve derived from 13 articles is close to the real values in most datasets. As can be seen in **Figure 5**, in 11 studies there was no significant difference in the mean straylight value between the study and the norm.

However, 5 studies did not seem to comply, of which 3 had somewhat better straylight levels than the norm. We think this might be related to patient selection. Van Bree et al.[11] Lapid-Gortzak et al.,[21] and Kinard et al.[27] enrolled only subjects with a high-quality state of their eyes. The 2 other studies reported relatively high average straylight values, of which Guo et al.[34] showed the highest. The reason for the high straylight numbers in the study by Guo et al.[34] might be that the straylight measurements were performed in a dark room with a subsequently large pupil diameter. Van der Meulen et al.[24] and van Gaalen et al.[35] separately found that intraocular scatter is closely related to pupil diameter in pseudophakic eyes. Their findings show that 1.0 mm of visible capsulorhexis remnant induces 0.52 log units of additional straylight. Nevertheless, Guo et al.[34] stressed that they found no differences in straylight values between natural pupils and dilated pupils. To clarify whether the natural pupil's response to scotopic light conditions can affect straylight measurements, additional studies are needed. The mean straylight value reported by van Gaalen et al.[32] was also statistically significantly higher than the normative line. However, we could not find a potential explanation for this difference.

Figure 6 shows that the relationship between the preoperative straylight value and its improvement after IOL implantation was different in the various age groups. The upper lines and the lower lines correspond to the age ranges 40 to 50 years and 80 to 90 years, respectively. This suggests that the older the patient is, the higher the breakeven point and that more preoperative straylight is required to achieve postoperative improvement. The age effect was rather clear and corresponds with approximately a doubling of the amount of straylight needed to obtain postoperative improvement between 40 years and 90 years. Thus, these findings imply a necessity of age classification of the breakeven point. Moreover, the breakeven point values in **Table 2** are close to the reference norm (**Figure 4**). Therefore, the established reference norm might be considered a predictive feature to improve the clinical decision-making process before crystalline lens exchange.

A considerable improvement in the amount of straylight after crystalline lens replacement (mean 0.27 ±0.30 log units) was observed in the subpopulations (see **Table 2**). However, there was an evident dependency on age. Approximately 40% of patients younger than 60 years had an increase or no change in ocular straylight after surgery. Roughly one half of these subjects had refractive lens exchange (RLE). These results suggest that when considering lens extraction in healthy subjects, preoperative straylight levels should be taken into account. On the other hand, patients older than 60 years had a mean clinical improvement exceeding 80%. Therefore, the probability of improving the straylight value following lens extraction increases with age. However, it is significant that the correlation coefficient (R^2) declined with age. The highest predictive power was observed for patients in their 40s ($R^2 = 0.81$); it gradually decreased to $R^2 = 0.42$ for patients in their 80s. The strongest predictability was in the subpopulation younger than 60 years, with a greater chance of negative results. Thus, the proposed model can help during preoperative planning to decrease the likelihood of visual disabilities after lens extraction.

The results presented in **Table 2** show that preoperative straylight values in the older subjects were higher than in the younger ones. This might suggest that in patients with cataract, preoperative straylight gradually increases with age in the same way as in normal phakic eyes. However, we think this is not the case. When Lapid-Gortzak et al.'s[21] refractive patients were excluded and only the van der Meulen et al.[22] and Rozema et al.[25] cataract studies were used, there was no such effect. In other words, in those cataract studies, young subjects were granted surgery only when, on average, their straylight was as high as in older subjects. Speculatively, this might be related to a reluctance to operate on young eyes despite significant hindrance from straylight compared with that in eyes of age-equivalent peers.

According to global statistics, approximately 10 million people annually have crystalline lens replacement because of the presence of cataract.[36] This number is increased by RLE performed to correct a refractive error or overcome presbyopia. The popularity of these practices is associated with a great variety of implanted IOLs. This must be realized when considering the general normative straylight function established in the present paper. However, the studies that we analyzed already had a great variety in the type of IOLs and showed relatively consistent behavior in the age-dependency of straylight, as shown in **Figure 3**. The effect of the type of IOL on straylight has been studied in the literature, especially for diffractive multifocal IOLs versus monofocal IOLs.[23,26,28,30,33] Optically, these IOLs are very different with respect to design and light distribution[37,38]; however, the literature has not been clear about the differences in straylight. De Vries et al.[23] and Peng et al.[33] found a considerable increase in straylight in a multifocal IOL subpopulation compared with their monofocal IOL counterparts. In contrast, Cerviño et al.,[26] Wilkins et al.,[28] and Hofmann et al.[30] report insignificant differences between those groups. Some authors speculate that constriction of the pupil during measurements could be an explanation for the lack of effect.[26] This might be in line with *in vitro* studies testing multifocal IOLs, underlining that the aperture has a substantial impact on optical performance.[38,39] Clinical reports of the effect of pupil size on straylight after multifocal IOL implantation have not been published until now; thus, further studies are needed to determine its potential effects.

In the current study, a reference curve for straylight values in normal pseudophakic eyes is presented. The new norm can be used in research as a reference criterion and clinically, in managing cataract patients for predicting the postoperative straylight level. The proposed approach might enhance patient selection as well as minimize the potential for disability glare and patient dissatisfaction.

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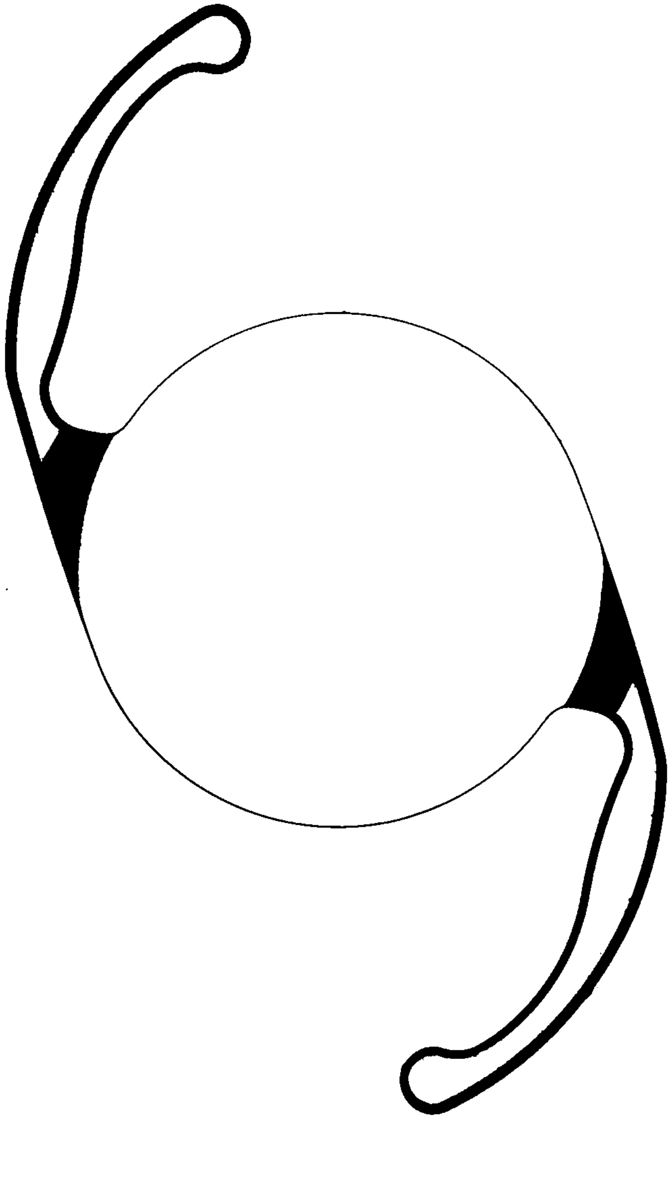

Chapter 4

Straylight measurements in two different apodized diffractive multifocal IOLs

Lapid-Gortzak R, Łabuz G, van der Meulen I, van der Linden JW, Mourits MP, van den Berg TJTP.

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ABSTRACT

Purpose

To evaluate differences in straylight between eyes implanted with a hydrophilic multifocal IOL (Seelens MF; Hanita Lenses, Hanita, Israel) and a hydrophobic multifocal IOL (SN6AD1; Alcon Laboratories, Inc., Fort Worth, TX).

Methods

In a prospective cohort study, routinely obtained straylight measurements (C-Quant; Oculus Optikgeräte, Wetzlar, Germany) 3 months after standard phacoemulsification for either cataract or refractive lens procedures were compared. Patients were implanted with either the SeeLens MF IOL or the SN6AD1 IOL. Postoperative straylight values, visual acuity, and refractive outcomes were compared.

Results

The SeeLens MF IOL was implanted in 84 eyes and the SN6AD1 IOL in 79 eyes. The difference in straylight was 0.08 (P = .01), with the SeeLens MF IOL having less straylight. Postoperative CDVA was logMAR -0.03 ± 0.06 in the SeeLens MF group, and logMAR -0.02 ± 0.08 in the SN6AD1 group. Mean postoperative refraction was +0.01 ± 0.43 and +0.06 ± 0.35 D, respectively.

Conclusions

The Seelens MF IOL showed a straylight of log(s) 0.08 lower than the SN6AD1 IOL. In terms of spherical equivalent and visual acuity the lenses performed equally. More study will aid in understanding the causes and clinical impact of this difference.

INTRODUCTION

Multifocal intraocular lenses (IOLs) were introduced in cataract surgery to address the problem of loss of accommodation following lensectomy and implantation of a monofocal IOL. There have been different multifocal designs, including diffractive bifocal,[1] apodized diffractive,[2] trifocal, refractive, zonal refractive,[1] rotational asymmetric refractive,[3] and accommodating IOLs in which the optic or optics need to move to achieve accommodation.[4]

Bifocal diffractive apodized IOLs have a circular pattern on the optic surface, which allows for diffraction of incoming light into two main distinct foci. One focus is for distance vision and the secondary focus is for near vision. The diffraction patterns distribute the light to both foci with loss of energy; approximately 18% of light is directed outside the far and near focal points.[2] As a result of multiple foci occurring in the eyeball at the same time and interfering with one another, the contrast sensitivity for both far and near foci decreases.[5] In apodized diffractive IOLs, the far focus is dominant and receives more light, whereas the near focus receives less light.[2] The patterns of the apodization can differ and not only allow changes in depth of focus with relation to the intensity of light distributed between the far and the near foci, but also changes in induced halos, contrast, and quality of vision with relation to the pupil size as a function of light intensity as part of the accommodative triad response.[6,7]

Straylight is a parameter of quality of vision, and is by definition glare disability. The light does not come to a focus on the retina because of imperfections in the optical system, but is forwardly scattered in the eye and veils vision. Straylight is known to increase with the development of cataract.[8] Corneal and vitreous turbidity may also increase straylight.[9] Elements in the capsular bag, such as the rhexis edge, posterior capsular opacification, and edges of YAG capsulotomies contribute to straylight after surgery.[10,11] Van der Meulen et al. showed that straylight decreases after cataract surgery and that preoperative straylight levels increase the predictability of the visual outcome of cataract surgery when used with visual acuity measurements.[12] Straylight improves significantly in many patients after phacoemulsification in eyes with good preoperative visual acuity.[13] However, the contribution of the IOL type to postoperative straylight has not yet been elucidated.

The effect of IOLs on straylight has already been studied by many authors, but the literature appears to be inconsistent. Dick et al.[14] showed that there is no difference between monofocal and multifocal IOLs in terms of straylight. This is in line with findings from Hofmann et al.,[15] Cerviño et al.,[16] and Wilkins et al.[17] However, de Vries et al.[18] found increased straylight of log(s) 0.078 in eyes implanted with the SN6AD3 (Alcon Laboratories, Inc., Fort Worth, TX) and Peng et al.[19] found an increase of straylight in eyes implanted with an apodized diffractive IOL. Ehmer et al.[20] found increased straylight in diffractive IOLs compared to refractive IOLs. The comparison of multifocal apodized diffractive IOLs from the same manufacturer, differing only in its effect on spherical aberration, have shown no difference in straylight.[21] Most of these studies were done with small cohorts, and have shown different results in terms of straylight when using different types of lenses. As a result, the effect of multifocality on straylight is unclear.

In this study, two types of optics of apodized diffractive IOLs were compared: the SN6AD1 (Alcon Laboratories, Inc.) versus the SeeLens MF (Hanita Lenses, Hanita, Israel). Both are bifocal apodized diffractive IOLs, but in one of these lenses the apodization pattern was adjusted in the number, distance, and height of the diffractive rings in an attempt to achieve a better differentiation of the foci, presenting allowance for intermediate vision and decreased halos and optical side effects. In this study, we compared the postoperative straylight in eyes implanted with either of these two lenses.

METHODS

Between April 2011 and May 2013 all consecutive patients older than 18 years undergoing a standard phacoemulsification for cataract or refractive lens exchange were included. The tenets of the Declaration of Helsinki were adhered to, the study was approved by the institutional review board, and all patients provided a signed informed consent. The following patients were excluded: patients younger than 18 years, patients incapable of or not willing to consent, and patients with diabetes, cornea guttatae, glaucoma, uveitis, macular disease, previous corneal laser surgery, or other significant eye disease.

Surgical Technique

A standard phacoemulsification procedure was performed using the infinity OZIL phacoemulsification technology (Alcon Laboratories, Inc.) with a 2.2-mm incision. After removal of the native lens, the posterior capsule was polished using the bimanual irrigation/aspiration headpieces. The anterior capsule was polished in the area of the optic adhering under the rhexis. The lens implanted was either an SN6AD1 or a SeeLens MF. The choice of IOL resulted from shared decision-making between the patient and the eye surgeon.

Lenses

The SN6AD1 is a hydrophobic apodized diffractive IOL, with a 6-mm optic and 13-mm haptic diameter and straight posterior optic edge, no angulation, blue blocker material, with a yellowish tint. It can be injected through a 2.2-mm opening into the bag via a cartridge system. The SN6AD1 has an apodized profile on the central 3.6 mm of the optic with 9 diffractive rings that have specific height and distance steps. The Seelens MF is a hydrophilic one-piece IOL, with apodized diffractive optics. The optic is 6 mm and the haptic diameter is 13 mm, with a 5° posterior angulation of the optic to the C-loop haptics. The optic has a 360° sharp edge to prevent posterior capsular opacification. The material has an ultraviolet blocking chromophore surface and is clear. The apodization pattern has a central diameter of 4 mm with 11 diffractive rings that have had the step height and distance adjusted for minimal halos and glare perception, and maximal visual acuity at distance and near.

Patient Examinations

A full preoperative ophthalmic examination was performed, including visual acuity and refraction, slit lamp and biomicroscopy examination, biometry (IOLMaster; Carl Zeiss AG, Jena, Germany), topography (Orbscan; Bausch & Lomb, Rochester, NY), tonometry, tear film diagnostics, and standard straylight measurements (C-Quant; Oculus Optikgeräte, Wetzlar, Germany). The above was repeated at 3 months, except for the topography and biometry.

Straylight Measurements

Using the C-Quant straylight meter, the straylight was measured twice before and 3 months after surgery and expressed in a logarithmic scale as log(s). The use of the technique has been extensively described elsewhere.[22] The straylight measurements were performed by the same optometrist under identical conditions. The optometrist was blinded to the fact that there was a study being done.

Statistical Analysis

Data were analyzed using statistical functions in Excel 2003 software (Microsoft Corporation, Redmond, WA). The parametric double-side *t* test was used as applied for normally distributed data. Correlations were calculated using normal regression analysis.

RESULTS

The refractive data are summarized in **Table 1**. Preoperative corrected distance visual acuity was similar in both groups, as was the postoperative corrected distance visual acuity and refraction. Demographic data are summarized in **Table 2**.

Table 3 summarizes the straylight data. There was an overall decrease of straylight in both groups, with an improvement of 0.01 ± 0.21 log(s) ($P = .61$) in the SN6AD1 group, versus a 0.07 ± 0.18 log(s) ($P < .003$) decrease in the SeeLens MF group. Postoperatively there was a difference between the SN6AD1 group and the SeeLens MF group of 0.08 log(s) ($P = .01$) in favor of the IOL with the adjustment in the apodization (SeeLens MF). When adjusted for age, this difference remained statistically significant at 0.06 log(s) ($P = .03$).

Table 1. Refractive data

Parameter	SeeLens MF	SN6AD1	*P*
No. of eyes	84	79	-
Preop CDVA (logMAR ± SD, range)	0.04 + 0.08 (0.3 to -0.1)	0.06 + 0.10 (0.4 to -0.1)	.171
Postop CDVA (logMAR ± SD, range)	-0.03 + 0.06 (0.2 to -0.16)	-0.02 + 0.08 (0.4 to -0.2)	.205
Preop refraction (SE ± SD, range), D	+1.30 + 2.05 (-6.625 to +5.75)	+0.48 + 2.65 (-10.75 to +6.00)	.027
Postop refraction (SE ± SD, range), D	0.01 + 0.43 (-1.375 to +1.25)	0.07 + 0.35 (-0.75 to +0.875)	.383

Preop = preoperative; CDVA = corrected distance visual acuity; Postop = postoperative; SD = standard deviation; SE = spherical equivalent; D = diopters;

Table 2. Demographic data

Parameter	SeeLens MF	SN6AD1	*P*
Refractive lens exchange (eyes)	35	31	-
Cataract (eyes)	49	48	< .752a
Male/female	46%/54%	41%/59%	< .61b
Age, y	59 ± 9	61 ± 7	< .14b

[a]z-test
[b]two-tailed t test.

Table 3. Preoperative to postoperative decrease in log(s) values.

Parameter	SN6AD1	SeeLens MF
Preoperative log(s)	1.19 ± 0.21	1.16 ± 0.20
Postoperative log (s)	1.17 ± 0.14	1.10 ± 0.19
Improvement	0.01 ± 0.21	0.08 ± 0.18
P (two-tailed *t* test)	.605	.003

Straylight improved most in eyes that had higher preoperative levels of straylight (**Figure 1**). When the change in straylight was plotted against the graph showing the normal phakic norm with age (**Figure 2**), it is clear that straylight was reduced postoperatively with both multifocal IOLs. The improvement was greatest using the SeeLens MF, as compared to the SN6AD1. None of the eyes had significant glistenings. At the 3-month follow-up visit, none of the eyes had posterior capsular opacification and none of the eyes had undergone a posterior capsulotomy for that reason.

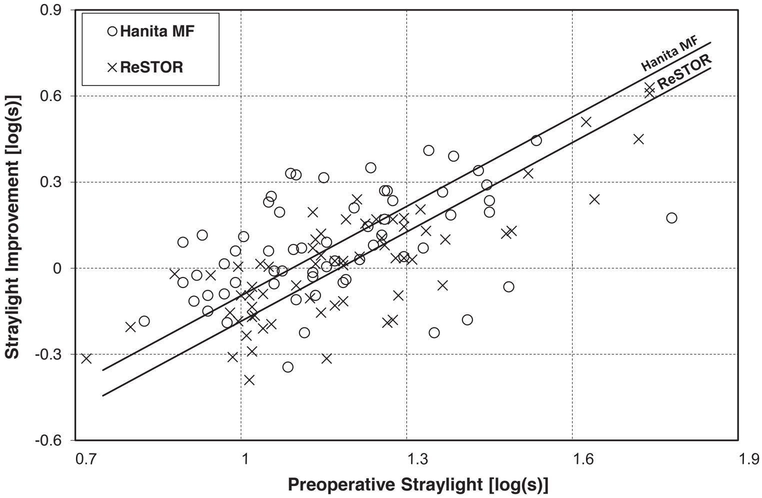

Figure 1. Straylight improved in the patient population overall. The improvement in straylight was greatest in eyes with higher preoperative straylight.

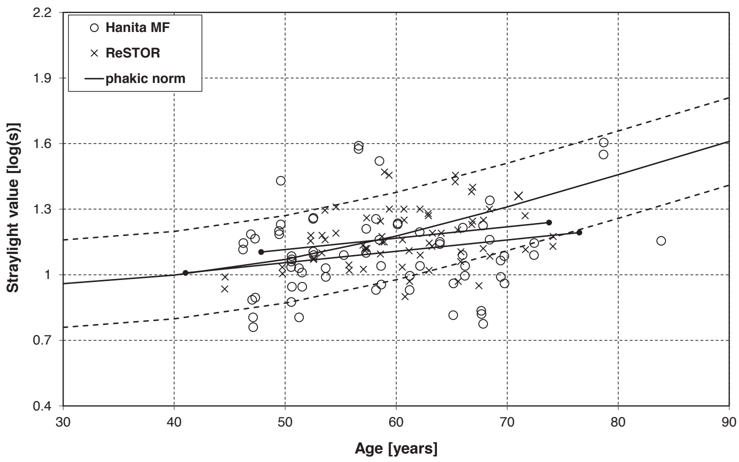

Figure 2. Straylight postoperatively in the multifocally pseudophakic eyes. The upper regression line is for the SN6AD1 (Alcon Laboratories, Inc., Fort Worth, TX) implanted eyes, and the lower regression line is for the SeeLens MF (Hanita Lenses, Hanita, Israel) implanted eyes. The latter have better straylight value than the former.

DISCUSSION

Straylight decreased postoperatively in both groups. The mean difference between age-adjusted groups was 0.06 log(s) ($P < .03$) in favor of the SeeLens MF IOL. A difference of log(s) of 0.06 can be compared to the logMAR scale on the visual acuity chart, and would in comparison be a difference of "3 letters" on the visual acuity chart. This is a small but statistically significant difference.

The explanation of this finding may lie in three factors. The first is the difference between the materials. Montenegro et al.[23] showed that the hydrophilic acrylic IOLs induce significantly less straylight than the hydrophobic IOLs. Moreover, the hydrophobic AcrySof material (Alcon Laboratories, Inc.) has a tendency for glistenings[24]—incorporating small inclusions of water and calcium in the open spaced polymer structure. However, the 'defects' caused by glistenings are deemed too small to influence straylight.[25] In this study, none of the IOLs showed significant glistenings in the 3 months of follow-up. As a result, glistenings do not seem to play a role in the higher straylight of the hydrophobic lens group. The second factor may be the apodization pattern, and the third factor is the manufacturing process of the hydrophilic lenses, which makes the optic surface of these hydrophilic lenses accurate.[26] One may be inclined to think that the asphericity patterns of the IOLs influence straylight, but because wavefront aberration affects the peak of the point spread function only and straylight is 1° or more off from the peak, there is no physical overlap between the two functions, and as such different asphericity will have no effect on straylight.[27]

The apodization pattern is the pattern in which the steps of the diffractive rings are spaced at different distances from the center of the lens and at different height to get a better energy balance. When the SN6AD3 with the +4.00 addition for runner of the SN6AD1 was designed, the primary guiding principle was that near vision is less important than distance vision, when in dim illumination when pupils are large. Clinically, this can be understood by the vision tasks in the dark (*i.e.* driving) where a distance dominance is important, as opposed to near tasks, which need better illumination, and will be accompanied by the synkinetic reflex. The second guiding principle was that glare and halo perception must be minimized under dim lighting conditions.[2]

The glare and halos mostly result from perception of the second unfocused near image in dim illumination. These principles are complementary on apodized diffractive lenses because the balance in the energy of light going for the distance and near focus together with pupil dependency allow for manipulation of image quality.[2]

Gatinel et al.[26] described the manufacturing process of the hydrophilic multifocal IOL in their study of the trifocal IOL. The hydrophilic multifocal IOLs are manufactured by a lathe-milling process, just like the monofocal IOLs, but the polishing step is omitted. High-precision lathes allow for low roughness and polishing-free IOLs. This is a well-accepted method for manufacture of hydrophilic multifocal IOLs and also the way the SeeLens MF lenses are manufactured. The hydrophobic IOL is cast-molded, as customary with acrylic IOLs. Surface roughness can be measured with atomic force microscopy and is possibly related to posterior capsular opacification.[28] Interestingly, in that study[28] the hydrophobic lenses had the least surface roughness and least posterior capsular opacification, but none of the IOLs measured in these studies were multifocal diffractive lenses, so empiric data on surface roughness of multifocal IOLs are lacking in the literature.

In comparison to the literature, this is the first study in which two different types of multifocal diffractive apodized IOLs were compared. De Vries et al.[21] showed that there was no difference between spherical and aspheric multifocal IOLs with a similar material and diffractive pattern with respect to the mean straylight value. Van Gaalen et al.[29] reported similar outcomes, but their study included only monofocal IOLs. Ehmer et al.[20] assessed three types of multifocal IOLs: the AMO ReZoom (Abbott Medical Optics, Abbott Park, IL), the AMO ZM900 (Abbott Medical Optics), and the LS-312 (Oculentis Optikgeräte). The diffractive IOLs showed a higher postoperative straylight value than the symmetric and rotational asymmetric refractive IOLs. [20] That study also reported the subjective photic phenomena, which correlated weakly with straylight. [20] The significance of the findings is difficult to gauge because there were 10 eyes in each group. [20] More often, comparisons between monofocal and multifocal lenses were made. It is clear that multifocal IOLs improve the depth of field at a cost of image quality;[30] however, there are still many doubts whether multifocality might be related to increase of straylight. Dick et al.[14] Cerviño et al.,[16] and Wilkins et al.[17] have all shown that there is no difference between monofocal and multifocal IOLs regarding straylight. Hofmann et al.[15] and de Vries et al.[18] separately reported more straylight by an average of 0.08 log(s) in the multifocal group, which in the report by Hofmann et al. [15] did not reach statistical significance. Peng et al.[19] demonstrated that the apodized diffractive IOLs were associated with increased straylight and the increasing prevalence of photopic disturbances (glare and halo) compared to the monofocal IOLs. There is no clear explanation for the discrepancies in outcomes of straylight measurements in multifocal IOLs. Some reports state that the pupil size is possibly important.[16] However, most reports have small sample sizes, and as such it is difficult to extrapolate the effect of multifocality on straylight. Optical bench systems will allow for more objective measurements.[15, 16]

The contribution of the IOL material versus the apodization pattern is unclear. It is clear that apodization allows for better enhancement of distance and near foci. By adjusting the pupil dependency of the diffractive rings, even an IOL with an optic of 11 rings such as the SeeLens MF shows less straylight than an apodized diffractive IOL with 9 rings (SN6AD1). Improved apodization patterns may have a good effect on side effects such as halos and glare (disability glare), [31] but more study is necessary to elucidate the exact contribution of the IOL material.

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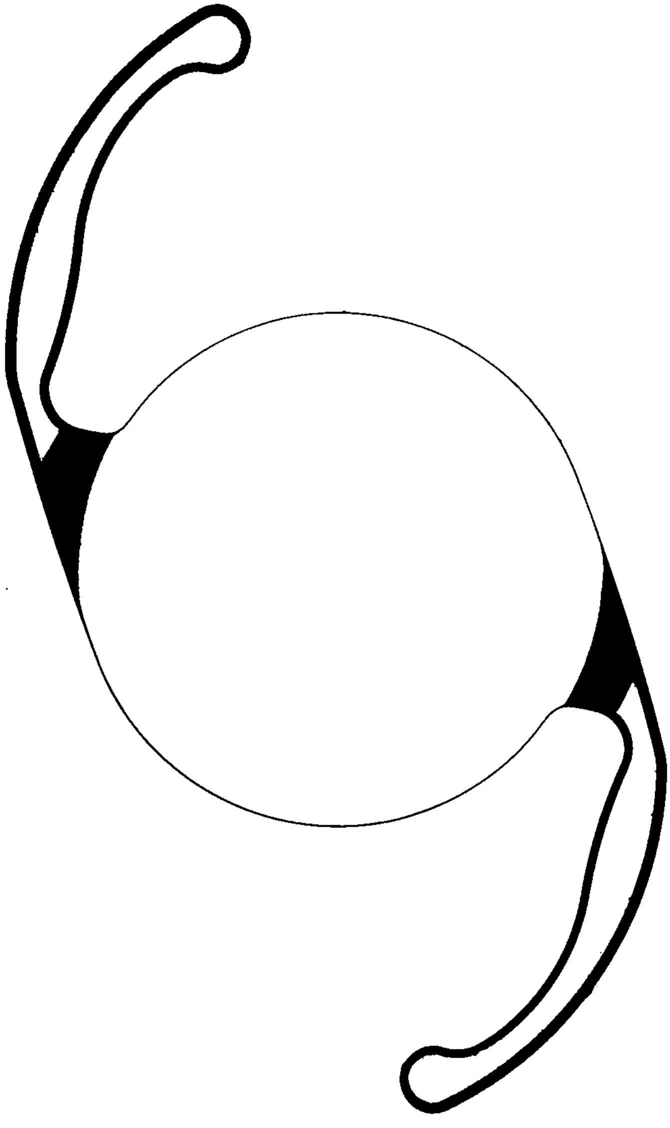

Chapter 5

Comparison of ocular straylight after implantation of various multifocal intraocular lenses

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ABSTRACT

A comprehensive review of the effect of multifocal intraocular lens (IOL) designs on post-operative ocular straylight was performed. Studies reporting straylight values obtained with the natural pupil using the C-Quant device after uneventful multifocal IOL implantation were included. The IOLs were categorized based on their material characteristics; that is, hydrophobicity and presence of colored chromophores. Age adjustment was achieved using the straylight age-dependency norm for pseudophakic eyes. This norm also served as a reference for comparing mean straylight levels of the various IOLs. The literature review identified 10 studies reporting 9 multifocal IOL designs. The hydrophilic IOLs showed less straylight than the hydrophobic IOLs by 0.08 log(s) (P = .001). Blue violet light–filtering IOLs showed less straylight than standard IOLs by 0.04 log(s), which was not statistically significant (P = .32). Hydrophobicity was a factor that significantly affected straylight in multifocal IOLs.

INTRODUCTION

Since the introduction of the first intraocular lens (IOL) in 1949,[1] tremendous advances in IOL technology have been made. Modern IOLs are not limited to correcting only post-operative aphakia. They can also reduce ocular aberrations, protect the retina against ultraviolet and blue light, and provide useful near and intermediate vision in addition to standard distance vision. Many IOLs that vary in optical design and material are available to healthcare professionals. This may influence not only the postoperative prediction error and visual acuity, but also other aspects of quality of vision such as the visual effects of light scattering; *i.e.*, straylight and disability glare.

Disability glare originates from light scattered in the eye due to imperfections in the optical media.[2] The scattered light causes a veil of light over the retina that degrades contrast of the retinal image. The visual effect of light scattered around a bright light source is called straylight.[3] Disability glare has been defined as identical to straylight by the Commission Internationale de l'Eclairage[4] and can be expressed by its (equivalent) luminance as the ratio of light scattered toward the retina at a certain angular distance and the total amount of light entering the eye. This is the basis on which straylight is measured by the C-Quant straylight meter (Oculus), an instrument that is commercially available for use in clinical practice.[5] The amount of straylight is expressed logarithmically as log(s). The effect on visual performance of an increase of 0.1 log(s) is comparable to that of losing 1 line of visual acuity on the logMAR scale.[6] Straylight elevation has been associated with several clinical conditions, particularly cataract, and with several corneal dystrophies, corneal haze, and vitreous turbidity[7] It causes numerous visual difficulties such as blinding by headlights of oncoming cars, halos around light sources, irritability to sunlight, and loss of color vision.[3,7]

Several authors have studied the effect of IOLs on postoperative straylight. Five studies compared monofocal and multifocal IOLs.[8–12] Two found a significantly lower straylight value in the monofocal population,[9,11] but the other 3 reported insignificant differences between the monofocal and multifocal IOLs.[8,10,12] The reason for this discrepancy is not understood. However, differences in multifocal designs and to what extent they affect the postoperative straylight have been investigated. Ehmer et al.[13] found that diffractive multifocal IOLs scatter more light than their refractive counterparts. In other studies,[14–16] straylight did not differ significantly between various diffractive multifocal IOLs. However, it is possible that not only optical design but also material properties such as hydrophobicity or the presence of colored chromophores influence the amount of straylight.

Because patients' expectations have increased over time, one challenge for multifocal IOLs is to optimize factors other than visual acuity, such as straylight, that affect visual quality. To address this issue, we looked at the potential effect on straylight of design and material differences between multifocal IOLs by meta-analysis of data from published studies.

METHODS

A comprehensive literature review of PubMed, ProQuest, Embase, Medline, and Google Scholar was performed to identify studies of straylight in pseudophakic eyes. The criteria of the selection process and data acquisition were as follows: Articles on multifocal IOLs were included if they fulfilled the following conditions: enrollment of healthy subjects with no ocular comorbidities or history of eye surgeries except cataract surgery or refractive lens exchange; absence of intraoperative and postoperative complications, for example, posterior capsule opacification; straylight measurements performed with the natural pupil using the C-Quant straylight meter; and disclosure of the implanted multifocal IOLs. Ten of the 230 records identified were included and analyzed (**Figure 1**).

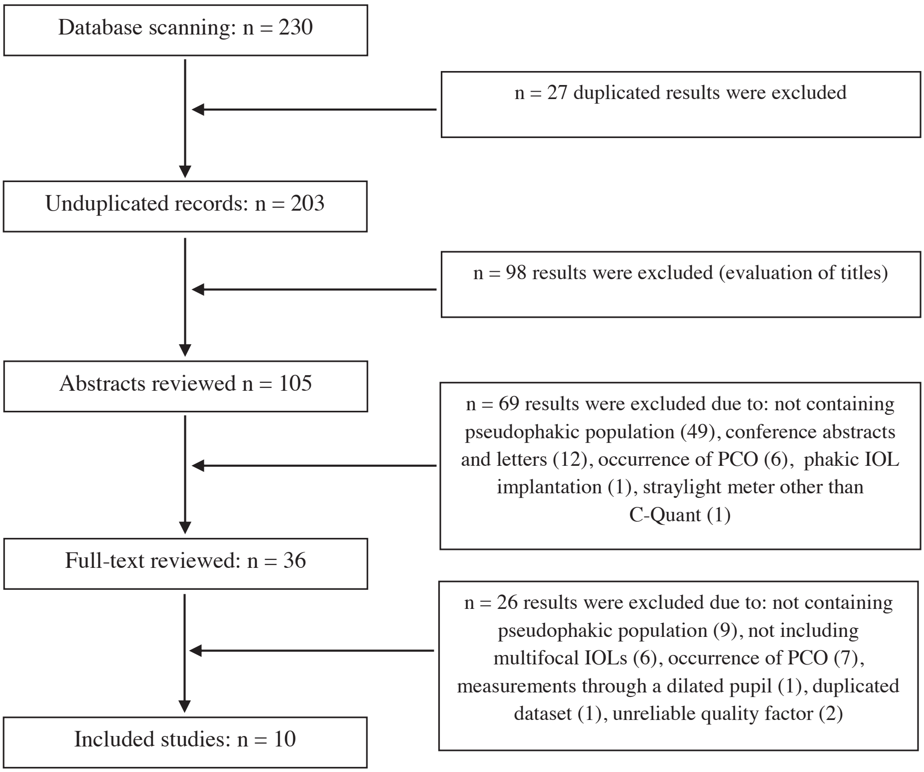

Figure 1. Illustration of the systematic literature review (IOL = intraocular lens; PCO = posterior capsule opacification).

Intraocular Lenses

Results of 9 IOL models from 5 manufacturers were available in the 10 eligible articles,[8–17] leading to 18 unique results. The IOL models along with their general features and the reported straylight values are presented in **Table 1**.

The IOLs use 4 technologies to achieve their multifocality. The Tecnis ZM900 (Abbott Medical Optics, Inc.) and the AT LISA 809M (Carl Zeiss Meditec AG) are full-optic multifocal diffractive IOLs; *i.e.*, the height of the diffractive steps remains constant, allowing a light distribution that is independent of pupil size.[18] The apodized diffractive pattern used in the Restor SA60D3, SN60D3, SN6AD3, and SN6AD1 (all from Alcon Laboratories, Inc.) and the Seelens MF (Hanita Lenses RCA Ltd.) is distinct from the full-diffractive IOL by a gradual decrease in the height of the diffractive steps from the center of the IOL, yielding a dominance of the far focus when the pupil size increases.[18] A drawback of using the diffractive technology is the energy spread up to 18% to higher-order foci.[18] This effect does not occur with the refractive multifocal IOLs. The Mplus LS-313 (Oculentis GmbH) is a rotationally asymmetric refractive multifocal IOL that contains a segment embedded for near vision. The Rezoom (Abbott Medical Optics, Inc.) is a rotationally symmetric refractive multifocal IOL.

The collected data were additionally categorized according to general properties such as the presence or absence of colored chromophores in the IOL material and the water content. Hydrophilic IOLs covered by a hydrophobic surface such as the AT LISA 809M and Mplus LS-313 were allocated to the hydrophilic group along with the Seelens MF, as these IOLs correspondingly contain 25% of water and are generally considered hydrophilic. In the study by De Vries et al.,[15] spherical (Restor SN60D3) and aspheric (Restor SN6AD3) diffractive multifocal IOLs were analyzed as a single set of data because it was shown that straylight did not differ significantly between these IOLs (**Table 1**).

Statistical Analysis

Because straylight has been found to be age dependent in pseudophakic eyes,[19–21] age adjustment of straylight values was performed to enable the evaluation of differences in light scattering between IOLs implanted in eyes of various age groups. The correction was achieved using the pseudophakic norm published in a review article.[19] To compare an average result of a single IOL model with that in the other included studies, the mean age of each population was used to calculate the straylight norm value based on the overall straylight norm formula in the pseudophakic eye as follows:

$$\text{Straylight} = 0.0044 \times \text{Age} + 0.89 \quad [\log(s)]$$

The difference between the mean straylight and the normative value, which is called the normalized difference, was then assessed. This resulted in a negative value or positive value depending on whether the postoperative value was below (less straylight) or above (more straylight) the pseudophakic reference, respectively (*i.e.*, negative values refer to less straylight). The cross-center comparison of straylight and its standard deviation (SD) involved the calculation of the arithmetic and weighted mean.

The significance of differences between the means of the IOL models was evaluated by the Kruskal-Wallis analysis of variance (ANOVA) test. The general properties of materials for IOLs listed in **Table 1** were compared with the Mann-Whitney U test. The nonparametric approach was chosen because of the possible inhomogeneous variance of the studied populations. For these tests, raw data were required. For 2[8,17] of the 10 articles, the raw data were supplied by the original authors; for 4 articles,[9,10,12,13] the raw data were supplied by digitization of the original plots using GSYS2.4 software.[A]

For the 4 remaining papers,[11,14–16] raw data could not be obtained and thus were not used for this part of the analysis; however, these papers were used for comparison of the mean straylight and its SD. Age adjustment of the results was done for each individual eye using the pseudophakic norm (**equation 1**). Subsequently, the residuals of the following

Table 1. Characteristics of the IOL models and clinical outcomes in the included studies.

IOL Model	Manufacturer	IOL Type	Material	
SeeLens MF	Hanita Lenses RCA Ltd	Diffractive apodized	Hydrophilic	Acrylic
AT LISA 809M	Carl Zeiss Meditec	Full diffractive	Hydrophilic (hydrophobic surface)	Acrylic
Mplus LS-313	Oculentis GmbH	Refractive (segment)	Hydrophilic (hydrophobic surface)	Acrylic
ReSTOR SA60D3	Alcon Laboratories	Diffractive apodized	Hydrophobic	Acrylic
ReSTOR SN60D3 Restor SN6AD3	Alcon Laboratories	Diffractive apodized	Hydrophobic	Acrylic
ReSTOR SN6AD1	Alcon Laboratories	Diffractive apodized	Hydrophobic	Acrylic
Tecnis ZM900	Advanced Medical Optics	Full diffractive	Hydrophobic	Silicone
ReZoom	Advanced Medical Optics	Refractive (zonal)	Hydrophobic	Acrylic
Total				

FU = follow-up; IOL = intraocular lens; NA = not available; VBL = violet blue light
*Intraocular lens names are listed as spelled by the manufacturer and not per journal style
†First author

groups were compared: hydrophilic versus hydrophobic and blue violet light–filtering IOLs versus standard IOLs. The significance level was a P value less than 0.05. The effect size was measured using the Cohen d parameter with the 95% confidence interval (CI). The analysis was performed using the statistical package Statistica 10 (Statsoft, Inc., 2011).

LITERATURE REVIEW

The mean straylight value of the 9 IOL models that were included in the 10 studies[8–17] (822 eyes) was 1.18 log(s) ±0.19 (SD), and the mean patient age was 66 ±9 years (**Table 1**). The individual postoperative straylight results in the study populations are presented in **Figure 2**.

Violet/ blue-light filter	Eyes (n)	Mean log(s) ±SD	Mean age (Y) ±SD [Range]	No. of eyes per study	Follow-up (Mo)	First author (year)
Yes	38	1.05±0.14	57 ±9 [46, 84]	38	3	Lapid-Gortzak (2014)[17]
No	109	1.13±0.18	55 ±7 [46, 67]	25	3	Lapid-Gortzak (2014)[17]
			67 ±9 [NA]	84	4 - 8	Maurino (2015)[16]
No	42	1.13±0.18	60 ±6 [51, 72]	32	3	Lapid-Gortzak (2014)[17]
			65 ±7 [52, 76]	10	> 3	Ehmer (2011)[13]
No	119	1.19±0.18	72 ±8 [55, 83]	37	18	Hofmann (2009)[10]
			75 ±10 [35, 88]	60	6	De Vries (2008)[9]
			64 ±11 [45, 83]	22	6	Cerviño (2008)[8]
Yes	92	1.16±0.16	68 ±11 [NA]	45	6	De Vries (2010)[15]
		1.19±0.19	65 ±10 [NA]	47		
Yes	304	1.21±0.18	62 ±7 [45, 72]	52	3	Lapid-Gortzak (2014)[17]
			64 ±9 [NA]	68	6	De Vries (2010)[14]
			66 ±8 [NA]	100	6	Peng (2012)[11]
			68 ±10 [NA]	84	4 - 8	Maurino (2015)[16]
No	95	1.21±0.26	59 ±10 [43, 70]	10	> 3	Ehmer (2011)[13]
			67 ±11 [32, 90]	85	4	Wilkins (2013)[12]
No	23	1.19±0.22	69 ±11 [56, 85]	13	6	Cerviño (2008)[8]
			60 ±14 [26. 78]	10	> 3	Ehmer (2011)[13]
	822	1.18±0.19	66 ±9 [26, 90]			

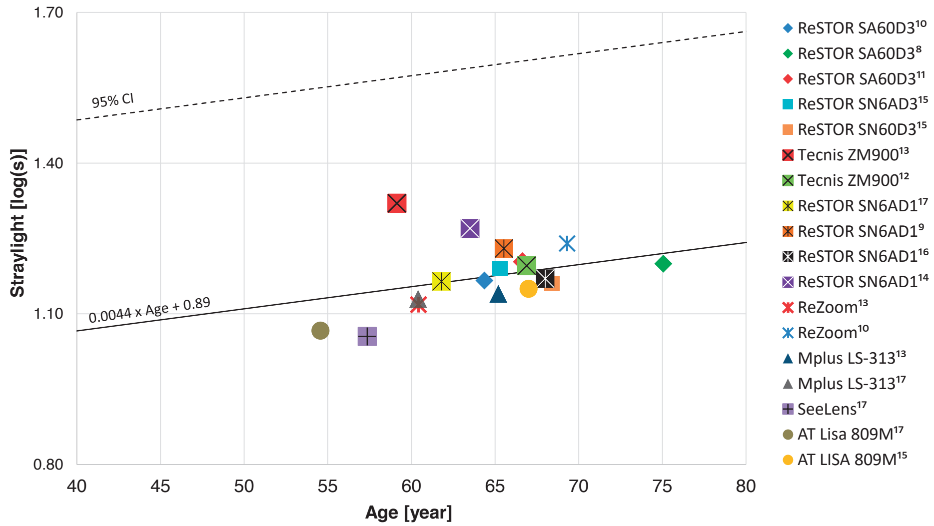

Figure 2. Mean straylight of the individual studies and IOLs as a function of age. The solid line represents the straylight pseudophakic norm and the dashed line, the 95% CI.

Figure 3 shows the SD level for the studied IOLs. This evaluation showed, on average, a slightly lower SD in the multifocal group (±0.19 log[s]) than in the overall normal pseudophakic population (±0.21 log[s]) as described in a recent review.[19]

After age correction, the mean straylight value remained at the same level of 1.18 log(s). The mean differences between the postoperative straylight values and the norm of the Seelens MF, AT LISA809M, Mplus LS-313, Restor SN6AD3 and SN60D3, Restor SA60D3, Rezoom, Tecnis ZM900, and Restor SN6AD1 IOLs were -0.088 log(s), -0.041 log(s), -0.029 log(s), -0.009 log(s), -0.005 log(s), 0.009 log(s), 0.028 log(s), and 0.035 log(s), respectively (**Figure 4**).

A total of 394 raw records were available. The differences between the IOL models proved to be statistically significant (P = .01). The statistical analysis of the material characteristics with the Mann-Whitney U test showed that the hydrophobic material was associated with significantly more straylight than the hydrophilic material by 0.08 log(s) (P = .001; d = 0.39; CI, 0.16-0.61). The 9 IOLs were therefore categorized into hydrophobic (289 eyes) and hydrophilic (105 eyes) groups, and the Kruskal-Wallis ANOVA tests of the IOL models were repeated for each group. The differences within the hydrophobic group (P = .22) and the hydrophilic group (P = .39) were insignificant. No effect of colored chromophores in IOL materials on ocular straylight was found. Although the blue violet light–filtering IOLs induced, on average, 0.04 log(s) less straylight than the standard IOLs, the difference was not statistically significant (P = 0.32; d = 0.16; CI, -0.07 to 0.40). The comparison between the hydrophobic and hydrophilic materials as well as between blue violet light–filtering and standard IOLs are presented in **Figure 5**.

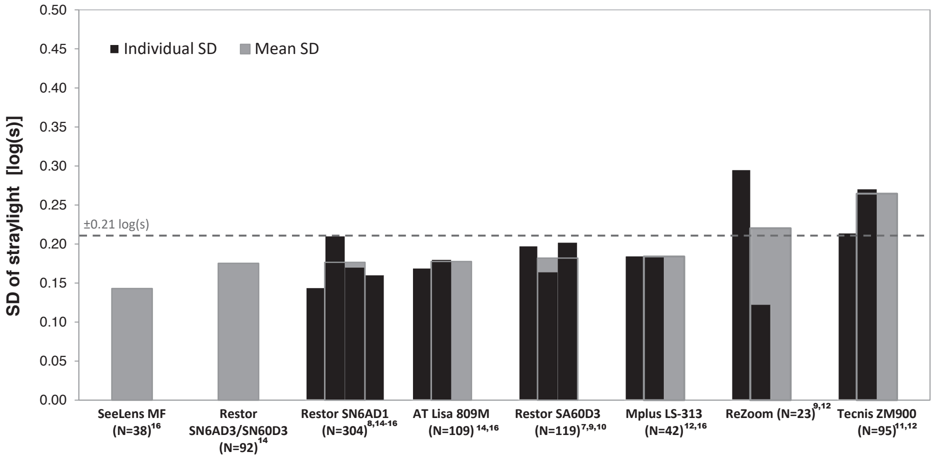

Figure 3. Standard deviation of log(s) for the studied IOLs. The black bars show the SD per study if the results were derived from different centers. The gray bars represent the pooled SD of the individual IOL models. The dashed line indicates the SD in the overall normal pseudophakic population.

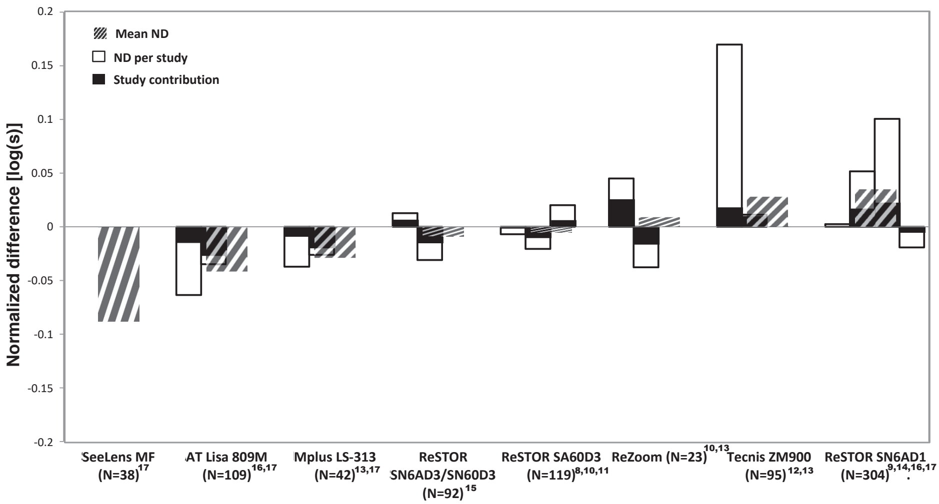

Figure 4. Normalized difference for each IOL group. Normalized difference shows to what extent a mean straylight result differs from the normative value. Note that the positive sign refers to straylight values above the norm. The gray bars describe the weighted mean normalized difference if more than 1 study was included; the empty bars indicate the mean normalized difference of an IOL group per study. The black bars give the contribution (weight) of each study to the mean normalized difference of the respective group by weighting over the sample size (the sum of black bars for a single IOL group equals the value of the respective gray bar).

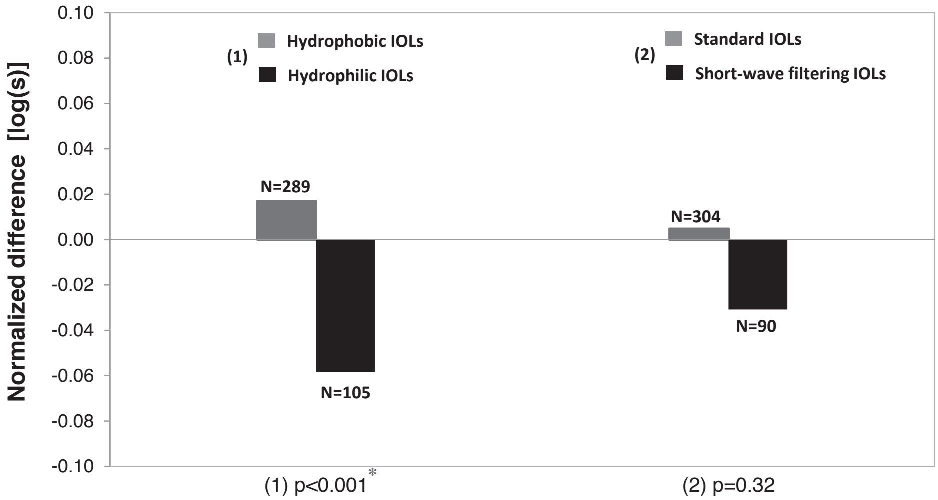

Figure 5. Normalized differences for different IOL material characteristics. Note that positive normalized differences indicate more straylight than the pseudophakic norm. The numbers (1 and 2) refer to the analysis of differences between the hydrophobic and hydrophilic materials and the standard and blue violet–absorbing IOLs, respectively (IOLs = intraocular lenses).

DISCUSSION

The current study shows that the type of implanted multifocal IOL affects the amount of postoperative straylight, and this can be partly explained by the differences in materials used for the IOLs, particularly when hydrophilic and hydrophobic IOLs are compared. In **Figure 4**, a clear distinction can be seen between hydrophilic and hydrophobic IOLs, with the hydrophilic IOLs (left side of figure) showing, on average, less postoperative straylight than the hydrophobic IOLs. When analyzed with the raw records from the 10 studies, the difference of 0.08 log(s) was statistically significant (P = .001). If this difference is compared with the effect of age on straylight in pseudophakic eyes (**equation 1**), it corresponds to a difference of nearly 2 decades. If the difference is compared with the logMAR scale, it corresponds to a difference of nearly 1 line (4 letters). Therefore, hydrophobicity appears a significant factor affecting intraocular straylight following multifocal IOL implantation. One earlier study also suggested that hydrophobicity increases straylight.[22] This study, however, investigated the effect of neodymium:YAG (Nd:YAG) laser capsulotomy on straylight. Although Nd:YAG laser capsulotomy is very efficient in reducing straylight, remnants can remain in the photopic pupil area and thus may have affected the study outcome.[20,22]

Straylight is the visual result of light scattered by inhomogeneity in the medium that light traverses. Extensive physical theory exists on the origin and properties of light scattering.[23] The relative size of the irregularities (*i.e.*, the ratio between size and wavelength) is an important parameter. If the ratio is (much) smaller than 1, scattering is isotropic but weak

(Rayleigh scattering). Larger particles cause an increase in scattering, especially in the forward direction.[23] The functional importance of particle size in human eye lenses was studied by van den Berg and Spekreijse.[24] The study found that particles with a radius of approximately 0.7 mm dominated forward light scatter, whereas particles much smaller than the wavelength (*e.g.*, single proteins) were more important at large angles (and dominate backward scatter).[24] These *in vitro* findings were in accord with *in vivo* straylight population study findings.[25] Similar to their existence in the crystalline lens, light-scattering particles may also exist in IOLs, according to several reports.[26,27] They can be large, seen as glistenings with the slit-lamp microscope,[27] or small, such as subsurface nanoglistenings.[28] A recent clinical study of the relationship between glistenings and straylight showed a significant, albeit not large effect.[29] Furthermore, another *in vitro* study demonstrated that the straylight effects of subsurface nanoglistenings is not significant.[B]

A clear difference can be found between the hydrophobic and hydrophilic materials in terms of surface roughness.[30] The difference between the average roughness of the acrylic hydrophilic IOLs (9.02 ±0.86 nm) and the acrylic hydrophobic IOLs (2.61 ±0.41 nm) was significant.[30] However, the values are so much smaller than the wavelength that these surfaces can be considered smooth surfaces and cannot be of significance in light scattering. This also supports our decision to include hydrophilic IOLs with a hydrophobic surface in the hydrophilic group.

Figure 2 shows that the individual mean log(s) values in most enrolled studies follow the norm for straylight in pseudophakic eye.[19] Moreover, the observed straylight age dependency in **Figure 2** underlines the necessity of using age correction when different age groups are compared. That was done and is presented in **Figure 4**, in which a significant variation is seen in the postoperative straylight in the IOL groups. Further subdivision led to a comparison of models within the hydrophobic and hydrophilic groups. Within these groups, the straylight differences between models were insignificant. **Figure 4** shows a difference of 0.12 log(s) in straylight between the models on the extreme ends (*i.e.*, Seelens MF versus Restor SN6AD1). The main difference between these IOLs is their material characteristics; *i.e.*, Seelens MF is an acrylate hydrophilic IOL and Restor SN6AD1 is an acrylate hydrophobic IOL. The difference in their optical designs seems to be minute. Both are diffractive apodized IOLs, although Seelens MF contains 12 diffractive zones versus 9 in the Restor SN6AD1. That these IOLs appear to be similar in their optical designs underlines the potential importance of hydrophobicity as a factor of postoperative straylight elevation. However, it must also be noted that the Seelens data come from 1 center in contrast to the multicenter results of the Restor SN6AD1.

A direct comparison in straylight between hydrophilic and hydrophobic IOLs was also made by Maurino et al.16 The Restor SN6AD1 and AT LISA 809M IOLs were studied, and the mean straylight value was, on average, lower in the hydrophilic group. De Vries et al.[14,15] studied apodized diffractive IOLs of the same manufacturer. In 1 study, the only difference was a spherical versus an aspheric design,[15] whereas in the other study, an addition power was the parameter that differed between the IOL groups.[14] No difference in ocular straylight was found between the evaluated IOLs. This can be expected since aberrations and refractive errors relate to a different part of the point spread function than ocular straylight.[2] A comparison of 3 types of multifocal IOLs was performed by Ehmer et al.[13] The Tecnis ZM900 showed more straylight than the Rezoom and Mplus LS-313, with relatively close outcomes between the refractive IOLs. However, the analysis was done without age adjustment, which could result in relatively better performance of the hydrophilic Mplus as the highest age was found in this group.

It is well known that not every patient is a good candidate for a multifocal IOL.[31] Therefore, patient selection requires a stricter approach than in the case of a monofocal IOL. This might lead to a patient selection bias, with a reduced SD and better postoperative straylight level for the multifocal population. However, it is well known that adverse photopic phenomena are more often reported with multifocal IOLs than with monofocal IOLs.[32] Since a multifocal IOL provides near and distance correction simultaneously, the secondary (out of focus) focus causes a blur circle around bright points. This blur circle is of the order of 10 minutes of arc in diameter. This is very small and, as a consequence, not a contributor to disability glare. Yet it is very noticeable to the patient and may lead to complaints. This phenomenon may confuse the issue of disability glare as studied presently. In the current review, the mean straylight value was 1.18 ±0.19 log(s), which was lower than the value in normal pseudophakic eyes; *i.e.*, 1.21 ±0.21 log(s).[19] The difference was even greater considering that the normative population included patients with multifocal IOLs. When types of IOLs are compared, care must be taken that patient selection does not differ, otherwise an inclusion bias can result in misleading interpretation of data. Besides the significance of the difference between IOL materials, inclusion bias might be a factor when multifocal and monofocal IOLs are compared. Five studies have reported the postoperative log(s) of multifocal and monofocal IOLs. Cerviño et al.[8] and Wilkins et al.[12] did not find a significant difference, whereas de Vries et al.[9] and Peng et al.[11] reported lower straylight values in the monofocal group. Moreover, Hofmann et al.[10] found a rather high difference of 0.08 log, also in favor of the monofocal group, but the difference was not statistically significant.

The wavelength dependency of straylight has been studied. The conclusion that yellow sources of light, in contrast to green and blue light, might attenuate disability glare has been presented.[33] However, there is no agreement about whether yellow-tinted IOLs might reduce postoperative glare.[34,35] In the current review, the effect on straylight of blue violet light–filtering and standard multifocal IOLs was studied. The mean result showed better straylight by 0.04 log(s) in the group of IOLs with short wave–absorbing chromophores in their material, but this difference was not statistically significant. In the study by Coppens et al.,[36] it was shown that ocular straylight can be modeled by 3 components with different wavelength dependencies. The base component showed the classic blue dominance of light scattering. Young and well-pigmented eyes may show this characteristic. With less pigmentation (as in white patients), a pigmentation-dependent component is added, dominating at long wavelengths. As a third component, an age-dependent addition was found with low wavelength dependency. Therefore, whether tinted IOLs might improve postoperative straylight may depend on a characteristic of an individual patient. As the individual characteristics within the studied populations were not available, the difference of 0.04 log(s) between the blue violet light–filtering and standard IOLs should be interpreted with caution.

In conclusion, the review showed that straylight of hydrophobic and hydrophilic multifocal IOLs differs significantly. The higher straylight level in the hydrophobic IOLs may originate from particles present in their material, since the observed surface roughness causes a negligible effect on light scattering. Although the optic design appears to be an important factor, if the hydrophobicity criterion is taken into account, only small differences between multifocal IOLs are seen.

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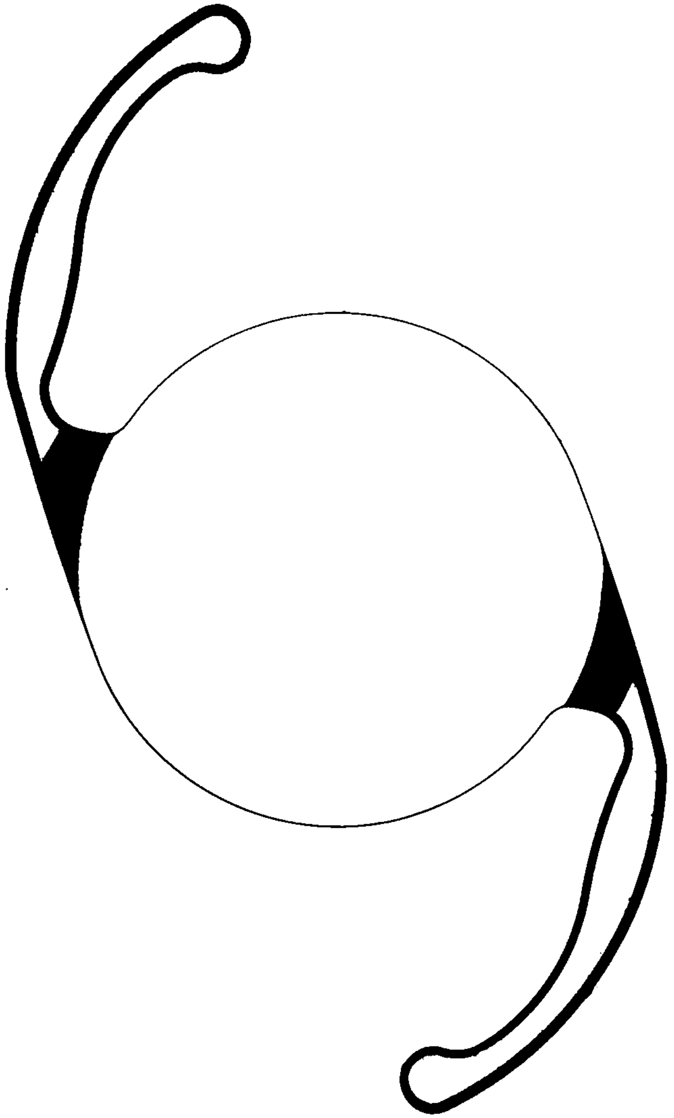

Chapter 6

Straylight from glistenings in intraocular lenses: an *in vitro* study

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J Cataract Refract Surg. 2017; 43:102–108.

ABSTRACT

Purpose

To assess light scattering from intraocular lenses (IOLs) with different numbers of laboratory-induced glistenings and create a model for predicting glistening effects on straylight.

Methods

Glistenings were induced in 7 Acrysof IOLs using an accelerated aging method. To create different numbers of glistenings, the IOLs were immersed in a balanced salt solution at temperatures ranging from 37°C to 60°C and cooled to room temperature. The glistenings were analyzed with a microscope. Light scattering from the IOLs was assessed using a commercial straylight meter (C-Quant) adapted for *in vitro* evaluation of IOLs at a 2.5-degree and 7.0-degree scatter angle. A model was proposed relating straylight increase to the total number and surface portion (total number x area) of glistenings. Results were compared to the Mie theory.

Results

The number of induced glistenings ranged from 114 to 12 386 per mm^2, and the surface portion ranged from 1.4% to 26.9%. At 2.5 degrees, the range in the straylight parameter was 1.49 to 72.49 deg^2/steradian (sr); at 7.0 degrees, it was 1.72 to 62.87 deg^2/sr. Straylight was proportionally related to the total number of glistenings (0.0046 x total number) (R^2 = 0.96) and the surface portion (217 x surface portion) (R^2 = 0.97). The measurements agreed well with the Mie theory.

Conclusions

Straylight from glistenings in IOLs had an accurate proportional association with their total number and surface portion. The proposed model proved effective in predicting straylight from glistenings. Numerous glistenings are needed to cause significant straylight elevation.

INTRODUCTION

The formation of glistenings (small fluid-filled vacuoles) in intraocular lenses (IOLs) has been a well-recognized phenomenon for more than 2 decades. Although this phenomenon has been studied extensively, the visual implications of the presence of glistenings for the patient remain a subject of debate.[1]

It is generally understood that glistenings have the effect of increasing light scattering. But how does that affect vision? A decrease in contrast sensitivity[2–4] and visual acuity[5] has been reported in isolated cases; however, most peer-reviewed studies[6–17] have found that glistenings affect contrast sensitivity and visual acuity only slightly or not. The lack of a tangible effect on visual acuity and contrast sensitivity might be counterintuitive, yet it can be simply explained. The situation is somewhat reminiscent of that for laser pits in IOLs (after neodymium:YAG laser posterior capsulotomy), which were also shown to have little effect on visual acuity or contrast sensitivity. The essence of the explanation lies in the fact that the light scattered by the IOL pits or glistenings involves only part of the light entering the eye.[18,19] The retinal image then consists of 2 parts; 1 part enters the eye properly, in between the scatterers, forming a proper image, which is superimposed on a background of light originating from the scattered light. In case of a visual acuity or contrast sensitivity test, the main effect of such light scattering is a veil of light projected over the visual acuity or contrast sensitivity target and, consequently, some loss of contrast. However, as a rule, the fraction of light hitting the scatterers is low (a few percent at most). Thus, the loss of contrast is small and does not appreciably influence visual acuity or contrast sensitivity.[18] For example, it has been shown that a 5-fold increase in light scattering results in a mere decrease of 0.1 log units in contrast sensitivity and no discernable effect on visual acuity.[18] Only in extreme cases can a significant effect on visual acuity and contrast sensitivity be expected. Scattering of light passing through glistenings might, however, give rise to the visual phenomenon called straylight, and thus disability glare.[20]

The visual phenomenon of straylight corresponds in a precise 1-to-1 fashion with light scattering.[19] Scattering has been measured *in vitro* in IOLs with laboratory-induced glistenings[20] and in explanted IOLs with glistenings.[21] In vivo straylight studies have, however, given rather inconclusive results. One study reported a lack of association with straylight,[12] but another found a significant, albeit small, effect.[22] The problem might be the amount of glistenings available in the studies. Proper quantification of glistenings is essential for understanding their importance. Henriksen et al.,[22] for example, showed that the total area of microvacuoles in the IOL correlates significantly with ocular straylight.

In this study, we assessed the relationship between straylight and glistenings *in vitro* with a clinical straylight meter. A model describing the relationship between straylight and the severity of glistenings was developed. The straylight measurements and the proposed model were compared with theoretically derived scattering based on the Mie theory and with straylight as known from the normal aging population and clinical studies.

MATERIALS AND METHODS

Accelerated Glistenings Formation

This study used 5 SN60WF IOLs and 2 SN60AT IOLs (Alcon Laboratories, Inc.) made of an Acrysof material. The IOLs were removed from their packages and inserted in screw-cap bottles filled with a balanced salt solution. The IOLs were placed separately in a laboratory stove (Tv25u, Memmert GmbH) and subjected to different temperature regimens. Because the primary goal of this study was to evaluate straylight at different stages of glistenings formation, the heating process was performed at different intervals (from 20 minutes to 2 hours) and temperatures (from 37°C to 60°C). The straylight measurements and image recording were performed when the IOLs had cooled to room temperature. For 1 IOL, data for 2 levels of glistenings were included.

Straylight Evaluation

Light scattering from IOLs was evaluated using the C-Quant (Oculus), a clinical device for straylight measurements. It gives straylight expressed as the logarithm of the straylight parameter "s," log(s). The straylight parameter directly relates to the peripheral part of the functional point spread function (PSF) of the eye. This device was adapted for *in vitro* straylight analysis of IOLs as described in a recent article.[23] In short, the C-Quant modification (**Figure 1**) has a plano-convex lens that ensures corresponding angular relations to *in vivo* measurements of the eye. An IOL is placed in a custom-made holder and inserted into a wet cell filled with a balanced salt solution. During the straylight meter measurement procedure, the plano-convex lens and the IOL project an image of the straylight meter test screen that is partly blocked by a diaphragm. The diaphragm intercepts the rays of the straylight source, while the central bipartite test field can still be seen through a magnifying lens. This enables the straylight meter test to be performed without interference from light scattering in the observer's own eye; thus, only straylight from the IOL is measured. Light scattering might also take place in the optical components of the setup. Therefore, straylight induced by the IOL (S_{IOL}) was calculated as the straylight value of the setup with the IOL (Set-up + IOL) minus the straylight value of the setup without the IOL (Set-up) using the following formula:

$$S_{IOL} = 10^{\log(\text{Set-up+IOL})} - 10^{\log(\text{Set-up})} \quad [\text{deg}^2/\text{sr}]$$

where sr stands for steradians.

In addition to the standard straylight meter used in clinics, an elongated straylight meter was also used (**Figure 2**). The elongation of the straylight meter tube enabled evaluation of light scattering at an angle of 2.5 degrees, instead of 7.0 degrees as applied in the standard straylight meter.

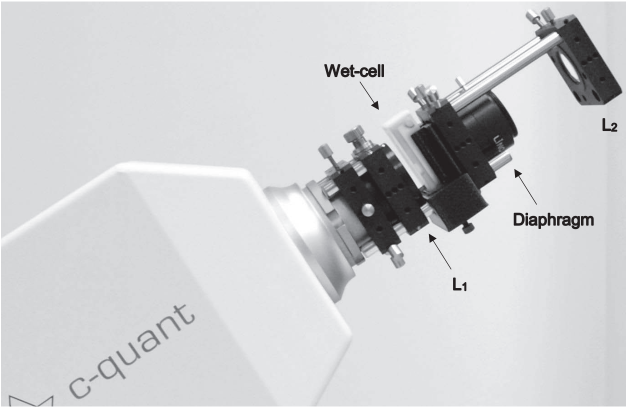

Figure 1. Adaptation of the C-Quant for assessment of straylight from IOLs. The plano-convex lens (L1) and magnifying lens (L2) can be seen.[23]

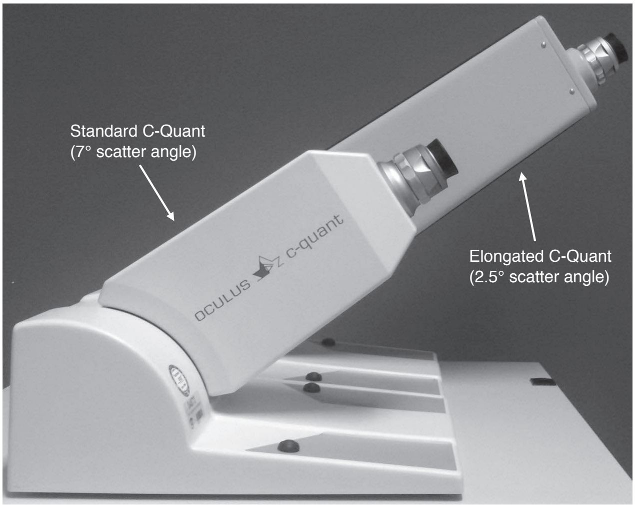

Figure 2. Standard straylight meter (7-degree scatter angle) and a straylight meter with an elongated tube for straylight measurements at a scatter angle of 2.5 degrees.

Image Recording and Analysis

Induced glistenings were recorded using a microscope (Optiphot 2, Nikon Instruments) equipped with a monochromatic camera (model PL-A641, Pixelink). Images were taken from the center of the IOL optic and analyzed with a custom-made software (Image Processing Toolbox, Matlab, Mathworks). Digital image processing involved the following steps: subtraction of background, median filtering, image binarization, morphological operations, and labeling of glistenings. Because some microvoids appeared blurred in microscopic images as a result of the limited depth of field of the system, 2 methods for evaluation of glistenings were used. The size was assessed with analysis of in-focus glistenings solely. The number of glistenings was derived from both in-focus and out-of-focus microvoids. This was achieved by varying the threshold of the binarization process and analyzing the shape of detected objects. The procedure was checked against a ground truth number of a manual counting. In cases of intense glistenings, the manual approach alone was applied because overlap between glistenings poses a problem for automatic analysis. The mean frontal surface area per glistening (mean area [mm^2]) and the total number per mm^2 were obtained based on the image analysis. These values were next used to calculate the surface portion of the IOL covered by glistenings as follows:

Surface portion = mean glistenings area x total number of glistenings per mm^2

After multiplication by 100, the surface portion is expressed as a percentage. In addition, slit-lamp images were collected using an SL-D 701 slit lamp with reverse illumination and a DC-4 camera system (Topcon Corp.). The slit was set at the maximum width, and x25 magnification was used.

Mie Theory

A theoretical prediction of light scattering by glistenings was calculated based on Mie theory.[24] The analysis was done for particles with an average diameter of 5 mm, 10 mm, and 15 mm and a Gaussian distribution with a standard deviation (SD) of 1.25, 2.50, and 3.75. A wavelength of 555 nm in air (the peak of the visual spectrum) was chosen, and an assumption was made that the refractive index of the medium (IOL material) is n_m=1.55 and that of glistenings was n_g=1.336. Because the straylight meter assesses straylight over 5- to 10-degree scatter angle (effective average 7.0 degrees), the results were averaged from 5 degrees to 10 degrees.

Statistical Analysis

Descriptive statistics and data analysis were performed using Excel software (2013, Microsoft Corp.). The mean area and size of the glistenings and their total number were derived from 3 regions close to the center of the IOL. The data were averaged and presented as the median ±SD and range.

The straylight value was based on the mean of 2 measurements. Straylight of the studied IOLs was compared with the level of a normal crystalline lens at age 20 years and 70 years and to that of a cataractous lens. For this comparison, the Commission Internationale de l'Éclairage (CIE) standard function for the PSF was used, which includes straylight and has age as a parameter.[25] Straylight of the eye includes contributions from ocular components other than the lens, and this is estimated to be two thirds for a young healthy eye. Correcting for this, the 20-year-old lens is estimated to have a log(s) value of 0.39 and the 70-year-old lens, 1.05. The age parameter of the CIE standard function for the PSF can also be used to model an eye with cataract.[26] To this end, the mean straylight level for a cataractous lens as found in a cataract population study was used as follows: log(s) = 1.52.[27] The equivalent age corresponding to the CIE's PSF model for this level is 95 years.[27] For comparison, norm values for the young healthy eye (log[s] = 0.9) and for early cataract extraction (log[s] = 1.4) are given.[28]

RESULTS

The median size of the laboratory-induced glistenings in the IOLs was 5.4 mm ±2.7 (SD) (range 4.6 to 12.5 µm), with total numbers varying from 114 to 12 386 per mm^2 between IOLs. The surface portion varied between 1.4% and 26.9 % within the studied IOLs.

The straylight parameter measured at an angle of 2.5 degrees and 7.0 degrees ranged from 1.49 to 72.49 deg^2/sr and from 1.72 to 62.87 deg^2/sr, respectively. **Figure 3** shows the straylight parameter as a function of angle for different surface portion values; for comparison, it also shows straylight levels of the human crystalline lens for different conditions as explained above. A surface portion of 1.4% showed straylight well below the level of that for a young crystalline lens. Surface portion values from 3.9% to 7.7% resulted in functionally significant straylight values that were close to the level of the aged (70-year-old) lens. For extreme glistenings, such as when the surface portion equaled 19.6% and 26.9%, the amount of scattered light was comparable to the effect of cataract. **Figures 4 and 5** show a nearly proportional relationship between straylight (at 7.0 degrees) and the amount of glistenings (R^2 = 0.96) and the surface portion (R^2 = 0.97). Thus, the glistenings effect on the straylight parameter can be modeled using the total number of glistenings or the surface portion value as follows:

$$\text{Straylight parameter} = 0.0046 \times \text{number of glistenings per mm}^2 \quad [deg^2/sr]$$

$$\text{Straylight parameter} = 215 \times \text{surface portion} \quad [deg^2/sr]$$

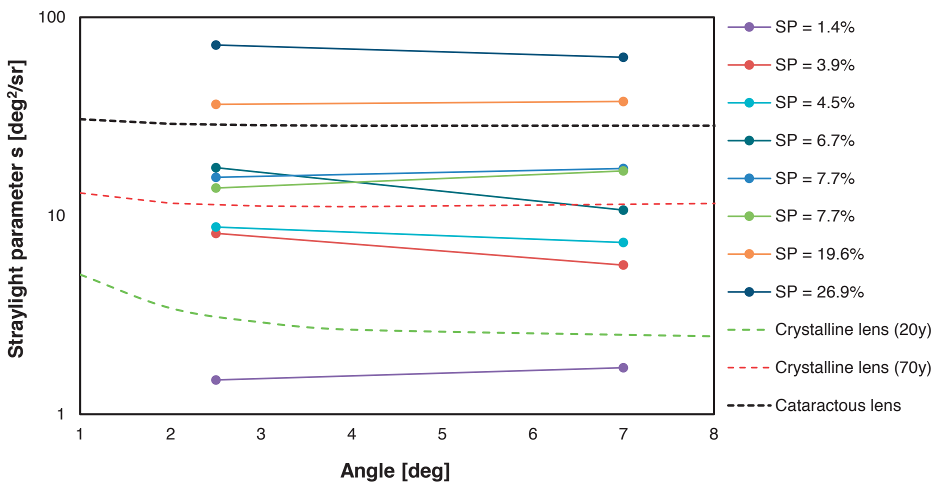

Figure 3. Straylight parameter for 2 angles for different grades of glistenings expressed by the surface portion. The surface portion indicates the IOL area covered by glistenings per mm^2. The dashed lines refer to straylight of a model crystalline lens at the age of 20 years (green) and years 70 (red) and to a model cataractous lens (black) (SP = surface portion; sr = steradians).

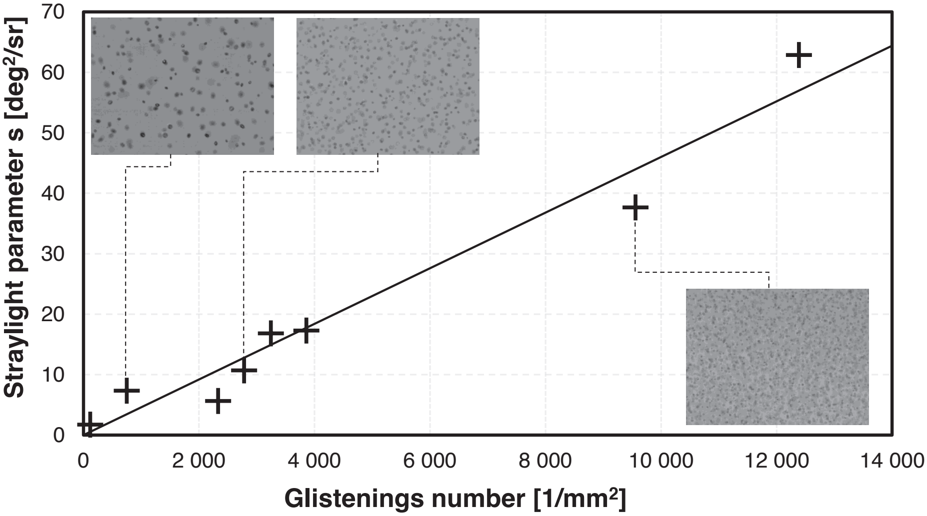

Figure 4. Straylight parameter (7-degree scatter angle) versus glistenings numbers. Three microscopic images of microvacuoles are connected (dashed lines) to respective data points. The solid line shows a directly proportional relationship between straylight and the number of glistenings (sr = steradians).

In **Figure 6**, the theoretical analysis based on Mie theory was compared with the proposed model and to the measured straylight values at 7.0 degrees (expressed in log units). The Mie calculation for 5 mm glistenings corresponded well with the individual data points and the model (*i.e.*, the yellow curve nearly overlaps the green one). A clear dependency of straylight on the glistenings size was found, with larger microvacuoles yielding more straylight.

DISCUSSION

The most important result that we found is a proportional relationship between the number of glistenings and their functional effect on straylight. Because straylight contributes to the functional PSF, potential effects on visual function, such as disability glare and loss of contrast sensitivity, can be derived from these data. Moreover, the present result can be used to understand the seemingly variable results reported in the literature.

The accelerated aging method of the IOLs proved effective, showing that it can be used to induce a wide range of severity of glistenings in IOLs. The correlation parameters were high for both the relationship between straylight and the number of glistenings and the relationship between straylight and the surface portion. A slightly better alignment can be seen for the surface portion in **Figure 5**, presumably because this parameter also accounts for glistening size.

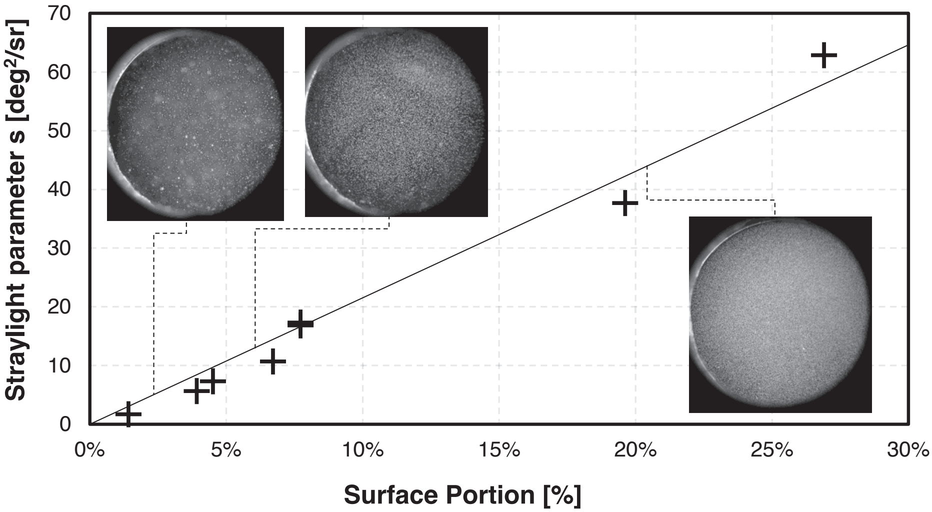

Figure 5. Straylight parameter (7-degree scatter angle) versus surface portion). The surface portion indicates the IOL area covered by glistenings per mm^2. Three demonstration slit-lamp images show IOLs with glistenings that are connected (dashed lines) to the measured straylight levels. The solid line shows a directly proportional relationship between straylight and the surface portion (sr = steradians).

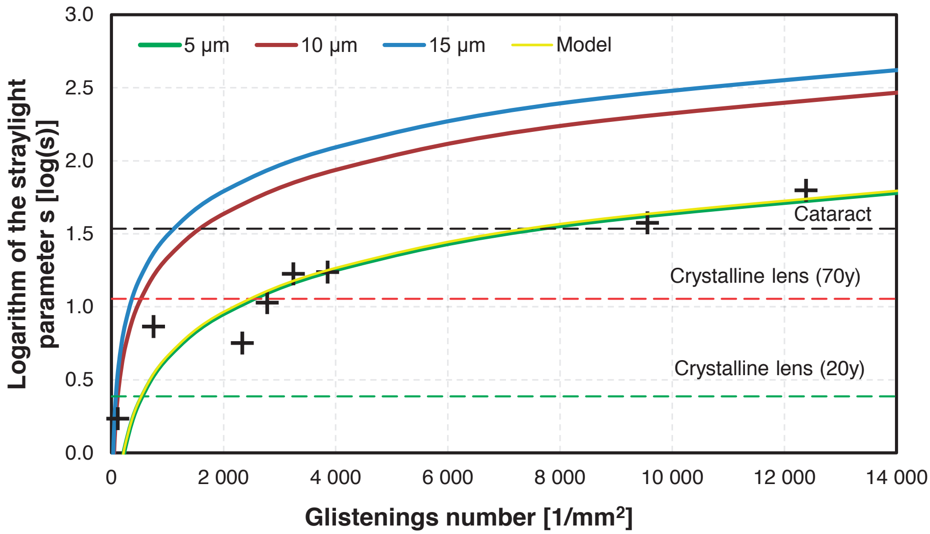

Figure 6. Logarithm of straylight as function of glistenings numbers for 5 mm, 10 mm, and 15 mm of size derived from the Mie theory. The black crosses indicate measured straylight for different glistening numbers. The dashed lines refer to straylight of a model crystalline lens at the age of 20 years (green) and 70 years (red) and to a model cataractous lens (black).

Table 1. Review of published used in clinical studies on glistenings.

First Author (Year)	Follow-up [Mo]	IOL Model	Grade (№)					Total (№)	GS
			Trace/0	1/1+	2/2+	3/3+	4/4+		
Dhaliwal[2] (1996)	NA	Undisclosed AcrySof model (Alcon, Inc.)	2	2	6	0		10*	I
	NA	Silicone lens (undisclosed model/manufacturer)	10	0	0	0		10*	
Christiansen[5] (2001)	29	AcrySof MA60BM and MA30BA (both from Alcon, Inc.)	27	5	5	3	2	42	II
Gunenc[3] (2001)	13	AcrySof MA30BA, MA60BA (both from Alcon, Inc.)	57	5	8	11	10	91	III
Miyata[29] (2001)	13	AcrySof MA60BM and MA30BA (both from Alcon, Inc.)	21	28 IOLs with grade ≥1/1+				49	IV
Wilkins[6] (2001)	98	Surgidev B20/20 (Surgidev Corp.)	8	30	34	1	-	73	V
Tognetto[7] (2002)	24	CeeOn Edge 911A (Pharmacia & UpjohnCo.); ACR6D (Corneal); AcrySof (Alcon, Inc.); Hydroview H60M (Storz); Sensar and SI-40NB (both from Abbott Medical Optics); Stabibag (Ioltech)	Glistenings were found in all studied lenses			0		249	I
Moreno-Montañés[8] (2003)	21	AcrySoft MA30BA (Alcon, Inc.)	91	15	18	5	-	129	I
Cisneros-Lanuza[9] (2007)	27	Artiflex (Ophtec BV)	16	1	1	0	2	20	II
Behndig[30] (2009)[P]	105	AcrySof MA60AT or SA60AT (both from Alcon, Inc.)	0	2	5	6	13	26	III
Colin[11] (2009)	<24**	AcrySof SN60AT, SN60WF and MA-type (all from Alcon, Inc.)	40	40	19	-	-	99	VI
	>24**		63	47	51	-	-	161	
Colin[12] (2011)	18	AcrySof MA-type, SA60AT, SN60AT, SN60WF (all from Alcon, Inc.)	39	31	27	-	-	97	VI
Mönestam[13] (2011)	>120	AcrySoft MA60BM (Alcon, Inc.)	9		8	23	63	103	III
Colin[14] (2012)	40	AcrySof SN60WF (Alcon, Inc.)	15	45	51	-	-	111	VI
Chang[15] (2013)	68	AcrySof SA60AT (Alcon, Inc.)	6	12	6	5	-	29	I
		AR40e (Abbott Medical Optics)	24	3	0	0		27	
Schweitzer[16] (2014)	35	AcrySof SA60AT and SN60AT (both from Alcon, Inc.)	4	9	12			25	VII
		AcrySof SN60WF (Alcon, Inc.)	22	4	16			42	
Xi[4] (2014)	24	AcrySoft SA60AT (Alcon, Inc.)	30	30	30	30	-	120	I

Table 1. Review of published used in clinical studies on glistenings. (continued)

First Author (Year)	Follow-up [Mo]	IOL Model	Grade (№)					Total (№)	GS
			Trace/0	1/1+	2/2+	3/3+	4/4+		
Biwer[31] (2015)	43	Akreos-Adapt (Bausch & Lomb), Lentis L-307 (Oculentis), undisclosed AcrySof models (Alcon, Inc.), AR40e and Clrflxc (both from Abbott Medical Optics)	24	11	8	7	13	63	II
Chang[17] (2015)	107	AcrySof SA60AT (Alcon, Inc.)	12	7	9	8	-	36	I
		BL27 (Bausch & Lomb, Inc.)	42	0	0	0		42	
Kahraman[32] (2015)	36	AcrySoft SA60AT (Alcon, Inc.)	7	11	32	-	-	50	VI
		ZCB00 (Abbott Medical Optics)	50	0	0			50	

I: Trace/0 (absence); 1/1+ (trace/countable vacuoles), 2/2+ (moderate); 3/3+ (severe).
II: Trace (<10); 1+ (10-20); 2+ (20-30); 3+ (30-40); 4+ (>40).
III: 0 (absence); 1 (a few); 2 (minor); 3 (moderate); 4 (pronounced).
IV: 0 (absence); 1 (50); 2 (100); 3 (200).
V: 0 (absence); 1+ (<10); 2+ (10-50); 3+ (>50).
VI: 0 (absence); 1 (moderate); 2 (dense).
VII: 0 (<50); 1 (50-150); 2 (>150).
[P] published plot analysis.
* Only subjects with an AcrySof lens in one eye and a silicone lens in the fellow eye.
** Mean follow-up = 33 months.

Figure 6 shows that larger glistenings result in more straylight. DeHoog and Doraiswamy[29] simulated the effects of glistenings on the quality of vision with optical software. They concluded that smaller glistenings (*i.e.*, 2 mm) have a greater impact on visual function than larger glistenings (*i.e.*, 20 mm). This seeming discrepancy with our results can be explained when realizing that DeHoog and Doraiswamy[29] compared, for example, 135 000 glistenings of 2 μm with 135 glistenings of 20 μm to keep the total volume that the glistenings occupied constant (*i.e.*, they assumed an equal volume fraction). We, however, looked at a cross-section of glistenings (expressed by the surface portion), which correlates more closely to what is seen at the slit lamp and also might be a more relevant parameter for determining the amount of light scattered. To relate their result to our findings, one can calculate the surface portion based on the given number of glistenings. This shows that when assuming an equal volume fraction, a surface portion of an IOL with larger glistenings (*i.e.*, 20 μm) is 10 times lower than of the IOL with smaller glistenings (*i.e.*, 2 μm). The reason is that the number of smaller glistenings is much higher than that of larger glistenings (*i.e.*, 135 000 versus 135) in cases of equal-volume fractions. Thus, for such comparison, smaller glistenings are more important. In practice, however, the opposite is the case; that is, larger glistenings are more important.

The best quantitative comparison of the present results can be made with a recent *in vivo* study by Henriksen et al.[22] They also found a significant correlation between surface portion (for which they used the term severity index) and ocular straylight. Looking at their plot of straylight versus surface portion (*i.e.*, severity index), we can deduce that they found, on average, 1.03 log(s) for a glistenings-free IOL (severity index = 0) and 1.26 log(s) for an IOL with glistenings with a surface portion of 3.5%. After conversion to the straylight parameter(s), the comparison of these values (1.03 log[s] versus 1.26 log[s]) results in a difference of s = 8 deg^2/sr. When surface portion = 3.5% is entered in our model for predicting straylight from glistenings, a value of 0.035 x 215 = 8 deg^2/sr is predicted, showing that our model agrees very well with their results.

To relate our findings to previously reported clinical results, a literature survey was performed. This showed that glistening severity is usually clinically quantified using a grading system. Seven grading systems have been published (**Table 1**).[2–9,11–17,30–33] The 3 most commonly used grading scales involve subjective grading (**Table 1**; grading scales [GS]: I, III, and VI). The subjective grades use terms such as minor, moderate, pronounced, and severe and make comparison with quantitative data difficult. The other 4 grading scales apply counting (**Table 1**; GS: II, IV, V, and VII), which might be considered a more reproducible and objective approach. However, Biwer et al.[32] showed only moderate agreement between rates of glistenings counted with a slit lamp versus subsequent assessment of slit-lamp images. It was concluded that the reliability of counting at the slit lamp can be limited by the examiner's experience, but they also pointed to difficulties in reproducibility of slit-lamp illumination.[32]

As knowledge of the quantitative amount of glistenings is clearly relevant, what does **Table 1** tell us? In the study by Miyata et al.,[30] up to 200 microvacuoles per mm^2 in IOLs were counted with a slit lamp. Based on our model for predicting straylight from glistenings based on the number of glistenings, the expected straylight parameter in such a case would be approximately 1 (log[s] = 0), which is very small compared with normal values in eyes of 10 (log[s] = 1) or more. It seems clear that straylight elevation will be significant only in cases with (much) larger numbers. The literature review showed that 19% of evaluated IOLs (limited to grading systems based on counting) fall into the highest grade, specified as having more than 40 to 200 glistenings per mm^2. Actual counting numbers are not given but would be needed for straylight estimation using our model. In the study by Colin and Orignac,[12] the highest reported number of microvacuoles per mm^2 was 597. The expected corresponding straylight value calculated with our model would be 3 deg^2/sr. If this value were added to the value 1.2 log(s) for their group with no glistenings (*i.e.*, grade 0), straylight would increase to 1.28 log(s). This is close to the straylight level of their most severe grade of glistenings severity (*i.e.*, grade 2) of 1.3 log(s).[12] Note that in terms of importance for quality of vision, a 0.1 log unit increase in ocular straylight is comparable to a loss of 1 line on the logMAR visual acuity test.[34] In the study of Colin and Orignac,[12] intense glistenings (grade 2) were found in 27 of 97 IOLs; however, the authors did not consider any of them to be extremely dense. This might partly explain why visual difficulties from glistenings have been observed in very few cases.[4,21,35]

Thus far, 2 studies of *in vitro* scatter evaluation of glistenings have been published.[20,21] In an experimental setting with off-the-shelf IOLs, glistenings were induced in the Acrysof material.[20] The mean glistening number was 1800 per mm^3; however, a direct comparison with our results cannot be made because the mean scatter level was not published in that study. The mean size of the microvacuoles (6.2 μm) reported by van der Mooren et al.[20] is close to the 5.4 μm (median) we found. In a case report of an exchange of a multifocal IOL because of glistenings, an *in vitro* light scatter analysis of IOLs (after several years in the eye) was also presented.[21] In the 2 cases described straylight was found to be higher than that of the 20-year-old crystalline lens, and this was considered the major contributor to the patient's visual complaints. Although a quantitative analysis of microvacuoles was not given and the analysis was limited to 2.5 degrees of scattering angle, a comparable effect can be found in our IOLs with a glistenings surface portion of 3.9% or 4.5% (**Figure 3**).

In conclusion, we found a proportional relationship between the number of glistenings and straylight. The relationship proved to agree with data in the literature. A large number of glistenings is needed to cause an increase in straylight that is clinically relevant to the patient. The relationship also clarifies the variable results published on (the lack of) functional effects of glistenings. Although effects on visual acuity or contrast sensitivity are improbable, effects on straylight and thus disability glare seem possible.

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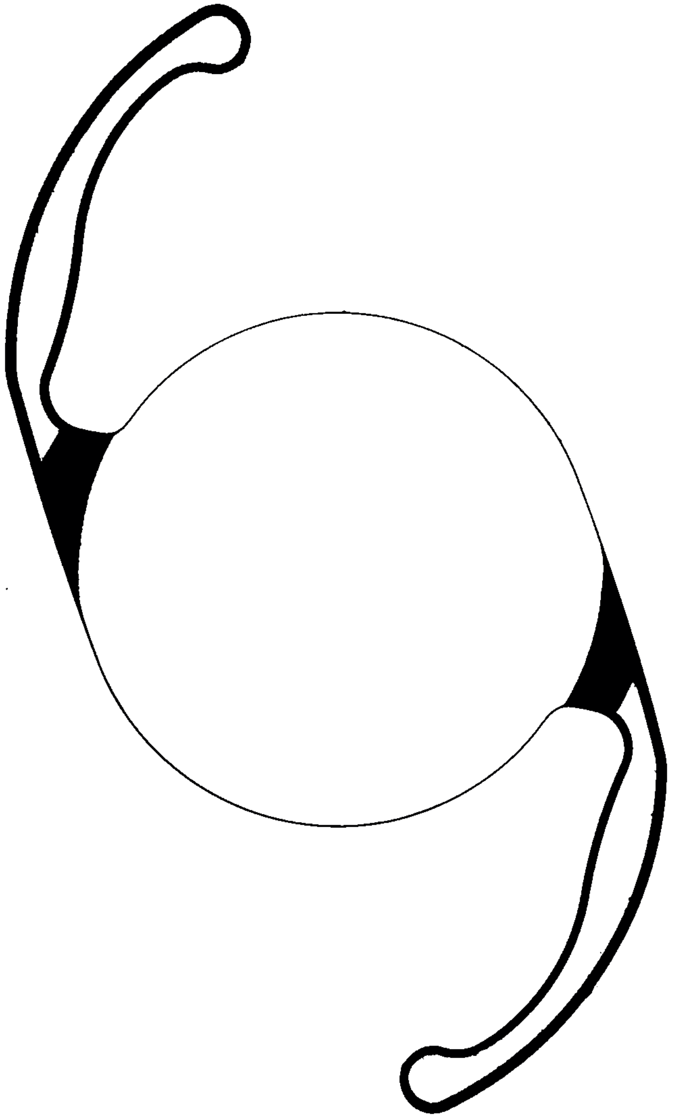

Chapter 7

Light scattering levels from intraocular lenses extracted from donor eyes

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J Cataract Refract Surg. (in press)

ABSTRACT

Purpose

To assess light scatter levels of intraocular lenses (IOLs) extracted from donor eyes, in order to understand straylight elevation documented earlier in pseudophakic population studies, and to identify potential sources of light scattering in IOLs.

Methods

Light scattering of 74 donor lenses was measured with the Oculus C-Quant device adapted for *in vitro* analysis of IOLs. Straylight was assessed at 2.5 and 7.0 deg scatter angle, and results were compared to straylight of a 20-year-old and 70-year-old crystalline lens, and to that of a lens with cataract. To identify potential changes to the IOL material, the IOLs were examined with a light microscope and a slit lamp.

Results

At 2.5 and 7.0 deg the straylight parameter (mean ±SD) was 5.78 ±4.70 deg^2/sr and 5.06 ±4.01deg^2/sr, respectively. Forty-one percent of the IOLs showed lower straylight than that of the 20-year-old lens; in 14% scattering intensity was higher than in the 70-year-old lens; none showed straylight comparable to that of the cataractous lens. Increased straylight was associated with surface deposits, snowflake-like degeneration, and glistenings. The incidence rate of lens-related complications differed between different IOL groups.

Conclusions

Microscopic structural alterations inside IOLs explains for an important part the straylight elevations found in pseudophakic eyes. A clear correlation with degeneration and/or alteration of implanted IOLs is found. Although these IOL-related complications are not likely to affect visual acuity, they give rise to straylight which is known to result in disability glare and other complaints.

INTRODUCTION

Straylight in pseudophakia has been studied since the 1980s. Ever since, it has been found that straylight of the pseudophakic eye does not, as a rule, return to the level of a young eye following surgery.[1-5] The literature shows that in the absence of posterior capsule opacification (PCO), straylight is increased up to a level known to be a serious hindrance to the patients' vision in 10% of the pseudophakic eyes.[5] The reason for straylight elevation in pseudophakia is yet unknown.

Straylight is a perceptual quantity corresponding with the functional effect of light scattering in the eye.[4, 6-9] In a young, healthy eye, the light is primarily scattered by the cornea and the crystalline lens. However, fundus reflectance and light transmittance of the eye wall are also deemed important.[4, 6-9] All sources of straylight in the eye but one (*i.e.*, the lens) are considered relatively independent of age.[4, 6-9] The straylight level of the young eye is 0.90 log(s) (s=7.9 deg^2/sr).[3, 4, 8-11] Aging of the crystalline lens causes straylight to increase, and an approximate 2-fold increase (1.20 log[s]; s=15.8 deg^2/sr) has been found at the age of 65 years.[3, 4, 8-11] For comparison, 1.52 log(s) (s=33.1 deg^2/sr), on average, has been reported in the eye with cataract.[12] Increased straylight results in disability glare, which is always exacerbated under dynamic light conditions.[3, 4, 6-9] It is depicted by the patient as blinding by light sources, hazy vision and/or as a loss of contrast.[3, 4, 6-9]

Clinical studies have shown a significant straylight decrease after cataract surgery. Yet, as previously mentioned, some pseudophakic patients experience high straylight levels.[5, 13-15] This could be attributed to postoperative complications related to the implanted intraocular lens (IOL). A main concern is biocompatibility of IOL materials, which might degrade or alter once placed in a dynamic eye environment. Several *in vitro* studies on lenses explanted due to IOL pathology have reported increased light scattering in most cases.[16-19] Changes to the IOL material that have been considered as important sources of light scattering are calcium and/or phosphate precipitations on the lens surface, snowflake degeneration, and glistenings.[16-20] An *in vitro* study on lens explants deemed free of any pathology has also shown higher straylight in 2 of 6 analyzed cases.[A] This indicates that the onset of IOL complications might occur in a subclinical form, and standard ocular examination might not be capable of early detection of this complication.

The aim of this study was to assess the contribution to straylight from IOLs obtained from donor pseudophakic eyes, and to identify potential underlying causes of increased straylight in pseudophakia. To this end, we measured light scattering in donor lenses and examined them with a light microscope and a slit lamp.

METHODS

Seventy-four monofocal IOLs from donor pseudophakic eyes were studied. The donor eyes were obtained from the Cornea Bank Amsterdam. No *a priori* data on the donor eyes and the IOLs were available. The lenses were stored in balanced salt solution (BSS) at room temperature. The IOLs were examined with the slit lamp and the light microscope. To separate different IOL groups, IOLs of the same model were matched based on slit-lamp images. Although the shapes of the haptic and optic may be clues to the specific IOL models, substitutes exist for well-known IOL brands that are available on the market. So, the authors could not identify lens types with certainty. For this, individual patient records were needed, which were not accessible to the authors.

Straylight of the IOLs was analyzed with an adaptation of the C-Quant (Oculus).[21, 22] **Figure 1** shows the optical diagram of the C-Quant adaptation.[21] The C-Quant device is a clinical straylight meter which uses a psychophysical approach to assess straylight.[4, 9, 23] In this instrument, straylight of the eye is measured by using the retina as null detector, and is defined and quantified by the concept of equivalent luminance.[4, 8, 9, 23-25] In essence, the test consists of comparing known light to (unknown) straylight. The adaptation includes optical components and a wet-cell (**Figure 1**). An IOL is placed in the wet-cell and submerged in BSS. An optical design of the adaptation enables a C-Quant test to be performed on an IOL (not the eye), yet by using the eye of an observer as null detector, regardless of the refractive power of the IOL. A diaphragm is placed behind the IOL to block light of a straylight source; hence, only the test field is seen to the observer where known and unknown straylight levels are compared (**Figure 1**). The observer's eye is used to judge the test field projected by the IOL. As the IOL is conjugated with the crystalline lens, the adaptation simulates "looking" through an implanted IOL. The only difference being the exposure to the straylight source, to obtain a pure measure of the light scattering aspect of the IOL.

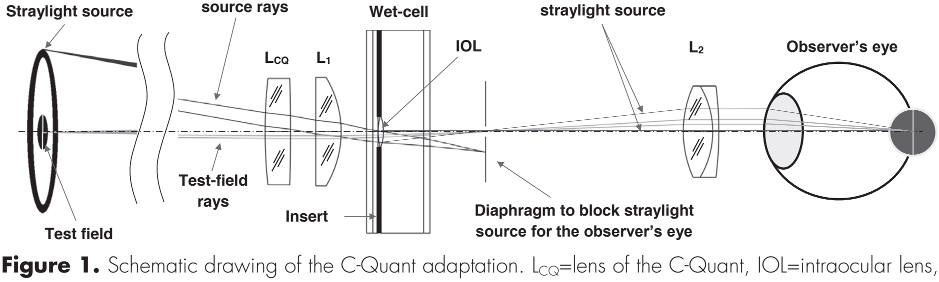

Figure 1. Schematic drawing of the C-Quant adaptation. L_{CQ}=lens of the C-Quant, IOL=intraocular lens, L=lens. For more details on the adaptation, please refer to the Methods section. Reprinted from *Biomed Opt Express 2017;8:1889-94.*

Straylight was measured at 2.5 and 7.0 deg scatter angle to study straylight-angular dependence.[26] A clinical C-Quant evaluates straylight at 7.0 deg.[23] A modified C-Quant with a tube elongated by a factor of 2√2 was also used to measure straylight at 2.5 deg.[20] Both the clinical and modified C-Quant give straylight results presented as logarithm of the straylight parameter, log(s). Note straylight can be expressed by either the straylight parameter "s" or its logarithm "log(s)," *e.g.* log(s)=1 equals s=10. Straylight of the donor lenses was compared to known (isolated) levels of the crystalline lens at the ages of 20 (0.38 log(s); s=2.4 deg^2/sr) and 70 (1.05 log(s); s=11.3 deg^2/sr) years, and to a 95-year-old lens (1.52 log(s); s=33.1 deg^2/sr) to simulate the effect of cataract.[12] These straylight levels were calculated based on the CIE model as described elsewhere.[24, 25]

RESULTS

The mean straylight (± standard deviation) at 2.5 deg and 7.0 deg was 5.78 ±4.70 deg^2/sr and 5.06 ±4.01deg^2/sr, respectively. Thirty (41%) of the 74 IOLs showed straylight that was below the level of that of the crystalline lens aged 20 years. Straylight was above the level of the 70-year-old crystalline lens in 10 IOLs (14%). However, none showed a straylight level that is close to that of the cataractous lens. **Figure 2** demonstrates the results graphically.

Eight IOL groups of the same model were identified that comprised 61 IOLs (82%). **Figure 3** shows overview images (one for each group) of the IOL models. **Table 1** reports the median straylight values of the 8 IOL groups at the 2.5 and 7.0 deg scatter angle **Figure 2** presents straylight for each group of IOL model as well as for the IOLs that could not be grouped, with the results compared to the straylight levels of the crystalline lens.

Thirty-four IOLs (43%) were free of any IOL pathology; the remaining 40 lenses showed different levels of lens opacification. **Table 1** presents incidence rates of lens opacification in the 8 groups. Surface deposits were found in groups 1 (one lens), 2, 3 (one lens) and 6. The observed white-brown foci of degeneration in groups 2 may also impress as snowflake degeneration. Glistenings were found in groups 4, 5 and 8. **Figure 4** shows slit-lamp and microscopic images of IOLs with snowflake-like degeneration, surface deposits, and glistenings.

Table 1. Straylight and the incidence rate of IOL complications in the 8 lens groups.

Angle [deg]	Median straylight parameter s ±SD [deg^2/sr]							
	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6	Group 7	Group 8
2.5	3.1 ±5.2	8.8 ±4.5	1.2 ±6.1	5.3 ±4.2	3.8 ±3.2	10.4 ±3.2	1.7 ±10.5	2.2 ±0.9
7.0	2.1 ±4.1	9.9 ±3.6	1.9 ±2.5	5.4 ±1.9	2.8 ±3.9	10.3 ±3.6	2.1 ±7.3	1.7 ±0.3
	IOL complications							
	1/5	7/7	1/8	5/9	6/10	10/10	0/6	4/6

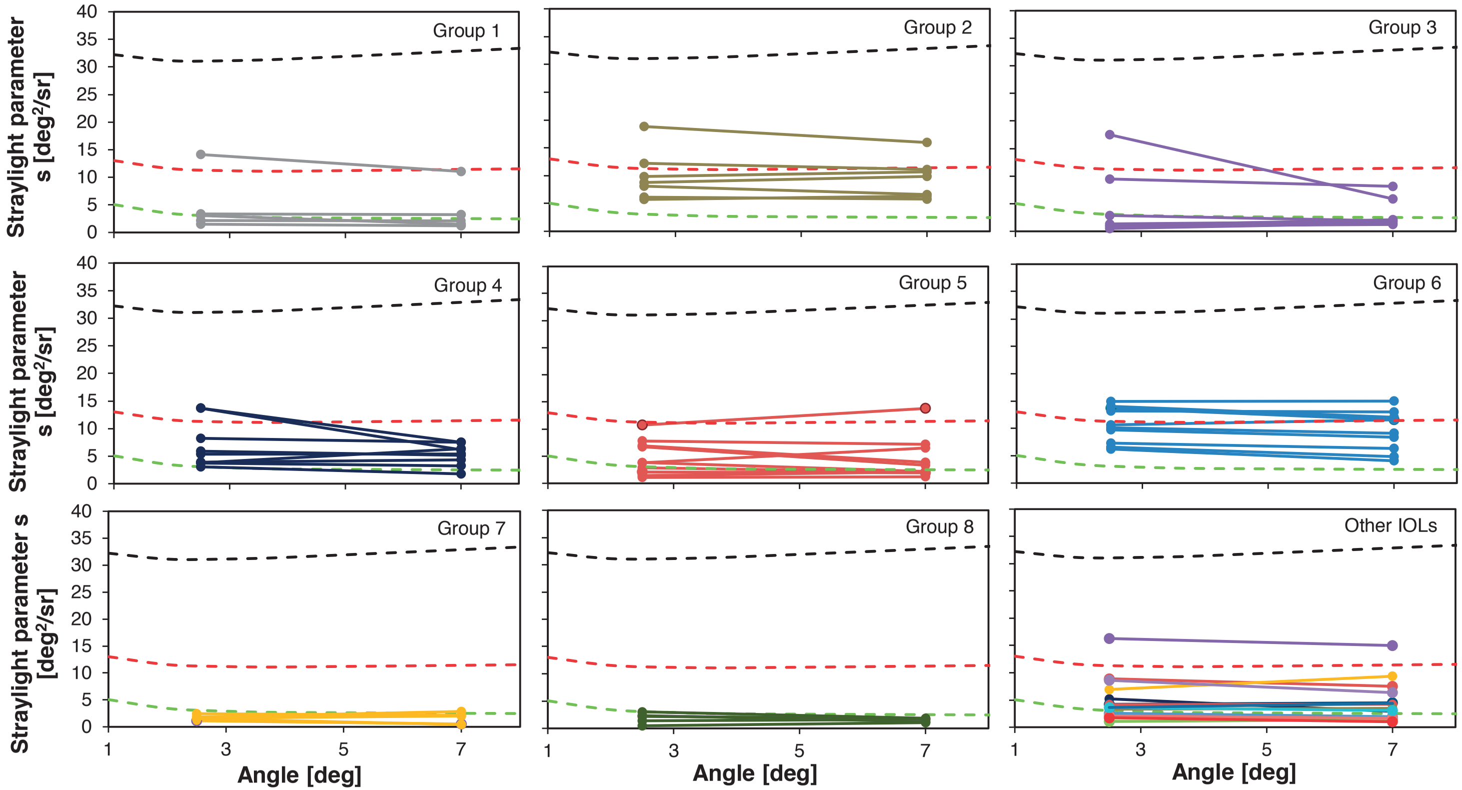

Figure 2. Straylight of donor IOLs measured at 2.5 and 7.0 deg scatter angle. The results are stratified by lens model. The green and red dashed line represents straylight of the crystalline lens at the age of 20 and 70, respectively. The black dashed line simulates the effect of cataract, which is comparable to a straylight level of a 95-year-old lens.

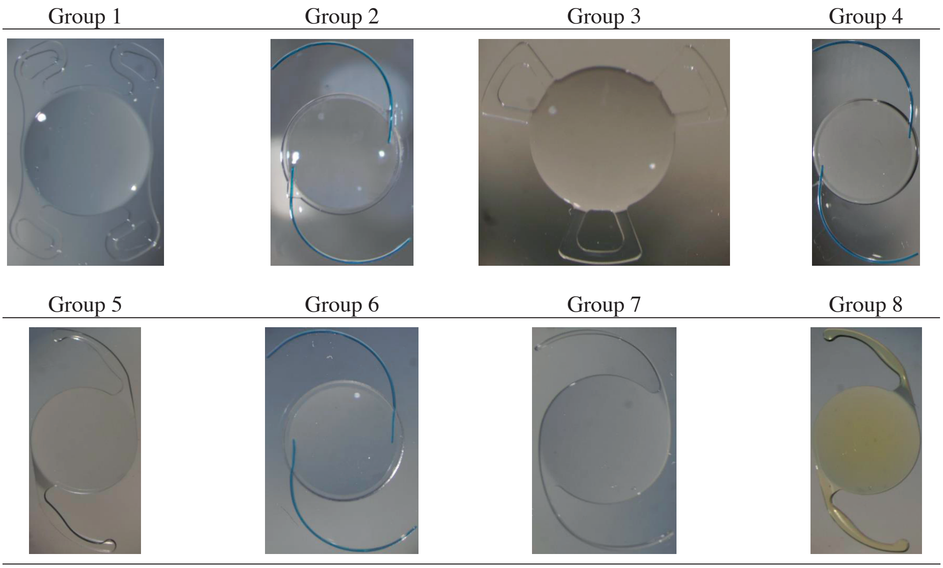

Figure 3. Exemplary photographs of matched IOL groups.

DISCUSSION

The study aimed to assess the contribution to straylight for a random sample of IOLs, in order to understand straylight elevation generally found in pseudophakic eyes.[5] The study found that IOLs from donor eyes are in general not free from straylight. Significant amounts of straylight were found, but differences seem to exist among the IOLs; both between groups of IOL models and within groups. This may be similar to the reported differences in straylight between pseudophakic eyes.[5] Scatter sources that are shown in **Figure 4** appear to be the most likely cause for the observed straylight increase. The incidence rate of the complications may differ between IOL models (**Table 1**).

A recent review paper on straylight in uncompromised pseudophakia (*i.e.*, without PCO) showed straylight elevation with serious straylight hindrance affecting 10% of the pseudophakic patients.[5] This must be compared to our current *in vitro* finding that seriously increased straylight occurred in 14% of the studied donor IOLs. Mean straylight has been found to be 1.21 log(s) in pseudophakic eyes, corresponding to s=16 deg^2/sr.[5] **Table 1** shows median s values in donor IOLs of about 0.3 to 1.0 log(s) (s=2 to 10 deg^2/sr). Since light scattering in the human eye is additive, we can approximate the straylight in an aphakic eye by subtracting the straylight value in our reported donor IOLs from that of the average pseudophakic eye. This would result in log(s)= 0.78 to 1.15, corresponding to s=6 to 14 deg^2/sr. These values must be compared to the values for the young normal eye, being on average log(s)=0.90 (s=7.9 deg^2/sr).[4] Therefore, the results of this study

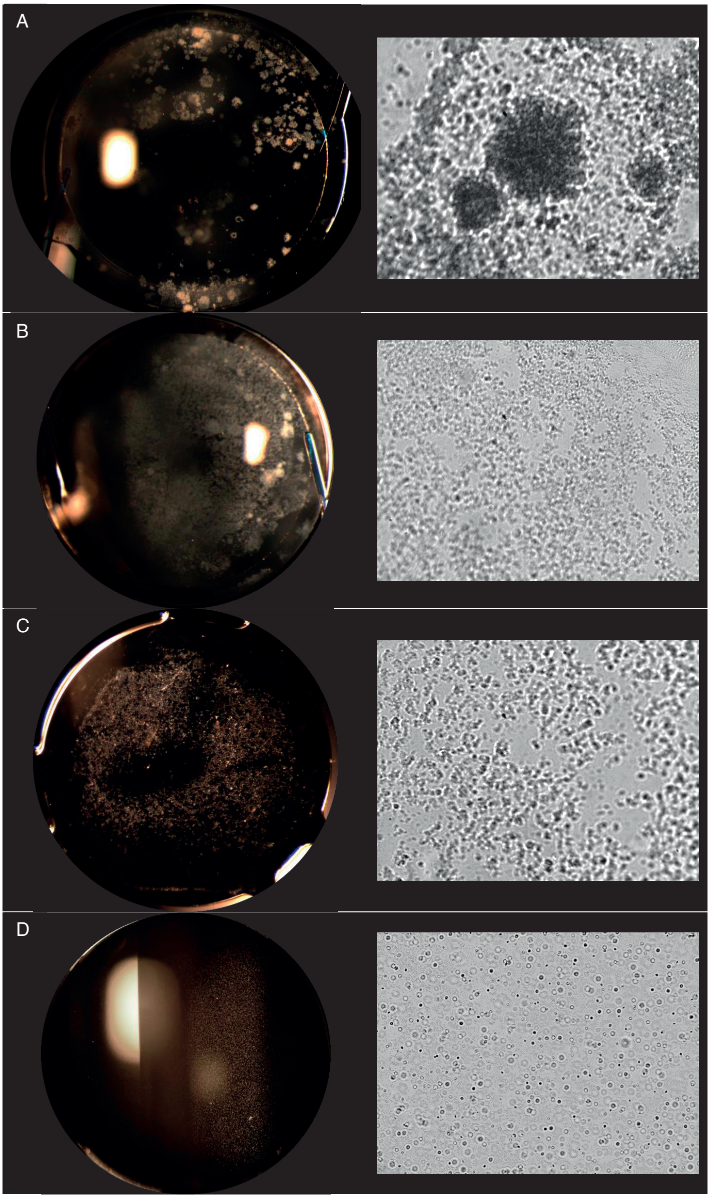

Figure 4. Slit-lamp (left) and microscopic (right) exemplary images of donor lenses with different types of IOL opacification. A) A 3-piece IOL (Group 2) with foci of white-brown opacification (left) that impresses as snowflake degeneration, and an isolated pattern of opacification (right); s(7deg) = 16.0 deg^2/sr. B) A 3-piece IOL (Group 6) with confluent whitish opacification located in the central and mid-peripheral lens area (left), with crust-like deposits (right); s(7deg) = 15.0 deg^2/sr. C) A 1-piece IOL (Group 3) with whitish deposits concentrated within the central and mid-peripheral area of the lens with irregular clearing in the center (left), with crust-like deposits (right); s(7deg) = 5.9 deg^2/sr. D) A 1-piece IOL (Group 5) with numerous glistenings within the IOL bulk seen with the slit lamp (left) and the microscope (right); s(7deg) = 13.8 deg^2/sr.

indicate that higher than expected straylight in pseudophakia may be caused by light scattering originating from implanted IOLs. Although this seems an important finding, this only partially explains straylight results of *in vivo* studies, as one may wonder why only 6% of the pseudophakic patients show straylight levels comparable to that of the young eye, if straylight of 41% of the studied lenses was low. This warrants further investigation.

It must be realized that the studies in pseudophakia relate to different IOL types. We, however, could not make a comparison of the present results with those studies on basis of IOL type. The reason is that data on the studied donor lenses were not accessible, so we were not able to identify the studied lenses with certainty. The mean straylight values found in those studies varies from log(s)=1.10 log(s) to 1.47 log(s), corresponding to s=12.6 to 29.5 deg^2/sr.[5] Individual log(s) values may differ much more (e.g. 0.68-2.13 log[s][15] = 28-fold difference). These ranges of variation seem to be larger than can be accounted for with the present study. The values found in the present study could only account for, say a 2- to 3-fold straylight difference. One may speculate about other potential sources of light scattering that might contribute to the reported differences between pseudophakic eyes, such as subclinical onset of PCO, pupil size and capsulorhexis diameter, age-related changes of the vitreous, and pigmentation level.

Light scattering characteristics depend on the size of the scattering particles (small vs. large particles).[26] **Figure 2** shows that relatively large particles (no less than of wavelength size) dominate scattering in the studied lenses, as straylight-angular dependence was found to correspond relatively well with the Stiles-Holladay approximation.[27] This was confirmed by the slit lamp and light microscopy examination, as large numbers of finite particles could be seen in some studied IOLs (**Figure 4**) revealing the presence of surface deposits, snowflake-like denegation, and glistenings.

Table 1 indicates that the highest rate of the IOL-related complications was found in Group 2 and 6. This finding also correlates with the highest straylight values found in these groups. Moreover, **Figure 2** demonstrates a consistent pattern of straylight elevation in the 2 groups. **Figure 4**A (Group 2) shows surface deposits and confined white-brown discolorations that might appear like snowflake degeneration[28, 29] The snowflake degeneration has been found in Poly(methyl methacrylate) (PMMA) lenses.[16, 28, 29] **Figure 4**B shows surface deposits that could be a potential reason for increased straylight in Group 6. Deposits were also found in one lens of Group 3 (**Figure 4**C) and Group 1 resulting in significant straylight elevation. Calcium and/or phosphate precipitates have been attributed to IOL surface deposits.[16, 17, 29-38] This postop complication has often been associated with hydrophilic lenses.[16, 17, 29, 33, 34, 36, 37] However, studies have reported calcium deposits on hydrophilic lenses with hydrophobic coating[30], silicone,[16, 29, 32, 35] and PMMA lenses[31] as well.

Straylight of explanted IOLs with calcium deposits/snowflake degeneration has been studied.[17, 19] One study showed straylight of 2 hydrophilic acrylic IOLs with severe opacification to be 1.8 and 2.9 log(s) (s=63.1 and 794.3 deg^2/sr) for 7.5 deg scatter angle.[17] Werner et al.[19] measured straylight of hydrophilic, silicone and PMMA IOLs that were explanted because of calcification/snowflake degeneration. They reported that average straylight (at 7.5 deg) of the calcified lenses (hydrophilic and silicone IOLs) was 1.63 log(s) (s=42.7 deg^2/sr); and of PMMA lenses with the snowflake degeneration it was 1.60 log(s) (s=39.8 deg^2/sr).[19] These values are much higher than straylight reported in the present study, as we found the highest value to be 1.20 log(s) (s=15.8 deg^2/sr). This, however, could be expected as those explanted lenses can be considered the top of the iceberg. IOLs are typically explanted when opacification affects visual acuity, but the donor IOLs might have provided satisfactory visual acuity throughout the donors' lifespan despite the presence of IOL degenerations and increased straylight. This may also indicate, that some IOL-related complications may go undetected, and so the incidence rate of lens complications might be understated.

Formation of glistenings is another postop complication that was found in the analyzed lenses. Glistenings are fluid-filled microvacuoles with a size ranging from 1 to 20 μm that have been especially, but not exclusively, associated with AcrySof IOLs.[39] Some cases of glistenings in other IOL materials have also been reported.[40, 41] Glistenings were found in Group 4, 5 and 8 with an incidence rate of 55%, 60% and 67%, respectively. Although the highest rate was found in Group 8, this group also shows the third lowest straylight among the 8 IOL groups. This finding may suggest that glistenings have lower potential for straylight elevation than surface deposits/snowflake-like degeneration. This is in agreement with literature, as explantation of lenses with the surface deposits/snowflake degeneration[16, 17, 28-38] has been more often reported than explantation of lenses with glistenings.[18, 42, 43]

Light scattering of 2 explanted, multifocal IOLs with glistenings has been studied by Van der Mooren et al.[18] They reported that straylight (at 2.5 deg) of the 2 analyzed lenses was below the level of that of the 70-year-old crystalline lens.[18] We also found that in Group 4, 5 and 8 all IOLs but 3 showed straylight below this level. A recent laboratory study on the relation between straylight and glistenings has demonstrated how the intensity of the scattered light depends on the size and number of the microvacuoles.[20] A model of the straylight effect of glistenings was proposed,[20] which can be used to estimate the number of microvacuoles. **Figure 1** shows a straylight value of s=13.8 deg^2/sr (1.14 log[s]) at 7.0 deg in Group 5, which is the highest among the IOLs with glistenings. If this value is entered in the model, the glistenings number is estimated to be (approx.) 2 800 per mm^2. Such a large number of microvacuoles would fall into the highest grade.

The slit-lamp and microscopic analysis, and the straylight measurements indicated that in the absence of structural changes to IOL material, light scattering remains at a low level. Forty-one percent of the studied lenses showed straylight below that of the 20-year-old crystalline lens, corresponding with 43% of IOLs that were free of any pathology. This is a likely reason for the observed difference between groups with the extreme straylight levels, *i.e.* group 2 and 6 (the highest) vs, group 3 and 7 (the lowest). As 100% complication rate was observed in groups with higher straylight, but in group 3 and 7 it was 7% (one lens).

In conclusion, it was found that straylight elevation in pseudophakic eyes may result from IOL-related complications. The presence of surface deposits/snowflake-like degeneration gives rise to a significant straylight increase, and should always be considered as a potential hindrance to patient's vision even if visual acuity remains unaffected. The reason for the observed differences in the incidence rate of postop complications between different IOL materials must be studied.

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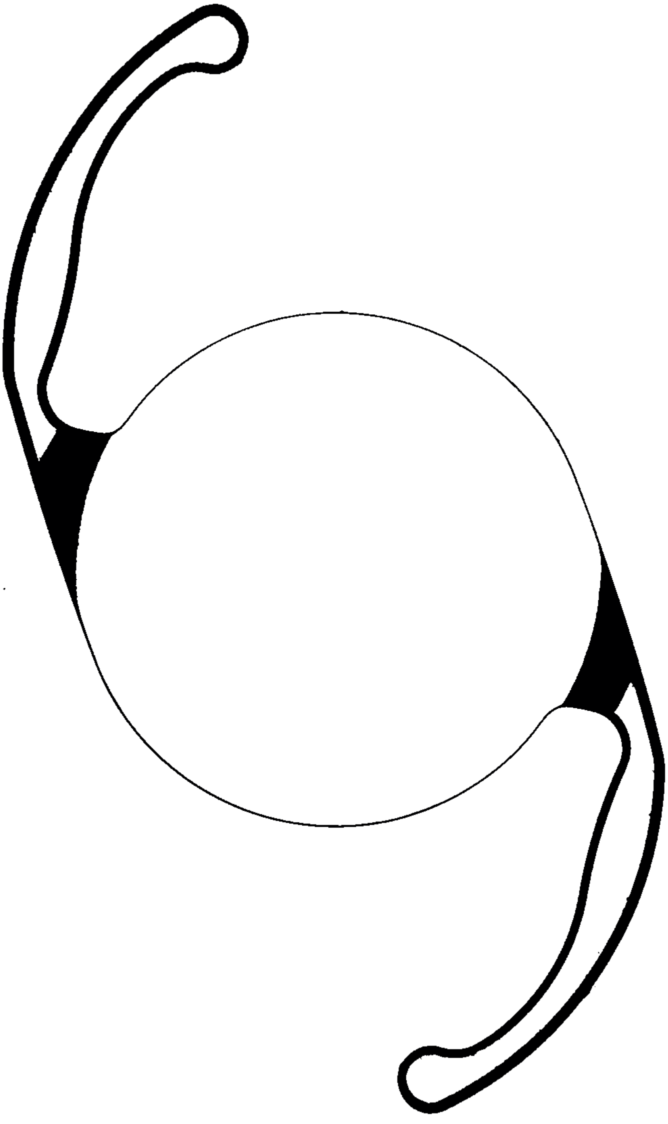

Chapter 8

Ocular straylight with different multifocal contact lenses

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Optom Vis Sci. 94.4 (2017):496-504

ABSTRACT

Purpose

Multifocal contact lenses have been growing in popularity as a modality to correct presbyopic eyes, although visual side effects such as disability glare have been reported. The objective of this study was to investigate the effect of multifocal contact lenses on disability glare by means of ocular straylight.

Methods

A prospective randomized, comparative study was performed that included 16 subjects free of ocular pathology. Straylight was measured using a commercial straylight meter with the natural and dilated pupil. Participants were fitted with Proclear Multifocal (Distance/Near), ACUVUE Oasys for Presbyopia, and Air Optix Aqua Multifocal randomized to the left or right eye. Straylight measurements were repeated with the contact lens in situ after the pupil dilation. Results obtained with the dilated pupil without contact lens acted as a control.

Results

Diameter of the natural and dilated pupil was 2.87 ± 0.40 mm and 7.45 ± 0.86 mm, respectively ($P < .001$). After pupil dilation, straylight increased from 0.92 ± 0.13 log(s) to 1.04 ± 0.11 log(s) ($P < .001$). Of the four studied lenses, a significant difference was only found between Air Optix and the control group ($P = .006$). The latter showed also slightly increased light scatter.

Conclusions

A difference in measured straylight was found between the studied multifocal lenses. The observed variability and the straylight-pupil size dependency should be taken into account to avoid elevated straylight in multifocal contact lens wearers. The reason for the observed differences in straylight must be the subject of future studies.

INTRODUCTION

According to the World Population Ageing 1950-2050 report,[1] issued by the United Nations, the ongoing process of population aging is a well-recognized global phenomenon. If the current trend continues, the percentage of older persons in the developed countries will exceed the proportion of young people by 2050.[1] This demographic shift has an important effect on the prevalence of age-related changes in the eye and will cause increasing demands of patients to maintain good quality of vision. The inability to change the focus of the eye becomes noticeable to the patient at around 45 years.[2] Spectacle lenses are commonly utilized to provide near vision in presbyopia.[3,4] However, for presbyopic patients who wish to have spectacle independence without undergoing a surgical procedure, multifocal contact lenses emerged as an alternative and have grown in popularity when compared to monovision correction.[5] The optical principle of these contact lenses is based on the projection of multiple images with different foci. As a result, a concern arose whether this could be a reason for elevated sensitivity to disability glare, particularly under low-light conditions because of the resulting increase in pupil size.[6]

Straylight is a visual handicap caused by inhomogeneities in the eye's optical media that scatter light in the forward direction.[7] The Commission Internationale de l'Éclairage reported that disability glare is defined as straylight and as the outer part of the functional Point Spread Function.[8] Straylight is quantified by means of its equivalent luminance, where the amount of light scattered over some angular distance toward the retina is compared to the intensity of a comparison light. This gives a functional straylight parameter presented logarithmically as log(s). In comparison to logMAR, an increase of 0.1 log(s) is comparable in visual quality to the loss of 1 line.[9] Straylight and visual acuity (VA) are quite independent aspects of quality of vision. Several studies have reported increased straylight in patients with good VA, but the reverse can also occur.[9-12] However, the importance to quality of vision is comparable.[9] Also quite independent from straylight is contrast sensitivity (CS).[7] This lack of correlation indicates that standard ophthalmic techniques cannot be used to assess ocular straylight. The concept of equivalent luminance has been developed and is now used instead. This has led to extensive studies on straylight and its relation to visual quality.[12]

It has been found that, in absence of ocular pathologies, approximately 10% of light is scattered in the normal eye.[13] The main sources of light scattering in the eye are the crystalline lens, the cornea, fundus reflectance, and light transmittance by sclera and iris.[13] In youth, the straylight value is on average 0.90 log(s), but as the eye ages, this increases 2-fold, to an average of 1.20 log(s), at 65 years of age.[10] Aging of the eye causes straylight increase in the normal eye, but log(s) elevation can be found in several other pathologies as well. Clinical conditions, such as cataract, vitreous turbidity, and corneal dystrophies, may lead to serious straylight-related visual difficulties.[12,14] Moreover, the literature has shown that corneal edema causes a significant increase of straylight, which may be caused by contact lens-related complications.[15] Because contact lenses alter the normal corneal shape and physiology of established users,[16] it is of importance to study how these changes affect the quality of vision in terms of ocular straylight. Increased straylight, which causes disability glare, is a real hindrance when performing everyday tasks and may occur under different light conditions, *e.g.* while driving. The typical problems are being blinded by the headlights of approaching cars and excessive irritation while driving towards a low sun.[12,14] However, other patient's symptoms may occur, such as hazy vision (typically described as looking through a fog), decrease in color discrimination, or elongation of light adaptation.[12,14] Because contact lens wearers are exposed to different light conditions on a daily basis, it is of particular importance to study how administration of a contact lens correction affects their ocular straylight and consequently their quality of vision.

In contrast to optical aberrations, such as defocus and astigmatism, straylight from different parts of the eye is additive and cannot be reduced with artificial optical devices. Thus, the use of the contact lens for refraction or presbyopia correction may increase ocular straylight. This has been studied in the past, though with variable results. In 1987, Applegate and Wolf[17] compared straylight of hydrogel contact lenses using eyeglasses as control. A significant difference in favor of the spectacles correction was found when a lower straylight value was observed in this group. However, this finding could not be verified.[18] Elliott et al.[19] evaluated hydrophilic and rigid gas permeable (RGP) contact lenses. In this study, no effect was observed for hydrophilic contact lens wearers. The RGP group performed worse, which resulted in a higher straylight value. When the lens was removed, straylight returned to a normal level. It was concluded that optical properties might be a factor affecting ocular straylight.[19] In contrast, a later study by Lohmann et al.[20] suggested that less straylight was associated with hard contact lenses as compared to soft ones used for correction of myopia. Nio et al. made a comparison of various modalities for myopia as well.[21] They found that spectacle correction and laser eye surgery outperform soft and RGP lenses when ocular straylight is concerned. However, differences were also found between the contact lens groups, as more (0.07 log(s)) straylight was observed in the RGP group than among soft contact lens wearers.[21]

One potential explanation for these variations between studies may be the differences in lens characteristics; another explanation could be the methodology used for straylight assessment. The Direct Comparison method, which was applied in these studies, has been considered reliable and discriminative,[22] but its accuracy varied when used clinically.[12] The new Compensation Comparison (CC) methodology, applied in a commercially available straylight meter (C-Quant; Oculus), provided a step forward by giving control over the reliability of the measurements.[12,23] This was improved by adding quality parameters to eliminate erroneous results. The appearance of the CC technique has led to a large number of clinical studies on straylight with documented reliability. With respect to contact lens studies, Cerviño et al.[24] employed the new instrument to investigate sensitivity to glare of subjects after fitting them with tinted and standard contact lenses. These lenses were made of the same material, and the only difference was the presence of an amber/gray-green tint in one group. A statistically significant straylight increase was reported with respect to the grey-green correction. In a previous study, no difference was found in straylight measured with/without monovision soft contact lenses.[25] Only established contact lens wearers were enrolled in that study and measured with their habitual correction. In addition, RGP contact lens users were investigated.[25] The findings of that study were in line with Fortuin et al.,[26] as straylight decreased after RGP lenses removal, albeit without reaching the level of the age-matched control group. It was suggested that corneal integrity could be affected by subclinical changes caused by long-time use of the RGP lenses because the straylight value remained elevated even after 24 hours of discontinuation of contact lenses.[25] Therefore, to avoid a potential confounding effect of the post-RGP contact lens use complication, the RGP contact lens wearers were excluded from the current study.

Several studies have been done to obtain straylight values of monofocal contact lenses,[17-21,24-26] but to the best of our knowledge, no report has been published to date on the relation between multifocal contact lenses and straylight. Although multifocal contact lenses have shown to give good VA and CS,[27] unwanted visual phenomena such as glare, which may result in patient dissatisfaction, have been reported.[28] The visual handicaps that subjects may experience raises the important question in how far the use of multifocal contact lenses may be a tradeoff between a near vision problem and a straylight problem. Taking this into consideration, discontinuity between different zones of a multifocal contact lens may scatter light beyond 1°.[7] Also, multiple abrupt changes in a power profile may contribute significantly to light scattering[29] because each transition might act as an independent source of straylight.

In the current study, straylight of four different present-day multifocal contact lenses were compared. Multifocal contact lens wearers most often complain about their night vision, and this can be related to scotopic pupil size. For this reason, the evaluation was performed after pupil dilation.

METHODS

Participants

Sixteen subjects (11 males and 5 females) were enrolled in this study. Their mean age ± SD (range) was 31 ± 8 (21-48) years. The mean spherical equivalent was¡1.53 ± 3.71D, with cylinder power ranging from -0.75 to +3.50D and best-corrected monocular VA of the studied eyes was 20/20 or better. Participants were mostly recruited among students and employees of the Optometry School of the University of Murcia. Only subjects without any ocular pathology, systematic disease, or history of eye surgery were included. There was no limitation regarding age, refractive error, or race of the participants. RGP contact lens wearers were excluded because of the potential confounding effect of subclinical corneal changes to straylight.[25] The habitual soft contact lens users were asked to abstain from contact lens use for 1 day before participation in the study.

The study was designed according to the tenets of the Declaration of Helsinki and was approved by the independent Ethics Committee of the University of Murcia. A written informed consent was obtained from each participant after thorough explanation of the purpose and nature of the study.

Contact Lenses

The study included four multifocal contact lenses that are currently available on the market. The distance (+0.25D) and addition power (2.50D) were equal among all lenses. This allowed exclusion of potential confounding factors related to lens geometry. For more details about technical parameters of each contact lens, please refer to **Table 1**.

Proclear Multifocal contact lens (Cooper Vision, Fairport, NY) is offered in two different optical designs, with the center dedicated to near (N) or distance (D) vision. The center and the surrounding area have spherical and aspherical designs, respectively, with a progressive power profile. The ACUVUE Oasys contact lens for Presbyopia (Vistakon, Division of Johnson & Johnson Vision Care, Jacksonville, FL) consists of five alternating distance and near rings with an aspheric progressive profile. The center of the lens is set for distance vision. AirOptix Aqua Multifocal (Alcon Laboratories, Fort Worth, USA) is a near-center contact lens with a surrounding intermediate zone and with the distance power situated at the outer part of the lens. This lens has an aspheric back surface design.

All included lenses were stored under the same conditions. The Ever Clean (Avizor S.A., Spain) solution was used to clean and sterilize the contact lenses.

Table 1. Descriptive characteristic of the included multifocal contact lenses.

CL Model	Material	CW [%]	BC [mm]	DA [mm]	RI	CT [mm]	Tint	Center	No. Rings
Proclear Multifocal	omafilcon A	62	8.7	14.4	1.39	0.16	Lightly blue	Near	2
Proclear Multifocal	omafilcon A	62	8.7	14.4	1.39	0.16	Lightly blue	Distance	2
ACUVUE OASYS for Presbyopia	senofilcon A	38	8.4	14.3	1.42	0.07	Lightly blue	Distance	5
AIR OPTIX Aqua Multifocal	lotrafilcon B	33	8.6	14.2	1.42	0.08	Blue	Near	3

CW, content of water; BC, base curvature; DA, total diameter; RI, refractive index; CT, center thickens (at -3.00 D)

Straylight Measurements

The evaluation of ocular straylight was performed using a commercial straylight meter (C-Quant; Oculus). The measurement principle is based on the psychophysical CC method,[23] which works as follows. A subject fixates on a central test field, which is surrounded by a flickering straylight source (alternating on- and off-phase, **Figure 1**). As a small part of the light entering the eye is scattered and falls onto the fovea, the subject perceives a faint flickering at the test field if the test field is dark. The test field is subdivided into two halves (left and right, **Figure 1**). One, randomly chosen, half is dark, and in the other half a counter-phase light is given, compensating straylight. The first half shows unmodified ocular straylight of the subject. While the subject fixates on the central field, short-lasting flickering stimuli (alternating on- and off-phase, **Figure 1**) are presented throughout the test. At each stimulus, the subject must decide which half (left or right, **Figure 1**) flickers stronger by pressing a button. Based on the subject's responses and the known value of the compensation light, a psychometric curve is plotted and used to determine the individual straylight parameter.[23] To estimate reliability of results, the instrument gives ''expected standard deviation'' (ESD). ESD is calculated based on a maximum likelihood fit of the psychometric function as the average width of the likelihood function.[30] As ESD closely corresponds to the actual accuracy of an individual value, it is used as a criterion of reliability.[30] Only results with ESD of 0.12 log units or less were accepted and included in the data analysis.[30] Independent studies have shown good reliability and repeatability of the C-Quant instrument.[31,32]

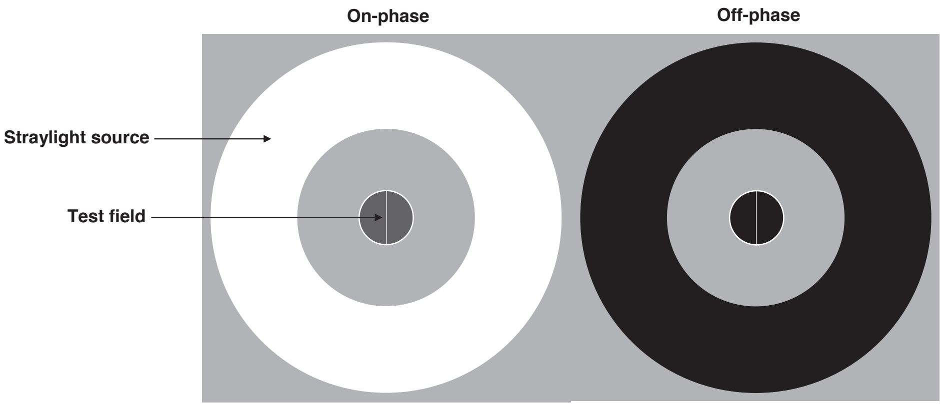

Figure 1. Test screen of the C-Quant. Please refer to the Methods section for more details.

Study Protocol

All participants underwent a complete ocular examination performed by an experienced optometrist. The flowchart of the data collection process is presented in **Figure 2**. An initial examination included refraction, best-corrected monocular visual acuity (VA) on a

Snellen chart, evaluation of the anterior segment of the eye with a slit-lamp biomicroscope, and straylight measurements (two times for each eye) using the C-Quant device. The eyes were photographed using a standard CCD camera attached to the slit-lamp unit. After preliminary evaluation including a first set of straylight measurements, subjects received two drops of tropicamide agent (1%; Alcon Cusi, Spain) to both eyes with an interval of 10 minutes. Thirty minutes after administration of the second drop, the straylight measurements were again performed. If necessary, refractive error was corrected using trial lenses inserted into the C-Quant ocular. The same correction was applied for the contact lens evaluation, as all studied contact lenses hold the same distance power of +0.25D and did not differ between subjects. Because even a single fingerprint on a spectacle lens might cause straylight increase,[33] trial lenses were thoroughly cleaned to exclude this potential effect. Pupil size was measured before and after pupil dilation based on analysis of the recorded photographs. Slit-lamp photographs of the studied lenses, with the reverse illumination, were taken as well. For this purpose, the contact lenses were placed into a wet cell and immersed in saline solution.

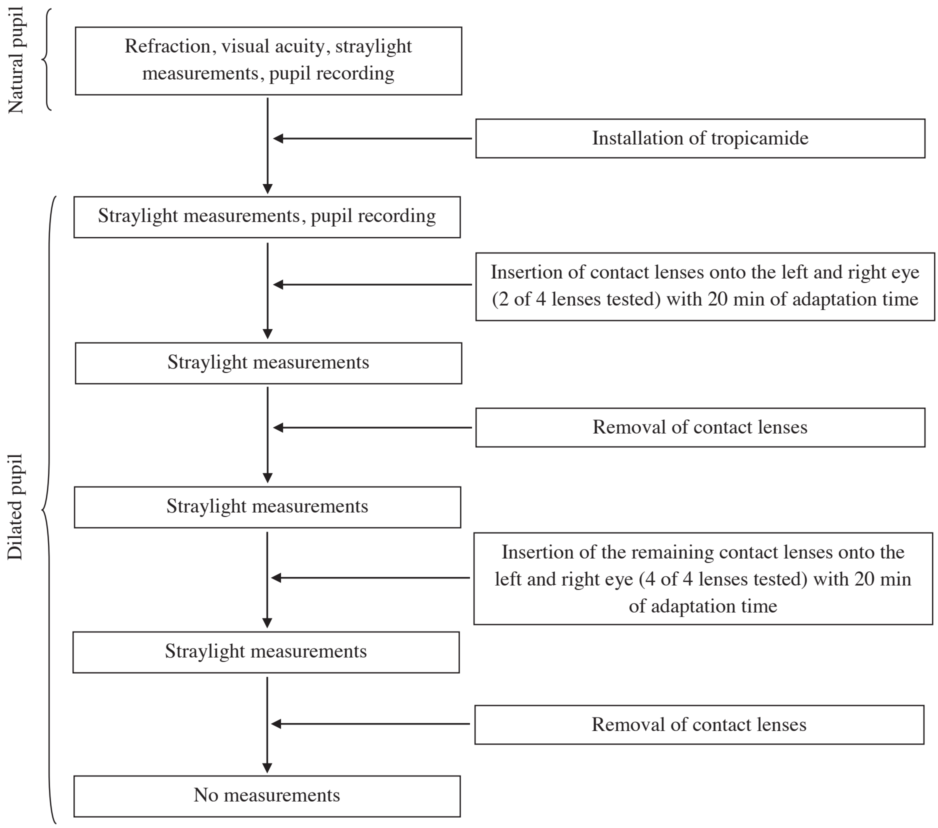

Figure 2. Flowchart of data collection.

Subjects were fitted with four different multifocal contact lenses, and each eye was evaluated with two randomly chosen lenses; therefore, the trial was divided into two parts. In the first part, two lenses were applied and tested monocularly, *i.e.* the left and right eye were always evaluated with different contact lenses present. The quality of a contact lens fit was assessed with the slit-lamp biomicroscope after the 20-minute adaptation time. The straylight measurements were performed with and without contact lenses. In the second part, the remaining two contact lenses were examined following the same protocol. Allocation was randomized by assignment of a random number generated by a computer to an individual contact lens. Subjects were not aware of the type of contact lens being tested. Both eyes of each subject were included in this comparative study because straylight values have been found to differ between fellow eyes by not much more than can be expected on the basis of the repeated measures standard deviation of 0.072 log(s).[34] The straylight values during multifocal contact lens wear were compared to those of a naked eye as controls. Earlier study has shown that soft contact lens wear (monofocal) does not affect straylight.[25]

Data Analysis

Straylight obtained with the natural and dilated pupil was compared. Because of the potential influence of pupil size on ocular straylight,[35] values measured after administration of tropicamide were considered to be a control. To exclude differences in preexisting straylight levels of the enrolled subjects, and (potentially) between the left and right eye, an analysis of residuals was performed. The residuals are defined as straylight of the eye with a contact lens minus straylight of the control value. The negative and positive sign of residuals refers to a decrease and increase of straylight, respectively, after a contact lens insertion.

Descriptive statistics were determined by calculation of mean, standard deviation (SD), and repeated measures standard deviation (RMSD) as based on the repetition of each measurement. Normality was assessed by the Shapiro-Wilk test and visual inspection of Q-Q plots. The paired double-side t-test was applied for statistical comparison of data. One-way analysis of variance ANOVA was used to evaluate significance of differences between groups, including the multifocal contact lenses and the control group. Tukey's HSD multiple comparison was performed as a post hoc test. Differences were deemed statistically significant if a p value was less than 0.05. Data were analyzed with the statistical packages STATISTICA 10 (StatSoft Inc., 2011) and Excel 2013 (Microsoft Corp.).

RESULTS

No significant difference was found between VA of the left and right eye (P = .94). The mean pupil diameter before and after dilation was 2.87 ± 0.40 mm and 7.45 ± 0.86 mm, respectively (P < .001). The mean straylight before administration of tropicamide was 0.92 ± 0.13 log(s). In mydriasis, the straylight value increased to 1.04 ± 0.11 log(s), and this difference was found to be statistically significant (P < .001). There was no significant difference between straylight of the left and right eye before (0.93 ± 0.14 log(s) vs. 0.91 ± 0.11 log(s), P = .58) and after (1.04 ± 0.11 log(s) vs. 1.04 ± 0.10 log(s), P = .85) pupil dilation. The mean log(s) results of the left and right eye before and after pupil dilation are presented in **Figure 3**.

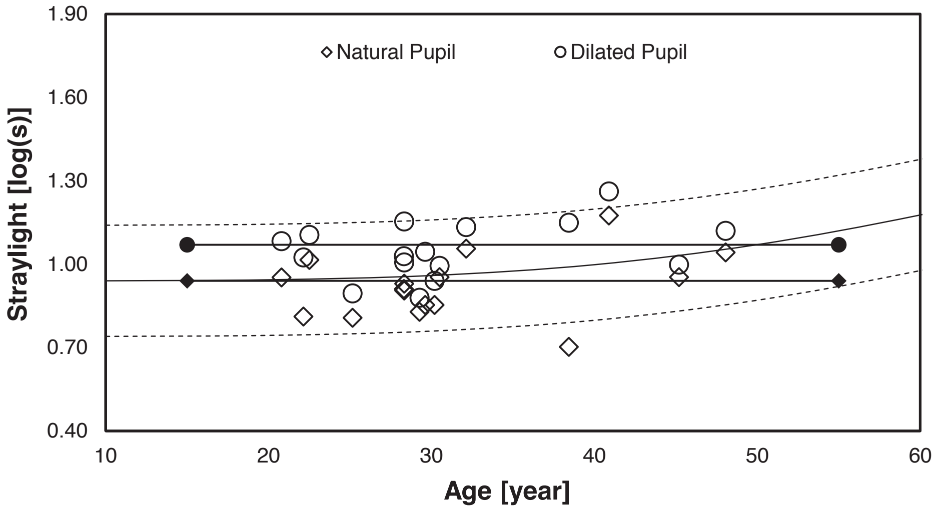

Figure 3. Individual straylight values before (diamonds) and after (circles) pupil dilation as a function of age. The lines with filled diamonds and round markers at their ends indicate the mean straylight level of the eye with the natural and dilated pupil respectively. The results were averaged over the left and right eye. Note that each data point for the natural pupil was based on 4 measurements (2 per eye; overall RMSD = 0.05 log); for the dilated pupil it was 8 measurements (4 per eye; overall RMSD = 0.06 log) as straylight before (2 per eye) and after (2 per eye) application of the first contact lenses was included. The black solid line gives the normal straylight function for phakic eyes with the 95% confidence interval (dashed lines).

The straylight level measured after removal of the first contact lens fitted was 1.06 ± 0.11 log(s). This difference did not reach the significance level (P = .13) when compared to straylight of the eyes before the first application. Therefore, these results (four measurements for each eye) were averaged and used as control.

One-way ANOVA indicated that a significant difference exists between the studied groups (P = .02). Tukey's HSD post hoc test showed that only the Air Optix straylight results differ significantly from the control (P = .006).

The calculation of residuals after the application of Oasys, Air Optix, Proclear (D), and Proclear (N) resulted on average in higher straylight by 0.02 ± 0.04 log(s), 0.11 ± 0.07 log(s), 0.05 ± 0.08 log(s), and 0.03 ± 0.07 log(s), respectively (**Figure 4**). One-way ANOVA showed a significant difference between residuals of the included multifocal lenses (P < .001). The post hoc analysis revealed statistically significant differences for the comparison of Air Optix with Oasys (P = .001) and Proclear (N) (P = .003). The remaining comparisons did not reach the significance level. The individual residuals are presented in **Figure 5** showing a larger number of the Air Optix results in the upper part of the graph (*i.e.* more straylight).

The slit-lamp images obtained with reverse illumination (**Figure 6**) show an increased intensity of scatter light from the Air Optix bulk (**Figure 6B**), dissimilar to that of the other studied contact lenses (please disregard the bright spots caused by dust particles). None of the analyzed multifocal designs showed increased scattering from the transition zones.

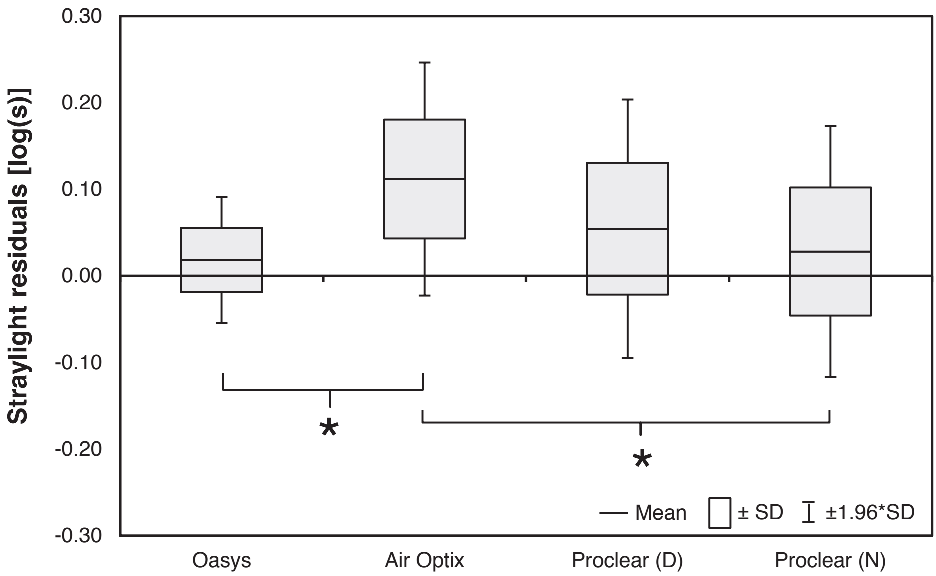

Figure 4. Straylight difference (residuals) following contact lens application. The straylight residuals are defined as a subtraction of straylight of the eye with a contact lens present and the control (base) value. Note positive residuals indicate straylight increase following the lens fitting. *, statistically significant.

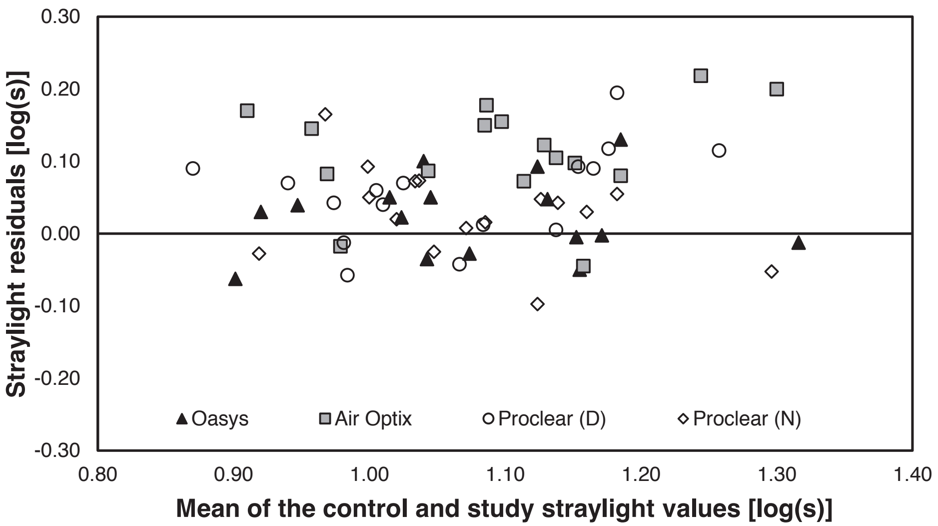

Figure 5. Bland-Altman plot of straylight residuals as a function of the mean straylight values. The residuals are defined as a subtraction of straylight of the eye with a contact lens present and the control (base) value. Note positive residuals indicate straylight increase following the lens fitting.

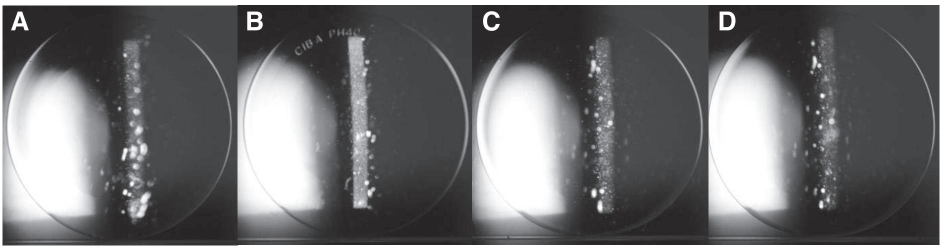

Figure 6. Slit-lamp photographs of the contact lenses used with reverse illumination. A, Oasys; B, Air Optix; C, Proclear (D); D, Proclear (N). AirOptix (B) shows a fine-grainy intensity pattern of the scattered light that cannot be found in the other studied lenses. Note uniform scattering from the AirOptix bulk irrespective of the different refractive zones.

DISCUSSION

As mentioned in the introduction, multifocal contact lenses are particularly prone to glare problems, but straylight has not yet been reported. To address this issue, four different types of present-day multifocal contact lenses were compared in the current study. The results varied significantly across the studied groups (P = .02), but the subsequent post hoc analysis revealed that, except for Air Optix (P = .006), straylight of the studied contact lenses did not differ significantly from the control. Oasys showed the lowest level of straylight increase by 0.02 log(s) whereas Air Optix caused the highest, 0.11 log(s) elevation. This difference was also found to be statistically significant (P = .001).

In this study, the lowest straylight was found in the multifocal with the highest number of optical zones. According to the manufacturer, this multiple-zones configuration cuts down visual side effects that are typically encountered by simultaneous-vision contact lens wearers, but no further explanation is given. Although complete information on optical designs of contact lenses is not available because of commercial confidentiality, some papers emerged that studied this issue, particularly in terms of power profiles. Various multifocal lenses were analyzed in the past and revealed considerable differences in their power profiles.[36,37] Interestingly, an analysis of AirOptix high addition showed a very smooth progression of optical power throughout the lens.[36,37] The power profile of Oasys with the same addition resulted in several abrupt changes,[36,37] and this could be considered as a potential source of light scattering.[29] However, the results of the current study rather contradict this hypothesis, as the lowest straylight was found in the Oasys group. The slit-lamp images did not reveal increased light scattering at the transition zones either. The optical power distributions themselves are unlikely reasons for the differences found because straylight and refractive errors affect separated aspects of visual performance.[7] The very close results of Proclear (N) and Oasys seem to confirm the validity of this assertion. Therefore, differences in optical design of the studied multifocals do not have an important effect on straylight. Moreover, the results of Oasys indicate that, despite its multifocal properties, straylight remains close to the level of the naked eye. Although the center thickness (at -3.00D) of the Proclear (D/N) lenses is twice as high as of Air Optix, straylight was lower in the Proclear group. This points to material characteristics as the suspect for increased straylight in Air Optix. Examination of the studied lenses with the reverse slit illumination (**Figure 6**) may also support this suggestion, as clearly there is some rather uniform light scattering taking place from the Air Optix bulk (**Figure 6B**). Thus, material properties may have important implications, and one would expect this to hold not only for multifocal but for soft contact lenses in general. However, Van der Meulen at al.[25] found no significant straylight effects for monofocal soft contact lenses. This seeming discrepancy might be caused by a difference in analyzed materials, as a random selection of various contact lenses was included in the Van der Meulen study.[25]

With respect to material properties, the literature has shown only small differences in surface roughness between analyzed contact lens materials. A microscopic examination of omafilcon A, senofilcon A, and lotrafilcon revealed average roughness values (mean ± SD) of 1.90 ± 0.39 nm,[38] 3.34 ± 0.28 nm,[38] and 4.50 ± 2.3 nm,[39] respectively. These values are much smaller than wavelength; hence, the potential effect of surface roughness on functional light scattering can rather be ruled out. It is also of interest to note that hydrophobicity has been suggested to affect ocular straylight when monofocal intraocular lenses are used.[40] However, the similarity between Oasys and Proclear (D/N) rather contradicts this for the case of contact lenses. In the current study, all investigated lenses were blue-tinted, and a possible confounder of contact lens tint[24] thus seems to be a nonfactor as well. However, the proposed potential relation of differences in material properties and straylight remains to be studied. Besides clinical studies, *in vitro* measurements with an optical bench set-up might be desirable to address these problems.

Only a small effect of pupil size on straylight has been found in the normal eye.[35] If light scattering is more or less uniform over the entire pupil, the proportion between the wanted and unwanted (scattered) light remains the same, regardless of pupil size. Hence, the straylight parameter is expected to remain at the same level as well. Franssen et al.[35] proposed a detailed model of straylight dependency on pupil size as the authors realized that not only light scattering in pupil opening contributes to straylight but also eye wall translucency. This second effect becomes more important for small pupils, especially below 2 mm. For large pupils, a small linear increase with pupil size was found.[35] In the present study, the mean pupil diameter changed from 2.87 to 7.45 mm resulting in 0.12 log(s) straylight elevation. According to the linear model, a 0.025 log(s) increase per 1 mm of pupil diameter may be expected,[35] hence, the difference of 4.58 mm in pupil diameter leads to the 0.11 log(s) theoretical straylight increase, which is very close to what the linear model predicts. In clinical practice, this finding can also be used as a reminder that patients with dilated pupils after, *e.g.*, eye examinations should avoid driving as their sensitivity to glare will be significantly increased.

LIMITATIONS

Inclusion of young subjects in the current study might be considered as a limitation despite the use of the cycloplegic agent as a presbyopia simulation because a multifocal correction is predominantly prescribed at an age that is older than the majority of the subjects enrolled in this study. The residual analysis, however, accounted for the straylight-age difference and other intersubject variabilities.

On the one hand, a refractive error correction using an ophthalmic lens instead of a dedicated contact lens correction might be seen as a deviation from the real-world situation. On the other hand, this approach enabled the researchers to maintain similarity among geometrical parameters of the studied lenses and, therefore, to exclude other potential confounders. One of the geometrical parameters associated with refractive power is lens thickness. **Table 1** presents the center thickness for the -3.00D lens, but one may wonder how this changes with increasing power.

Mydriasis was used to mimic night vision, so as to maximize potential effects of the multifocal designs on ocular straylight. Because it was shown that the bulk scattering (which is irrespective of pupil size) rather predominates over scattering from the optical (multifocal) design, the presented results could also be considered as a good approximation for straylight under daylight conditions.

In conclusion, we studied and compared ocular straylight of four multifocal contact lenses. Most of the studied multifocal designs showed a rather weak scattering effect. Thus, the observed increased straylight of Air Optix is more likely to be related to its material than to the optical design. More research is needed to determine the importance of material properties to ocular straylight. The results of this study could advise which type of multifocal contact lens might be more beneficial for a specific group of people, *e.g.* professional drivers, when straylight is taken into account.

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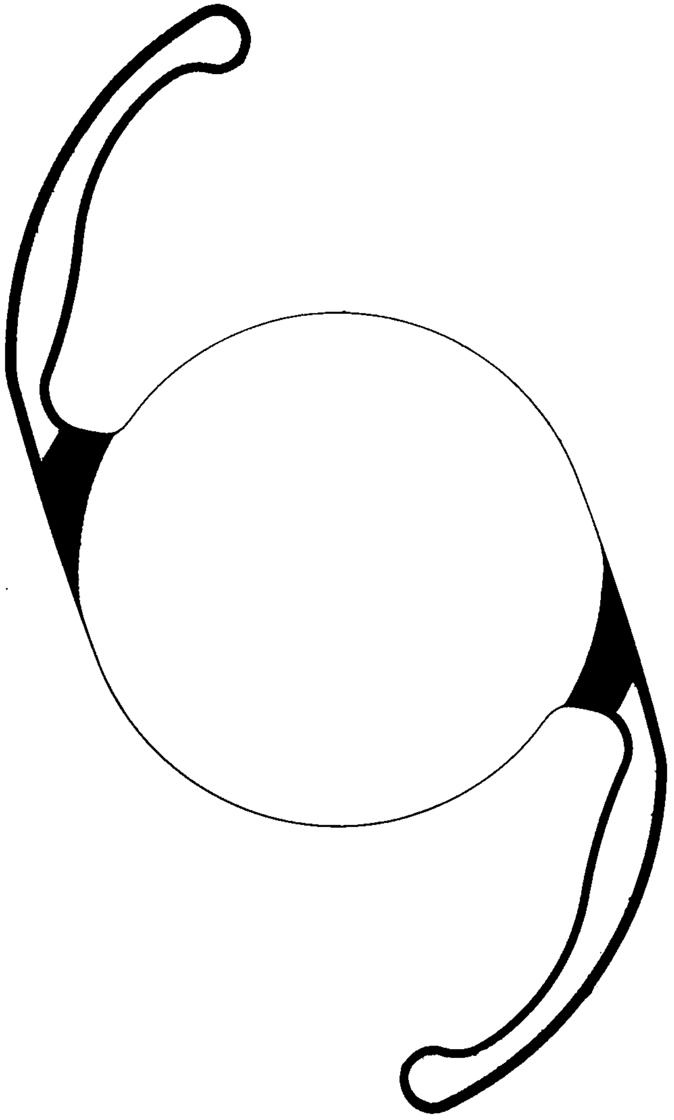

Chapter 9

Method for *in vitro* assessment of straylight from intraocular lenses

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ABSTRACT

Ocular straylight has been measured by means of psychophysical methods over the years. This approach gives a functional parameter yielding a straight comparison with optically defined light scattering, and the point spread function. This is of particular importance when the effect of intraocular lenses (IOLs) on postoperative straylight is sought. An optical system for straylight measurements of IOLs was adapted to a commercial device (C-Quant, Oculus), which employs such psychophysical method. The proposed modifications were validated using light-scattering filters and some sample IOLs. The measurements were performed by 3 observers to prove that results are independent from straylight of the eye. Other applications will be discussed.

INTRODUCTION

Intraocular straylight refers to the effect that light scattered (forward direction) by the ocular media is projected on the retina and decreases contrast of the in-focus image. According the CIE (Commission Internationale d'Éclairage) must disability glare be quantified by means of straylight, as (the outer) part of the Point Spread Function (PSF).[1] The PSF is defined as the fraction of light scattered per steradian. This is a 2-dimensional function, but the PSF is by approximation radially symmetric, certainly for larger radial angle θ in most eyes. For that reason the CIE standard is given as function of radial angle only, as PSF(θ).[2] The straylight parameter is defined as:

$$s = \theta^2 \times PSF(\theta)\ [deg^2/sr], \qquad (1)$$

with θ the visual angle in degrees, and is as a rule presented logarithmically as log(s). Straylight of the eye can be assessed by measuring the eye's PSF at the respective angular distance of a light source. By using an annular light source the radial average value of the PSF can be obtained. This approach has been applied in many studies on ocular straylight that involved various techniques,[3] however, recently a commercial apparatus (C-Quant, Oculus) has become a standard used in laboratory and clinical practice.[3] This instrument delivers the straylight parameter based on the psychophysical compensation comparison method and provides repeatable and reliable straylight values.[4, 5]

The C-Quant has also been used to measure straylight from optical materials like light-scattering filters[6] or corneal implants[7] without interference from scattering of the eye. This application can be understood as follows. In the C-Quant a flickering ring serves as source of straylight. It induces straylight at the fixation point in the middle of the ring. This flickering straylight is compared to a comparison field. Now suppose that we place in front of the eye a piece of light scattering material, and block at the same time the flickering light from entering the eye. Then the eye will only see the straylight originating from the piece of material and not its own straylight. This method was checked against optically measured values and found to reproduce the optical values precisely.[6]

Straylight values whether assessed inside or outside the eye can be considered by good approximation the same. Straylight from an eye can be addressed as the addition of the straylight from different scattering layers, for instance, a layer placed at the cornea. If one considers scattering sources deeper in the eye (limited to the anterior segment), only the effective angle of the incident light changes. This is however of little consequence if straylight is assessed by means of the straylight parameter, since the straylight parameter is by good approximation invariant with angle.[8, 9] Therefore, the C-Quant can be used to measure straylight originating from other structures, such as an intraocular lens (IOL). Nevertheless, it is important to point out that the assumption of invariant angle is limited to relatively small errors in the angular distance, but this will be discussed later in the manuscript.

In the normal young eye the straylight parameter is at a level of 0.9 log(s).[10] As the eye ages intraocular straylight increases, and at 65 years a 2-fold increase can be expected and a 3-fold increase at the age of 77.[10] But an elevated straylight level is also associated with many ophthalmological conditions such as: corneal dystrophies, vitreous turbidity, cataract, posterior capsule opacification and IOL opacity.[3] These pathologies lead to decreased visual quality and functional difficulties like hazy vision, disability glare, halos around light sources and loss of color vision.[11, 12]

In most cases cataract removal and IOL implantation succeeds in lowering intraocular straylight, albeit that up to 15% of cataract patients experience increase or no-improvement in straylight after the surgery.[13] It is speculated that the observed increase might be related to implanted IOLs depending on their materials, optical designs and manufacturing processes.

Straylight of IOLs has been studied solely on an optical bench set-up.[14, 15] The use of the C-Quant in straylight evaluation of IOLs can make these measurements more accessible for researchers. This method gives a straylight value that can directly be compared with the clinical measurements. This can *e.g.* be used when the effect of explanted IOLs on ocular straylight is sought.[16, 17]

The purpose of this study was to develop a method to measure straylight of IOLs objectively using the C-Quant and deliver the functional straylight parameter that can be applied in clinical practice.

METHODS

Psychophysical measurements

The C-Quant straylight meter evaluates ocular straylight by means of the psychophysical compensation comparison method. The basics of this methodology have been thoroughly studied. [18, 19] In short, an annular straylight source (from 5° to 10° radius) is presented flickering at different intensities in black and white. A central test field with diameter of 3.3° is presented, subdivided in 2 halves one of which flickers in counter-phase with different modulation depths. No flicker is presented in the other half, and as consequence only light scattered from the straylight source is seen in that half. The opposite part comprises scattered light, and additionally, the counter-phase compensation light. The patient fixates the central field and indicates which of the observed halves flickers stronger using two buttons. The ratio between the intensities of the compensation light and the annulus is varied during evaluation. At a certain moment, both halves appear to be equal and the subject must guess which one flickers stronger. Therefore, this approach is called a two alternative forced choice method. It provides a psychometric curve from which the straylight parameter can be determined.

This method can also be used for evaluation of light-scattering objects without interference by the light scattering properties of the eye being used.[6, 7] Because normally only a very small fraction of light is scattered in total, different sources of straylight in the eye and of scattering objects are additive in the standard C-Quant measurements. However, if the object is exposed to the straylight source but the observer sees only the central field by blocking the straylight source for his eye, then an independent straylight parameter can be obtained for the object. In this case, the eye only judges the light scattered by the object against the comparison test field without any contribution to the straylight produced by his/her own eye. This can be achieved by positioning the observer at a certain distance from the C-Quant where the flickering annulus is not perceived, or alternatively, by using an additional field-stop.

Adaptation of the psychophysical system

The C-Quant straylight meter was proven to give the precise value of the straylight parameter by using scattering filters in this manner,[6] but the evaluation of straylight from IOLs requires an adaptation. The main reason for the adaptation is the high refractive power of IOLs as well as the small size of their optical zone, which rarely exceeds 6 mm diameter. In order to estimate the clinical importance of straylight produced by IOLs, the angular relation between the scattering source and the evaluated sample must comply with the condition when straylight of the eye is measured. As it was mentioned before, in order to avoid the influence of straylight of the observer's eye, his/her eye cannot be exposed to the straylight source.

The adaptation was designed using the OpticStudio 15 software (Zemax LLC, Kirkland, WA, USA). The Liou & Brennan eye model[20] was assigned to find at what angle the crystalline lens "sees" the image, produced by L_{CQ}, of the scattering ring (**Figure 1**).

The performed calculation resulted in an angle of 8.8° for the outer rim of the flickering annulus. The resulting C-Quant system adjusted to the IOL measurements is presented in **Figure 2**.

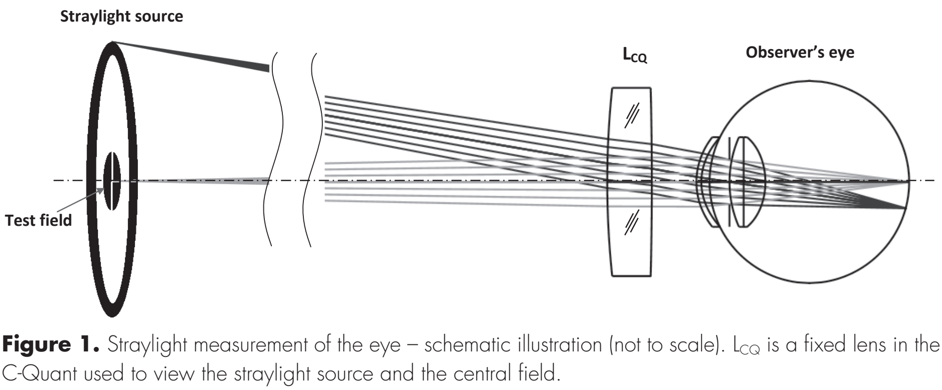

Figure 1. Straylight measurement of the eye – schematic illustration (not to scale). L_{CQ} is a fixed lens in the C-Quant used to view the straylight source and the central field.

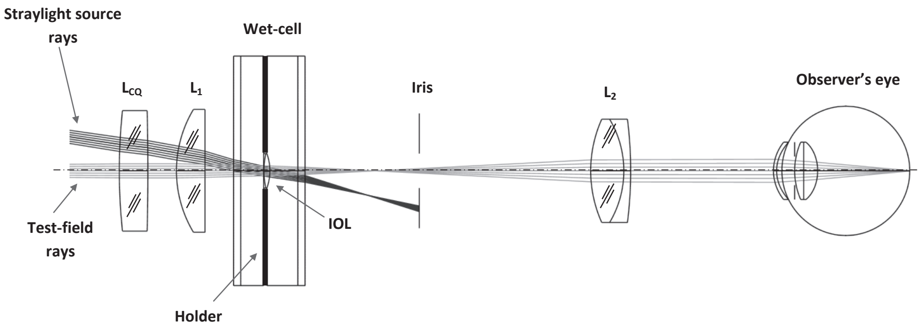

Figure 2. The C-Quant adaptation to measure straylight of IOLs (not to scale). L_1 is placed 5 mm behind the C-Quant lens (L_{CQ}). The front of the wet-cell and the back of L1 are at a distance of 5 mm as well. The holder with an IOL is set at 1 mm to the cuvette's inner-surface. The iris acts as a field-stop intercepting the rays that come from the flickering annulus while the test field can still be seen with help of the magnifying lens L_2.

The adaptation of the C-Quant system included a plano-convex lens (L_1; f'_1= 40 mm, Linos-Qioptiq, Göttingen, Germany), and a wet-cell (6030-UV-10-531, Hellma GmbH & Co. KG, Müllheim, Germany) with a sample IOL. These components allow the light from the flickering ring to arrive at the IOL at 9.3°, a value similar to the 8.8° obtained in the human eye model (**Figure 1**). The system also contained an iris acting as a field-stop and an achromatic lens (L_2; f'_2= 40 mm, Linos-Qioptiq, Göttingen, Germany) to generate an image of the test field at the observer's far point. All components were mounted using standard rods and holders as presented in **Figure 3**.

Figure 3. Adaptation of the C-Quant to evaluate straylight from IOLs.

A sample was prepared as follows; the IOL was gently mounted in a steel-made holder, then the IOL-holder set was submerged in a saline solution of 0.9% that filled the wet-cell. The IOL holder acts as natural pupil with an aperture of 5.5 mm. The wet-cell was inserted in a rectangular opaque component created using a 3D-printer to block any parasitic light reflected by the walls of the cuvette. The iris constraints the light that comes from the straylight source, but the test field still reaches the observer's eye, and this enables to perform straylight measurements of IOLs.

With this system, the straylight value both with and without the IOL could be obtained. In both cases, the test field can be seen in focus by the observer by moving L_2 inward (with IOL) or outward (without IOL) with respect to L_1. Neither of the system's components was removed at any stage of the trial, therefore, the same conditions can be maintained through the complete experiment. Straylight of the IOL was calculated as a linear subtraction of 2 straylight parameters using the following formula:

$$\log(S_{IOL}) = \log(10^{\log(Sset\text{-}up+IOL)} - 10^{\log(Sset\text{-}up)}). \quad (2)$$

The values $\log(S_{set\text{-}up+IOL})$ and $\log(S_{set\text{-}up})$ are provided by the C-Quant and denote straylight with and without IOL respectively.

Measuring a commercial intraocular lens

The monofocal Softec HD (Lenstec, Inc., USA) and Tecnis ZCB00 (Advanced Medical Optics) IOL were used with a power of 22.00 D and 24.00 D respectively. The Softec HD lens is a hydrophilic acrylic, aspheric IOL with 5.75 mm optical size. Tecnis ZCB00 is a hydrophobic acrylic IOL with an aspheric surface and 6mm optical diameter. Moreover, the multifocal Tecnis ZM900 (Advanced Medical Optics) with 10.50 D of distance power and 4.00 D addition was evaluated. Tecnis ZM900 is a hydrophobic silicone, aspheric IOL with a diffractive pattern situated on its posterior surface and 6 mm optical diameter.

Validation of the system

In order to validate the proposed methodology 2 commercially available scattering filters were used: Black Pro Mist (BPM) 1 and 2 (Tiffen, New York, USA). Straylight of both filters have been found to comply with the normal eye and are proposed as validation standard.[6, 21] The filters were evaluated by 3 independent observers along with their own straylight using the unmodified C-Quant. The measured log(s) values of the filters were used to calculate an expected straylight increase after their insertion into the system based on the following formula:

$$\text{Expected straylight} = \log(10^{\log(Sset\text{-}up)} + 10^{\log(SFilter)}) \quad (3)$$

Each filter and the sum of both (3 different conditions) were placed between L_1 and the wet-cell. Three repeated measurements of the log(s)-value were performed for all 3 filter conditions and the C-Quant adaptations without the IOL. The same was done with the IOL present using this formula for the expected straylight value:

$$\text{Expected straylight} = \log(10^{\log(Sset\text{-}up+IOL)} + 10^{\log(SFilter)}) \quad (4)$$

Both for setup alone and set-up+IOL 2 observers completed the experiment.

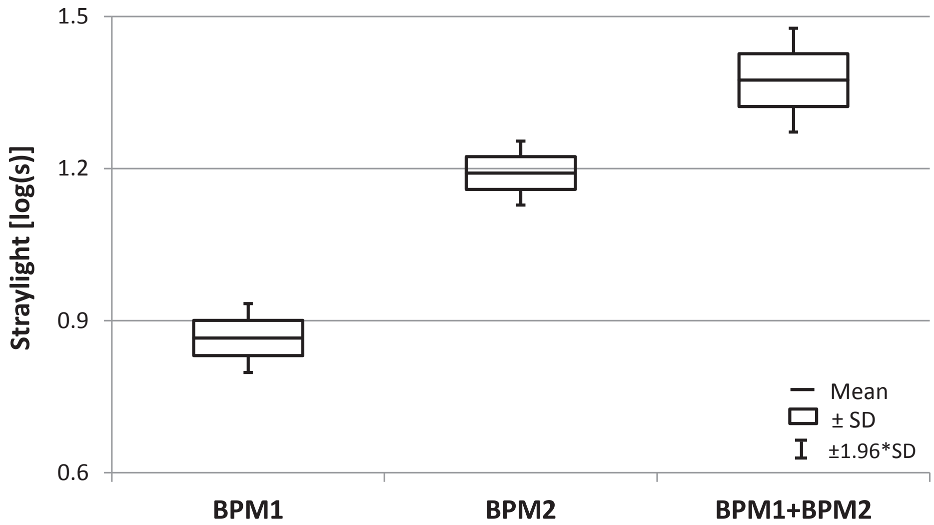

Figure 4 .Straylight of the BPM filters. The left, middle and right box refer to BPM 1, BPM 2 and the combination of the 2 filters respectively. Each box is based on 9 observations (3 observers, 3 times each).

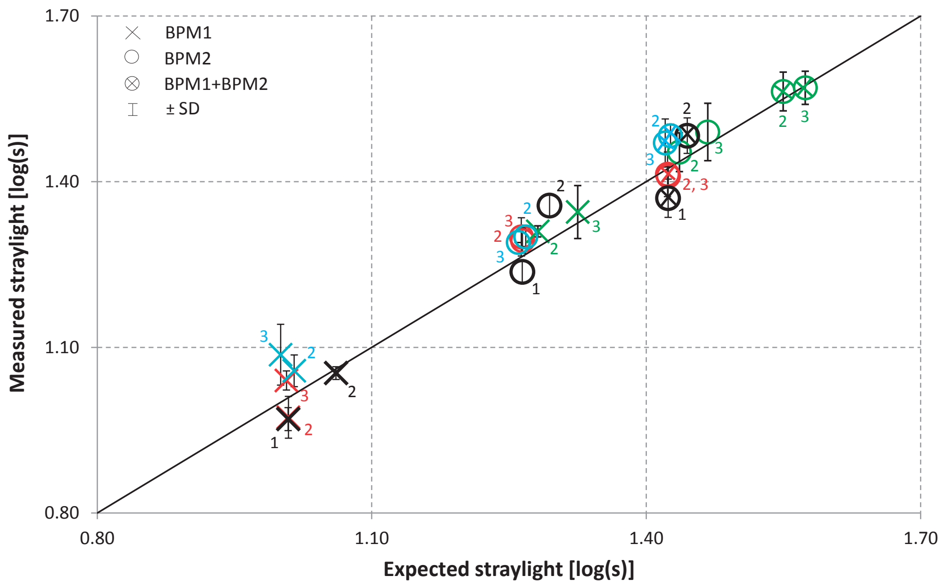

Figure 5. Validation of the set-up using the BPM filters. The results measured by observer 1, 2 and 3 (vertical axis) are plotted against the expected straylight values (horizontal axis). The black markers indicate the values of the set-up with filters, without an IOL. The green, red and blue markers refer to measurements of the complete set-up including the Softec HD, Tecnis ZCB00 and Tecnis ZM900 IOL respectively and the BPM samples. Please note that each condition was tested by two observers, each 3 times. Small differences between observers result from the fact that setup straylight differs each time the cuvette is filled.

RESULTS

The individual straylight values (mean ±standard deviation [SD]) of the 3 observers were 0.91 ±0.02 log(s), 1.07 ±0.02 log(s) and 1.12 ±0.03 log(s). Straylight of the filters BPM1, BPM2 and BPM1+BPM2 was 0.87 ±0.03 log(s), 1.19 ±0.03 log(s) and 1.37 ±0.05 log(s) respectively (**Figure 4**). Please note that linear addition of 0.87 log(s) and 1.19 log(s) yields 1.36 log(s), which is very close to the observed value of 1.37 log(s), underlining the additivity rule mentioned above.

A very good absolute correspondence and high correlation (R^2=0.97) was observed when measured and expected log(s) were compared using the BMP filters and the set-up with and without the IOLs (**Figure 5**).

The mean difference between the expected straylight value and straylight of the set-up without an IOL as well as with the Softec HD, Tecnis ZCB00 and Tecnis ZM900 IOL was -0.01 log(s), 0.02 log(s), 0.01 log(s) and 0.05 log(s) respectively.

The straylight level of the measured IOLs obtained by the 1st and the 2nd observer are presented in **Table 1**.

Table 1. Straylight of the used IOL models.

	Straylight value ±Standard error [log(s)]	
IOL Model	Observer 1	Observer 2
Softec HD	0.67 ±0.04	0.74 ±0.07
Tecnis ZCB00	-0.46 ±0.58	-0.61 ±0.35
Tecnis ZM900	0.38 ±0.07	0.48 ±0.05

DISCUSSION

In the present study, a new methodology to evaluate straylight of IOLs was proposed and tested. The precision of this approach was tested, and a high agreement was found when measurements with standard filters was performed. This technique uses the human eye as an optical detector, capable to establish identity with a good precision. Influence of straylight from other sources could be controlled for. Indeed, the results show that, although the 3 individual straylight values of the observers differ, a close correspondence between the expected and measured results was obtained. This is in line with the study of Van den Berg et al.[6] where 7 light-scattering filters were compared using the C-Quant instrument and 2 other optical methods that involved the use of a CCD camera and photodiode instead of the observer's eye. This study demonstrated that the psychophysical technique is able to provide as accurate results as the optical measurements, since the obtained results were almost identical.

With IOL in the system that scatters light also similar results were obtained when tested with 2 different observers and the 3 filter conditions (**Figure 5**). This indicates that the straylight measurement of IOLs is robust independently from straylight of the eye and the system components. The mean straylight level of the Softec HD IOL was 0.71 log(s), and this might be considered as an increased value if compared to other, non-explanted IOLs studied.[15] The reason of the observed elevation may be that the Softec HD IOL used contained deposits in its material. Since the logarithmic scale was used, the negative straylight values of Tecnis ZCB00 signify that the straylight parameter was less than 1 and that can be considered as functionally unimportant. This is in line with the study of Langeslag[15] where the straylight parameter of the Tecnis ZCB00 IOL was found to be at the tenths level. The evaluation of the multifocal IOL resulted in 0.43 log(s) as mean value. Although, straylight of Tecnis ZM900 has not been measured objectively until now, the found effect is comparable to the previously published data on certain diffractive IOLs.[15]

The C-Quant instrument delivers the straylight parameter of the eye for a fixed visual angle. This might appear as a limitation as one may wonder about the straylight value at smaller or larger angular distances of the glare source. On the other hand, a straylight measurement at the pre-set angle is advantageous when results from different centers are evaluated, or particularly, when the relation between *in vitro* and *in vivo* straylight parameter is sought. This might be beneficial, for instance, when a comparison between scattering of an opacified IOL and the straylight level before its explanation is made.[16, 17] Moreover, there is another reason of using the fixed angle. A series of studies carried out in the 1990s showed that the straylight parameter of the eye is approximately invariant with angle.[8, 9] However, this is applicable only if differences in angle are limited. The relation of log(s) to visual angle has been investigated extensively and proved to follow a parabolic shape with minimum at 7°.[8, 9] An error of 1.5° to either side gives less than 0.03 log of error in log(s). Therefore, while measuring straylight, a small error in observation angle causes only little effect on the straylight value. To perform in-vitro straylight measurements of an IOL in a way comparable with that of an IOL implanted in the eye, an optical set-up was used to simulate the *in vivo* angle of 8.8° at which light falls onto the crystalline lens of the eye model. The experimental angle was 9.3° and that is 0.5° higher than the calculated *in vivo* value. This difference is acceptable taking into account the above arguments. Therefore, the potential effect of an IOL on straylight of the eye after its explanation/implantation can be predicted. Suppose the presently used Softec HD IOL was removed from an eye that suffered a straylight hindrance of 1.50 log(s). If we assume that a new, implanted IOL does not scatter light, then the expected postoperative, *in vivo* log(s) can be calculated as follows: $\log(10^{1.50} - 10^{0.71})$ and that gives 1.43 log(s). A similar prediction can be made when this IOL is implanted in an otherwise clear eye with 0.75 log(s) [9], then an expected postoperative straylight of 1.02 log(s) results.

The methodology of this study can also be applied to measure straylight of other optical elements besides IOLs like contact lenses (CLs). The optical power of CLs might also cause that the unaided observer's eye cannot see correctly the test field when a CL sample is introduced into the system. The presented approach solved this problem using the high-power lens (L_2) that can be moved by the observer, and by this, also correcting his/her refractive error. In contrary, straylight of objects that do not present any optical power such as scattering filters [6] or flattened corneal implants[7] can be measured using the unmodified C-Quant instrument. Since the magnification of the test field is not altered, this eliminates the need for using any special lenses and significantly reduces complexity of the system

In the present study, an adaptation of the C-Quant device for straylight measurements of IOLs was proposed and validated. This methodology used a relatively simple optical set-up that allows to take measurements of the IOL that can be compared to the *in vivo* situation. The methodology is not restricted to IOLs, as it can be employed for assessing straylight of other optical or biological components. The C-Quant delivers a functional parameter which enables a straight comparison between *in vitro* and *in vivo* outcomes, therefore, it can be directly applied in clinical practice and research on light scattering in the human eye.

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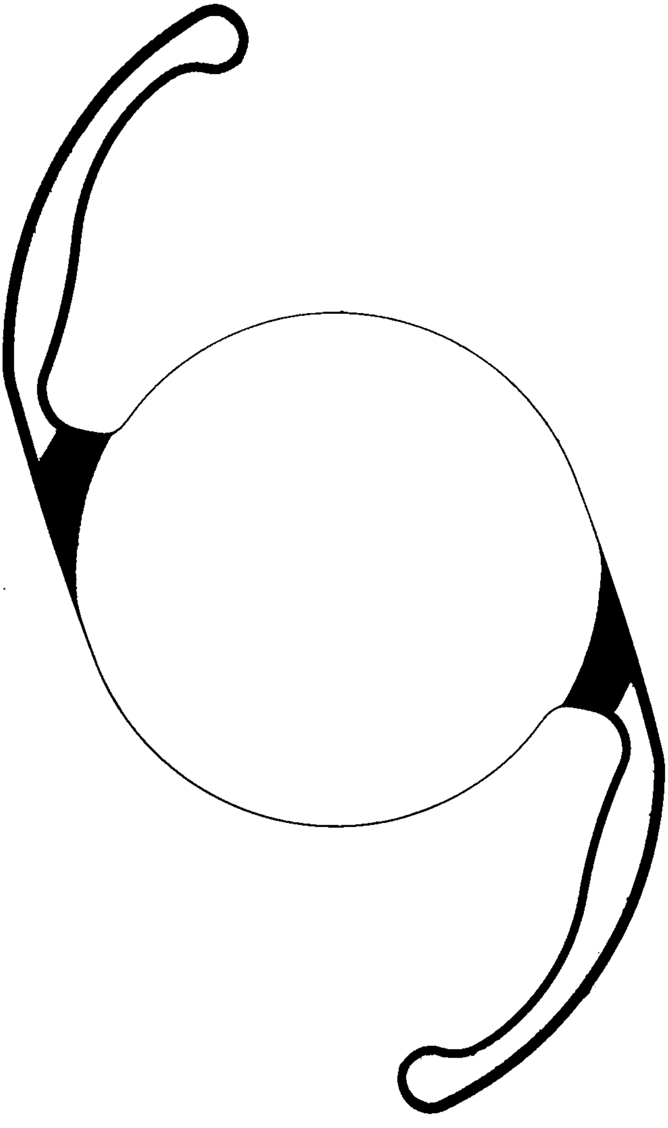

Chapter 10

Validation of a spectral light scattering method to differentiate large from small particles in intraocular lenses

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ABSTRACT

A psychophysical approach has been designed to measure straylight from intraocular lenses (IOLs) *in vitro*. This approach uses a clinical straylight meter (C-Quant) and an observer's eye as optical detector. Based on this, we introduced a method for study of straylight-wavelength dependency for IOLs. This dependency can be used to distinguish between 2 types of scattering particles (small and large) as defined by Mie theory. Validation was performed using a turbidity standard and scattering filters. Several IOLs were analyzed to identify potential scattering sources. Large particles were found to predominate in scattering from the studied lenses. This was confirmed by straylight-angular dependency found in these IOLs.

INTRODUCTION

A survey on explanted intraocular lenses (IOLs) has shown that optical phenomena (*e.g.* glare) is a common reason for IOL exchange.[1] Glare is caused by increased forward light scatter (straylight).[2] In pseudophakic eyes, increased straylight may originate from the implanted IOL as a result of the presence of large and/or small (*e.g.* submicron) particles. Straylight from larger particles (*e.g.* glistenings, surface deposits) has been studied.[3-6] Submicron particles have also been found in IOLs (*i.e.* nanoglistenings), but their potential straylight effects have received little attention,[7, 8] partly because of the difficulty of detecting submicron particles, and also because clinicians have limited access to objective straylight measurements.

Nanoglistenings cannot be resolved under a slit lamp or with light microscopy, so Scheimpflug imaging has been used for their assessment.[7] This approach measures backward scatter, although forward scatter (straylight) is the important type, as it falls onto the retina and causes glare symptoms.[9] A clinical device (C-Quant, Oculus Optikgeräte GmbH) has been introduced to measure *in vivo* forward scatter of the eye based on a psychophysical approach.[10] This device has also shown potential for *in vitro* evaluation of light scattering by IOLs.[11] If the C-Quant could be adapted for assessment of straylight-wavelength dependence, this could also be used to assess particle size, as important for functional (forward) scattering effects.

In this study, we have proposed and validated further modifications of the C-Quant adaptation[11] to differentiate between large and small (<λ) particles in IOLs, by means of their spectral light-scattering characteristics.

METHODS

Straylight measurements

Straylight was assessed using a commercial straylight meter (C-Quant) adapted for *in vitro* evaluation of light scattering from IOLs.[11] The description and validation of the C-Quant adaptation have been presented in a recent article.[11] In short, this adaptation works as follows. A complete C-Quant test screen is projected by Lens 1 (L_1) and an IOL immersed in balanced salt solution (BSS). A diaphragm partly obscures this image to block rays of a straylight source (**Figure 1**). A test field (**Figure 1**), however, can still be seen by an observer's eye through a magnifying lens (L_2).

Because of straylight originating from the IOL, part of the light is scattered and superimposed over the image of the test field. Since the straylight source flickers, a weak flicker is also perceived in the test field as a consequence of the superimposed image. The test field consists of 2 halves. In both halves the perceived flicker results from the superimposed

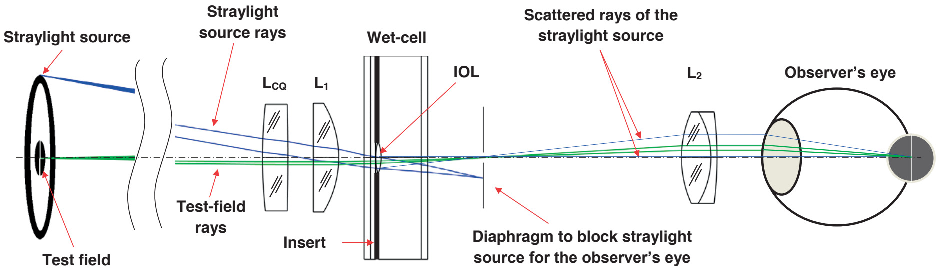

Figure 1. Schematic illustration of the C-Quant adaptation (not to scale). L_{CQ}=lens of the C-Quant, IOL=intraocular lens, L=lens.

image, but in one counter-phase compensation light is also added. During the C-Quant test, the observer is asked to indicate which of the 2 halves flickers stronger. Based on these responses, a psychometric curve is drawn, where the minimum of the curve corresponds to the sought straylight level.[10] The observer performs the C-Quant test in a similar way as her/his own eye would be tested. The difference is that the observer's eye is not exposed to the straylight source (as it is blocked by the diaphragm), thus only straylight of the IOL is measured. In this set-up, the eye only acts as a detector.[11]

The straylight parameter of the IOL is derived using this formula:

$$S_{IOL}= 10^{\wedge}\log(S_{set\text{-}up+IOL}) - 10^{\wedge}\log(S_{set\text{-}up}) \quad [deg^2/sr]$$

Where $S_{set\text{-}up+IOL}$ and $S_{set\text{-}up}$ are the straylight parameter of the set-up with and without the IOL in place, respectively. Note straylight can be expressed by either the straylight parameter "s" or its logarithm "log(s)".

A standard C-Quant measures straylight at 7.0° scatter angle.[10] To test angular dependency of IOLs, a modified C-Quant was also used to add straylight at 2.5°.[3] To this end, a C-Quant tube was elongated by a factor of 2√2. Although one may wonder about scattering intensity at other scatter angles, 2.5° and 7.0° were used because these angles are also used to assess the functional effect.[12] Moreover, *in vivo* studies have shown rather smooth angular dependence of ocular straylight.[12] Results taken at 2.5° and 7.0° angle were compared with straylight values for levels of normal crystalline lenses, known to originate from particles of around 1.4 μm in size.[13] Straylight of the crystalline lens was calculated using the CIE standard for the age of 20 and 70 years.[14]

Spectral analysis

Three interference filters (IF) of 468, 550, and 650 nm (10 nm bandwidth, Thorlabs, USA) were used to analyze the size of scattering particles by means of their straylight-wavelength dependence. The blue and red filters were chosen to approach the visible range; the green filter corresponds to the peak of the visual spectrum. This method enables to detect small (compared to wavelength) scatterers in IOLs. It has been shown that scattering from particles that are much smaller than wavelength of light has strong wavelength dependence. As defined by Rayleigh theory, intensity of scattered light from these small particles is inversely proportional to the fourth power of wavelength (λ^{-4}).[15] Angular dependency of light scattering from small particles is virtually zero, apart from a "natural light" correction at 90°.[16] On the other hand, light scattering from large particles has strong angular dependence, but weak or no dependence on wavelength. Scattering from large particles is defined by Mie theory.[15] The IFs were mounted on a rotational wheel and introduced into the system after L_2 (**Figure 2**). Because only a fraction of light is transferred by the IFs, a camera (C5405-50, Hamamatsu, Japan) was used as light amplifier to enable the suprathreshold psychophysical test, as intended with the C-Quant. The C-Quant test was then performed by the observer looking at an external screen where the test field was projected in real time. **Figure 2** shows the complete set-up for detection of submicron particles in IOLs. For very low straylight levels, spectral analysis was not possible.

The camera evaluation was done with and without the IFs. Results obtained with the camera but without the IFs (white light) were compared with results obtained with the observer's eye. Outcomes of the spectral analysis were compared to Rayleigh-type scatter.

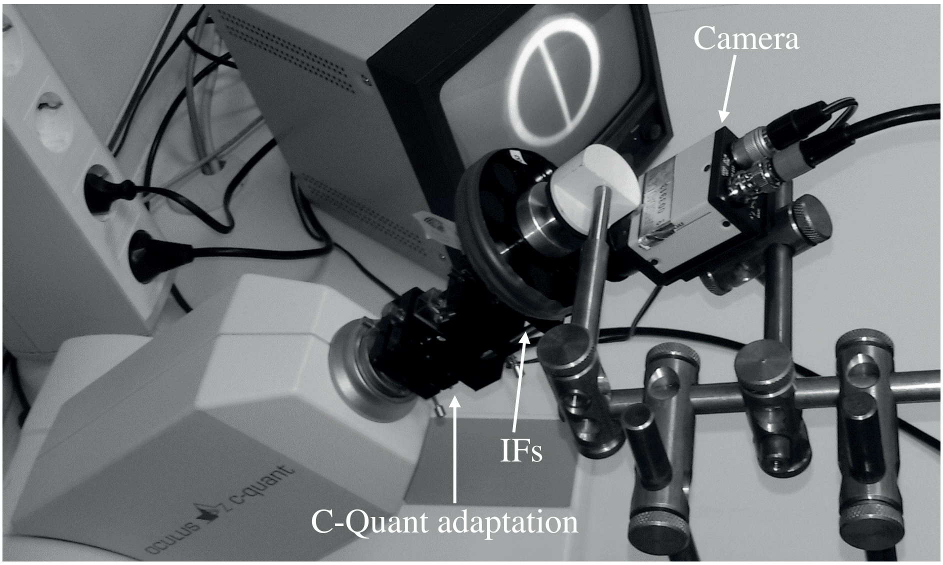

Figure 2. Complete set-up for assessment of straylight-wavelength dependence of intraocular lenses.

Validation test

The AMCO Clear 4000 NTU turbidity standard (GFS Chemicals Inc., USA) was used to test the ability of the set-up to detect submicron scatterers. In the eye research, AMCO Clear has been proposed as standard for corneal haze, as the cornea shows Rayleigh-type scatter.[16, 17] AMCO Clear contains numerous styrene divinylbenzene microspheres with an average size of 0.2 μm (0.1-0.3 μm). The AMCO solution was diluted with BSS by different factors.

Black Pro Mist filters (BPM) (Tiffen, USA), which contain various numbers of large particles, were also measured to exclude false positive results. Three BPM filters (1, 2 and 3) were used. They differ in the particle number, and consequently, in the scattering effect. It has been shown that straylight-angular dependence of the BPM filters agrees well with that of the human eye.[18]

Intraocular lenses

Six explanted IOLs and 5 IOLs from pseudophakic donor eyes were measured, all monofocal. The explanted IOLs were removed from the eye for other than straylight reasons. All IOLs but 1 are made of hydrophobic material. No *a priori* data (*e.g.* material properties) were available on the donor lenses. The lenses were rinsed and stored in BSS at room temperature. The hydration level and the temperature did not change throughout the measurements.

For each measurement session, an IOL was removed from a bottle and placed on a rectangular-shape custom-made insert. The insert contains a 5-mm opening to mimic a natural pupil. The IOL was centered with respect to this aperture, and that was assured by visual inspection. The IOL-insert combination was then introduced into a glass cell filled with BSS. The cell was placed on a custom-made holder that was designed to 1) baffle parasitic light 2) provide correct alignment of the glass cell (and the IOL) with the adaptation and the C-Quant.

RESULTS

The mean difference (± SD) between the straylight results with and without the camera was 0.00 ± 0.05 log(s) showing a good correspondence between the 2 measurements. Individual comparisons are presented graphically with a Bland-Altman plot in **Figure 3**.

Figure 4 presents the results of validation of the set-up. Straylight of AMCO Clear measured at 468, 550, and 650 nm closely followed Rayleigh theory. The BPM filters showed virtually no change in straylight with wavelength.

Straylight results of the studied lenses obtained at 2.5° and 7.0° angle are presented in **Figure 5**. All IOLs (the solid lines) showed angular behavior that differed considerably from straylight-angular dependency of AMCO Clear (the dashed black line), suggesting the presence of large particles. Five IOLs demonstrated straylight that is close to the level of the 20-year-old crystalline lens. The remaining 6 lenses showed increased straylight levels close to that of an aged lens (70y).

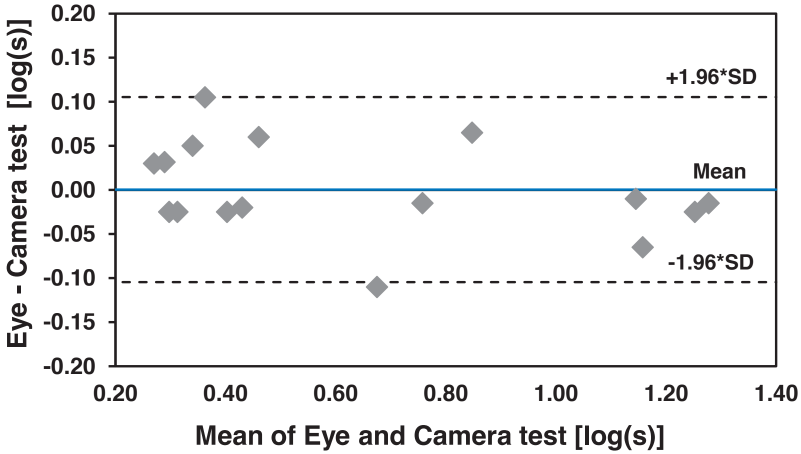

Figure 3. Comparison between straylight measured with the observer's eye looking at the camera projection ("Camera test") and with the observer's eye looking directly through the C-Quant adaptation ("Eye test").

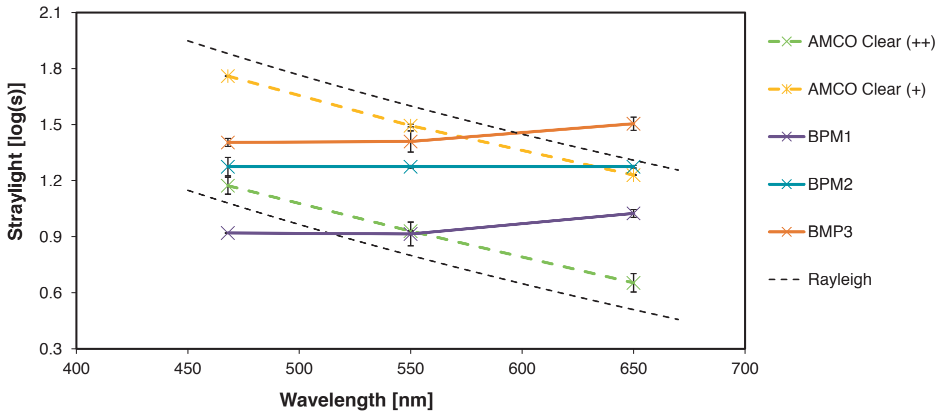

Figure 4. Validation of the set-up for detection of submicron particles. Straylight of AMCO Clear and Black Pro Mist (BPM) filters was measured with interference filters of 468, 550 and 650 nm. The "+" and "++" signs refer to different dilutions of AMCO Clear. Error bars = standard deviation.

Straylight of 4 IOLs was low hence, they were excluded from spectral analysis. The other 7 IOLs showed rather weak spectral effects, much less than Rayleigh-type scattering (**Figure 6**).

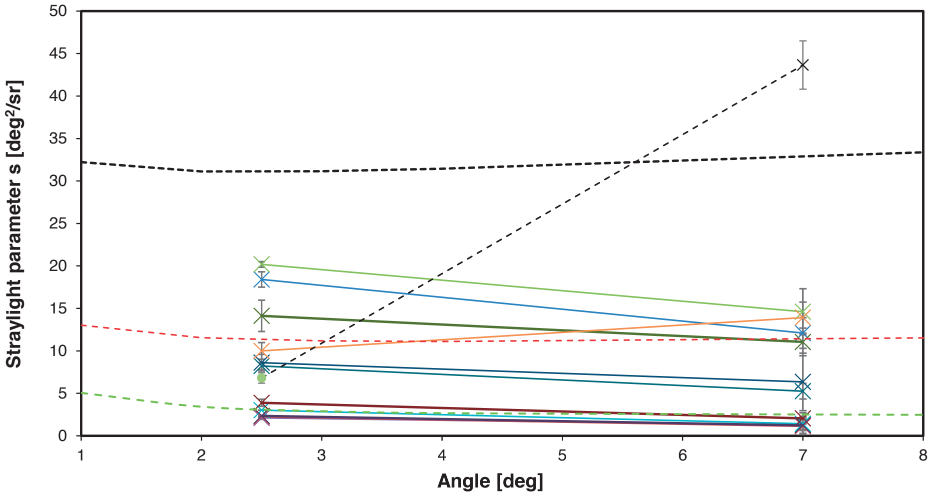

Figure 5. Straylight of the studied IOLs at 2.5° and 7.0° scatter angle. The dashed green and red line indicate straylight levels of the normal crystalline lens at age 20 and 70, respectively. For comparison, results of AMCO Clear are also presented (dashed black line). Error bars = standard deviation.

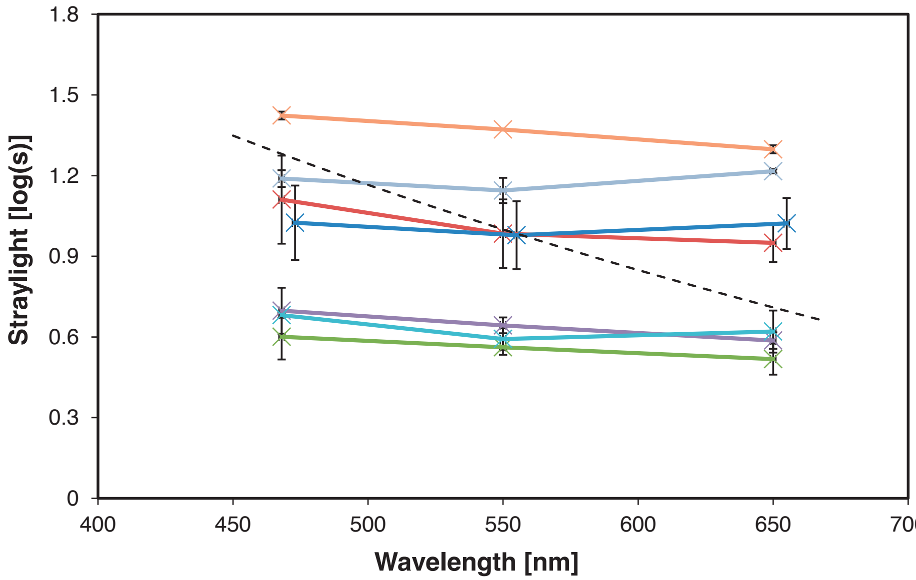

Figure 6. Analysis of straylight-wavelength dependency of IOLs. Straylight was measured at 7.0° scatter angle.The dashed black line corresponds to Rayleigh-type scatter (λ^{-4}). Error bars = standard deviation.

DISCUSSION

The proposed method for spectral analysis of light scattering in IOLs proved effective, as the straylight-wavelength dependency of AMCO Clear agreed well with the Rayleigh λ^{-4} law (**Figure 4**). As expected, the BPM filters did not show spectral effects. **Figure 3** indicates that the C-Quant adaptation and procedure gives proper absolute values and can be considered as an objective measure for straylight assessment in IOLs.

One potential application of this method is to identify small scattering particles, such as subsurface nanoglistenings. It has been reported that the diameter of nanoglistenings ranges from 0.03 nm to 0.19 μm.[19] The size distribution of AMCO Clear microspheres is about the diameter of nanoglistenings. Hence, the proposed methodology can be used to study straylight from such particles. Das et al. assessed straylight from IOLs with artificially induced nanoglistenings, using a modified Complete Angle Scattering Instrument scatterometer.[7] They found lower scattering intensity at a wavelength of 633 nm than at 488 nm, corresponding to Rayleigh behavior. In our study, none of the analyzed IOLs showed the Rayleigh-type scatter. This can be explained by differences in types of lenses and in aging process, as Das et al.[7] used artificially aged IOLs of a type that is most often associated with nanoglistenings. We, however, studied the IOLs of various types that had aged naturally in the eye.

Figure 5 indicates that straylight of the studied IOLs is mostly higher at 2.5° than at 7.0°, and this can be attributed to Mie scattering. Rayleigh-type scattering shows a different behavior as the straylight parameter of AMCO Clear steeply increases with angle. Please note how the straylight parameter (s) is defined, that is:

$$s = \theta^2 \times PSF(\theta) \quad [deg^2/sr]$$

where θ is the visual angle (*e.g.* 2.5°, 7.0°), and the PSF is the Point Spread Function. Thus, if pure Rayleigh scattering takes place, the PSF does not change at different angles (*e.g.* 2.5° vs. 7.0°), but the θ^2 coefficient causes the straylight parameter to increase at 7.0° as compared to 2.5°. For larger particles, however, the PSF at 7.0° is much lower (generally by order[s] of magnitude) than that at 2.5° hence, the straylight parameter at 7.0° is relatively close to that at 2.5°, and this points to strong angular dependency.

It has been shown that light scattering from IOLs prior to implantation is low.[20]

Figure 5 demonstrates that 4 of the 11 IOLs showed straylight below the level of that of the young crystalline lens. This indicates that only a few lenses preserved their low scattering properties. Higher straylight in the remaining 7 IOLs can be attributed to the presence of large particles (Mie scattering), as these lenses showed clear angular dependence (**Figure 5**), but no Rayleigh-type dependence on wavelength (**Figure 6**). Although (weak) wavelength dependency can be seen in some of the IOLs studied (**Figure 6**), this can be expected, given Mie scattering, which shows weak dependence on wavelength.

In summary, this paper has validated a new method to distinguish between large and small ($<\lambda$) particle scatter in IOLs. The main advantage of this technique is that it is based on a fairly straightforward modification of the C-Quant. An advantage of the present system compared to benchtop measurements is that results can be more directly compared to data acquired *in vivo*. Moreover, the use of the clinical device may increase the accessibility of objective straylight measurements for researchers and clinicians who do not enjoy access to the optical bench. Although it has been primarily developed to assess straylight from IOLs,[11] this approach can also be applied to study straylight from different types of scattering materials.

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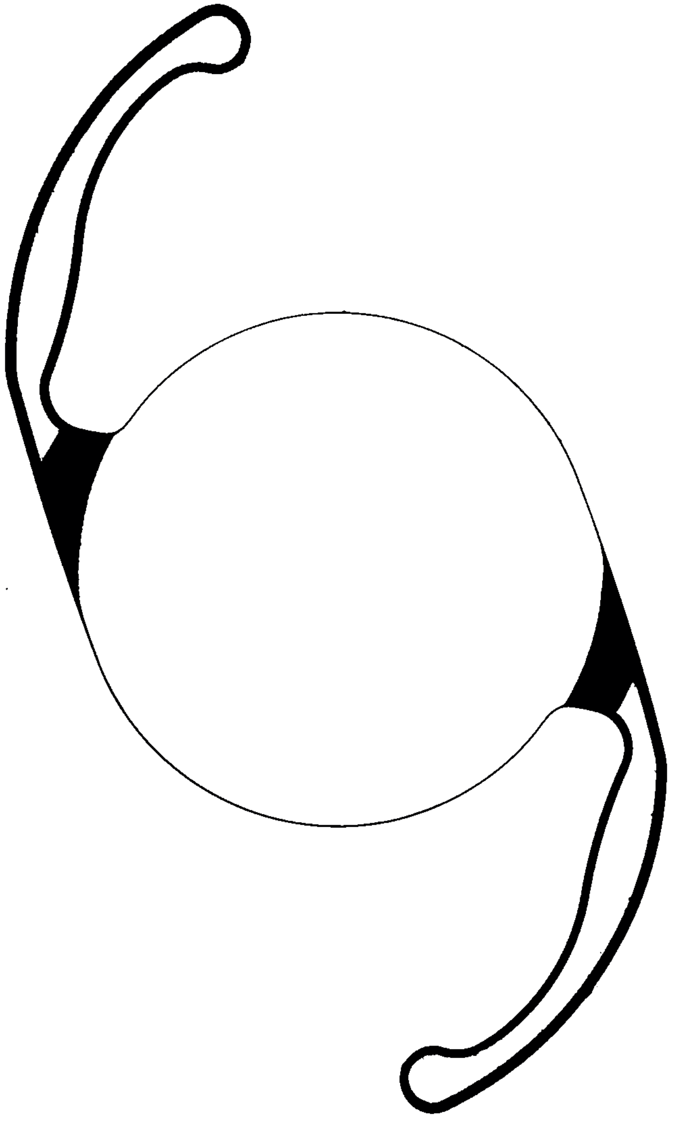

Chapter 11

Conclusions

Both intraocular lenses and corneal contact lenses have proven to be a significant contributor to ocular straylight (**Chapter 3-10**). Their composing material appears to be as the main factor determining their light-scattering characteristics (**Chapter 4-8**). Although the optical design is very important for the overall quality of vision, differences in terms of straylight between the studied lens designs seem to not be of much significance (**Chapter 4, 5** and **8**). The contribution of the optical design (especially in case of diffractive lenses) should, however, be further studied using a technique that could identify morphological sources of light scattering, and be able to differentiate between bulk scattering and scattering originating from the optical features.

Straylight of IOLs can be affected by the water content of lens material, as hydrophilic multifocal IOLs have shown *in vivo* to scatter less than the hydrophobic ones (**Chapter 4-5**). Increased straylight in the hydrophobic lenses might be related to the formation of glistenings. Based on the proposed model for the relationship between straylight and severity of glistenings (**Chapter 6**), the number of microvacuoles that would have an equivalent effect on light scattering could be estimated. To this end, the 0.08 log(s) difference between the hydrophobic and hydrophilic lenses must be applied to the mean straylight value (1.18 log[s]), and the difference obtained entered in the model **(Chapter 5-6**). This results in a glistenings number of 652 per mm^2. The literature review showed that such a large number can be found *in vivo*.[1] This can however not be the full explanation for the hydrophilic lenses to perform better in terms of straylight, and more study is needed.

Glistenings appear to be the most prevalent IOL degeneration/alteration, but only a large number of microvacuoles may yield a significant straylight increase (**Chapter 6-7**). A proportional relationship between straylight and the glistenings number was found (**Chapter 6**). Based on this relationship, scattering effect of clinically observed glistenings can be estimated. This finding points to the objective counting as a preferable method for assessing glistenings severity and progression. To demonstrate to what extent the presence of (*in vivo*) glistenings affects visual quality, one would need an actual range of the glistenings number. Given, however, that subjective grading has most often been used in clinics, the range of the number of glistenings is difficult to assess, and this warrants further study.

Other IOL abnormalities may be related to significant straylight elevation as well. Besides well documented cases of serious IOL opacification,[2, 3] surface deposits/snowflake degeneration may appear in a subclinical (early) form shown to affect ocular straylight (**Chapter 7**). The total incidence rate of IOL degeneration was 53%, but in some IOL groups it was 100% (**Chapter 7**). Since IOL opacification even at its early stage causes ocular straylight to increase, such a large incidence rate of lens abnormalities may (partly) explain general straylight elevation in the pseudophakic eye. This finding, however, cannot explain the high intersubject variability in ocular straylight reported in the literature (*i.e.* from 0.64 to 1.82 log[s][4]), and this remains to be elucidated.

The development of a clinical instrument for straylight assessment of the eye provided a new parameter to the existing metrics of visual quality (*e.g.* visual acuity).[5] The current thesis shows that now this instrument (the C-Quant) can also be used to *in vitro* assess straylight of IOLs (**Chapter 9-10**). The proposed C-Quant adaptation has proved effective in measuring straylight from the IOLs, but also in differentiating between large and small particles (**Chapter 9-10**). This may prove to be of clinical value as the proposed method could be used for screening new lenses or evaluation of lens explants. The latter application may improve understanding of subjective visual complaints, as now *in vivo* and *in vitro* straylight can be compared directly. The C-Quant, however, measures straylight at a fixed angle of 7.0° (average)[6] and this could be viewed as a limitation. A C-Quant adaptation that enables straylight to be measured at different angles would be advantageous and could be a step forward in intraocular lens research.

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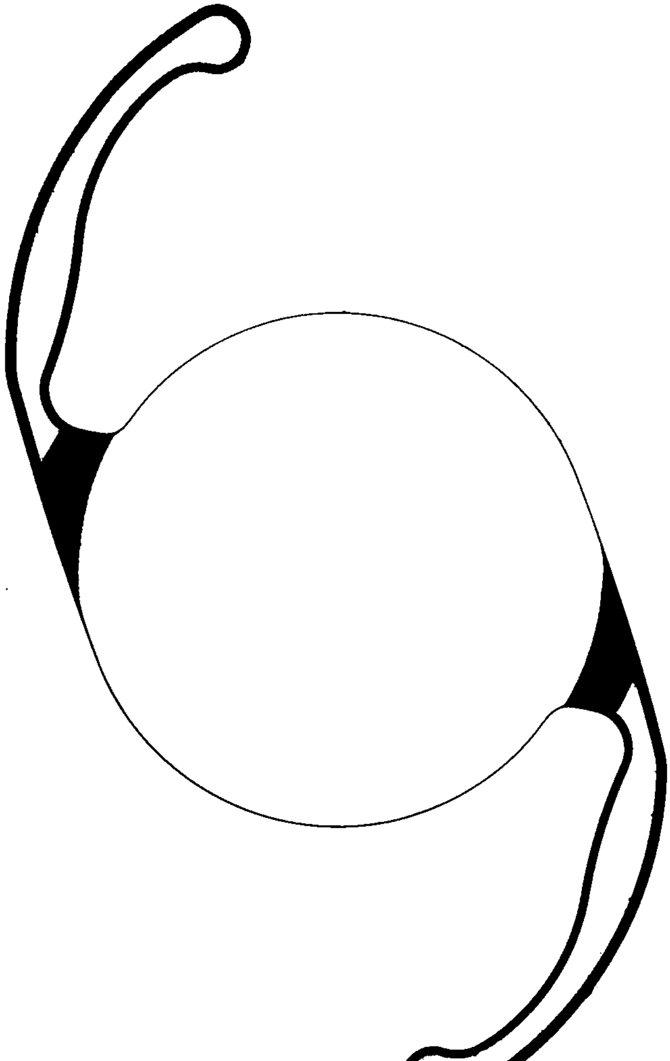

Chapter 12

Summary and general discussion

Summary in Dutch - Samenvatting

SUMMARY AND GENERAL DISCUSSION

Higher (than expected) straylight has been reported in patients after implantation of a monofocal or multifocal intraocular lens.[1-17] Among the typical complaints related to elevated straylight glare plays an important role. Glare is the subject of this thesis. Our reported research on straylight from IOLs may shed new light on potential causes of straylight elevation in pseudophakia. A new method for assessing light scattering from IOLs is proposed and validated.

A literature review of studies on straylight in pseudophakic eyes (with no comorbidities) is presented in **Chapter 3**. A new norm for straylight in pseudophakia is proposed, which was derived from 13 studies (1,533 eyes), that is

$$\text{Straylight} = 0.0044 \times \text{Age} + 0.89 \quad [\log(s)],$$

where s is the straylight parameter. This norm was compared to the phakic reference showing that straylight-age dependency of the phakic eye differs from the pseudophakic one. That is, on average, a 0.15 log(s) straylight increase per decade for the phakic norm[1] vs. 0.044 log(s) per decade for the pseudophakic norm. This finding indicates that, although the phakic reference has often been used for assessment of straylight in pseudophakic patients,[2, 4, 6, 16, 18] this could potentially lead to uncertain conclusions. Instead, the new pseudophakic norm should be used as a reference in such studies.

An average 2-fold increase has been found in pseudophakia as compared to the normal value for a young eye of 0.90 log(s).[1] This was confirmed by the results presented in Chapter 3, as mean straylight of the pseudophakic eye was found to be 1.21 log(s) (average of 1,869 straylight results from 16 studies). Three studies allowed comparison of pre- to postoperative data. It was found that postoperative straylight improvement depends not only on preoperative straylight values but also on age. A model for predicting straylight improvement that is presented in Chapter 3 was established based on data of these 3 studies (558 eyes):

$$\text{Straylight improvement} = 1.04 \times \text{preop straylight} - 0.006 \times \text{age} - 0.84 \quad [\log(s)]$$

This model indicates that for younger patients (<70 years old), postoperative improvement can only be reached if preoperative straylight is higher than that of an age-matched normal population. The model gives a break-even point (BEP) for straylight improvement of patients aged 40 to 50 years of 1.06 log(s), and this increases to 1.29 log(s) at the age of 80 to 90 years. As this corresponds to the pseudophakic norm, the BEP demonstrates that the pseudophakic norm can also be used as criterion for predicting postoperative straylight improvement. The analysis of pre and postoperative straylight results revealed that 18% of pseudophakic patients experienced an increase of straylight following surgery in the included studies. To address this issue, the new pseudophakic norm could be used for better prediction of postoperative straylight. The application of the pseudophakic norm in clinical practice may improve the decision making process and minimize potential for postoperative straylight increase, and serve as a general reference for assessment of postoperative results.

Chapter 4 reports on postoperative visual outcomes (with a focus on straylight) of 2 groups of patients treated with 2 different diffractive multifocal intraocular lenses (SeeLens MF, Hanita vs. Restor SN6AD1, Alcon). Postoperative corrected distance visual acuity (logMAR) in the SeeLens and Restor groups was -0.03 ±0.06 and -0.02 ±0.08, respectively. Mean postoperative refractive error was +0.01 ±0.43 D in the SeeLens group, and +0.06 ±0.35 D in the Restor group. Although visual acuity and postoperative refraction did not differ significantly, straylight was found to be higher in the Restor group (1.17 ±0.14 log[s]) than in the SeeLens group (1.10 ±0.19 log[s]) (p=0.003). Following age adjustment, the mean difference was 0.06 log(s) (p=0.03). A straylight improvement of 0.08 ±0.18 log(s) was found in the SeeLens group, in the Restor group it was 0.01 ±0.21 log(s), noting that those were relatively good eyes, as most were refractive procedures.

Modern multifocal IOLs most often provide good visual outcomes in terms of visual acuity and postoperative refraction, showing only little differences when different IOL models are compared.[8, 17, 19] This study, however, showed that a difference can be found in terms of straylight, which is an additional visual function parameter. Although the SeeLens and Restor IOLs are very close in their optical design (both are diffractive apodized lenses), straylight was found to differ significantly with lower straylight in the SeeLens group. It was suggested that the difference reported here can be attributed to material properties (hydrophobic vs. hydrophilic) or manufacturing process (cast molded vs. lathe milling).

To further delineate potential sources of straylight in multifocal IOLs a literature review was performed that is presented in **Chapter 5**. The review included 10 papers where 9 different multifocal IOL models were studied. A mean straylight value of 822 eyes was 1.18 ±0.19 log(s). Statistical analysis showed that patients with hydrophobic IOLs have higher straylight than patients with hydrophilic ones by 0.08 log(s). The comparison between optical designs showed insignificant differences when the material type (hydrophobic and hydrophilic) was accounted for, and this emphasizes potential importance of material characteristics to straylight. IOLs featured with a blue/violet filter demonstrated, on average (0.04 log[s]), lower straylight than standard IOLs. This difference, however, was not statistically significant.

An association between higher straylight and hydrophobic monofocal lenses has been reported before on a more limited data set.[18] The current study showed that a similar effect can also be observed in multifocal IOLs. This might be related to a difference in glistening numbers. In addition, the lower refractive index of the hydrophilic IOLs, reduces the ability of microvacuoles to scatter light because differences between the refractive index of the lens material and the medium (the aqueous humor) are smaller.[20] This finding implies that the type of material for the IOLs can be an important factor that may significantly affect postoperative ocular straylight

Several studies have reported on scattering effects from lenses of different designs.[2-6, 8, 9, 14, 15, 17] Although it might be expected that multifocality gives rise to straylight increase, comparative studies on multifocal vs. monofocal IOLs have shown rather inconclusive results. Two of 5 clinical studies reported a significant straylight difference between multifocal and monofocal IOLs.[2-4, 9, 14] The discrepancy in results between those studies can possibly be explained by the differences in material for IOLs, as suggested in Chapter 5. Another reason could be patient selection bias, as candidates for multifocal IOLs must meet stricter requirements than those for monofocal IOLs. Indeed Chapter 5 reports that the amount of variation in postop straylight of patients after implantation of the multifocal IOL was smaller than that found in a general pseudophakic population (0.18 log vs. 0.21 log). Although this difference is small, this might play a role when multifocal and monofocal lenses are compared.

Several studies have tested the ability of yellow-tinted IOLs to reduce glare with rather mixed results.[21, 22] The literature review presented in Chapter 5 shows that patients with the blue/violet filter IOLs have on average lower straylight than those with standard IOLs. Individual characteristics of the patients' eyes were, however, not available, and that would be needed for better understanding of this finding.[23] The study concluded that blue/violet IOLs failed to prove clearly that they can reduce postoperative glare.

It has long been debated whether glistenings may adversely affect vision.[24] **Chapter 6** elaborates on the effect of glistenings on visual performance by means of straylight measurements. To this end, 7 IOLs made of AcrySof material with laboratory induced glistenings were analyzed. Straylight was measured at different stages of glistenings formation to establish how straylight and glistening severity are related. A wide range of the total number of glistenings (114 to 12 386 per mm^2) and the surface portion (1.4% to 26.9%) were induced. The straylight parameter ranged from 0.24 to 1.80 log(s). A proportional relationship was found between straylight and the number of glistenings, as well as between straylight and the surface portion of glistenings (mean glistening frontal area x glistenings number per unit of pupil area). A model was proposed to predict straylight effects of glistenings based on either the total number or the surface portion:

$$\text{Straylight parameter} = 0.0046 \times \text{number of glistenings per mm}^2 \quad [\text{deg}^2/\text{sr}]$$

$$\text{Straylight parameter} = 215 \times \text{surface portion} \quad [\text{deg}^2/\text{sr}]$$

The model proposed here was compared with Mie scattering calculation[20] for the observed mean particle (glistenings) diameter of 5 μm, showing good agreement between the experimental and computational results.

This study contributes to the understanding of the lack of significant effects of glistenings on visual acuity/contrast sensitivity on physical grounds as proposed earlier.[25-28] It shows that glistenings may be a significant source of light scattering though. The proposed model gives a precise estimation of the straylight effects of glistenings, and can be used when straylight analysis of an IOL with glistenings is not possible. The study presented in Chapter

6 also explains seeming discrepancy between results reported in the literature. Problems with different grading systems for glistening severity are discussed in Chapter 6. It is concluded that subjective grading as used in several studies makes a comparison of results very difficult as those grades are not sufficiently defined.[29-39] More quantitative grading systems have also been proposed.[40-45] However, in several studies the actual glistenings count for the highest grade is not reported, and only given as "more than" a certain number (*e.g.* 50, 200 per mm^2). This applied to 19% of the cases reported in literature, and as result the data of this most important group cannot be used. The limitations of the grading scales could be overcome by the use of a strict quantitative method instead, as proposed by Colin and Orignac.[31] This could make possible the comparison of multicenter results, and also the use of our model to predict scattering effects of glistenings. In Chapter 6 is shown that scattering of approximately 2,500 glistenings per mm^2 is comparable to a straylight level of a 70-year-old crystalline lens. This finding indicates that only a large number of glistenings can lead to visual disturbances and patient complaints.

In **Chapter 7**, we present results of straylight measurements and microscopic examination of 74 lenses removed from donor pseudophakic eyes. This chapter reports that only 41% of the studied lenses showed low straylight levels. Although none of the studied lenses showed straylight that was close to a straylight level of a cataractous lens, it was seriously increased in 14% of the IOLs. The slit lamp and light microscopy evaluation revealed the presence of IOL degeneration, such as snowflake-like degeneration,[46] surface deposits,[47] and glistenings.[24] Increased straylight was found in IOLs affected by these abnormalities, however, the extent of the straylight increase differed between different conditions, and IOL types. The snowflake-like degeneration and surface deposits appeared as important sources of light scattering in 2 lens types that showed the highest straylight among 8 studied IOL groups. Despite a high prevalence of glistenings (3 of the 8 groups), the presence of glistenings showed lower potential for a significant straylight increase than surface deposits/snowflake-like degeneration, as straylight was found to be above the level of a 70-year-old crystalline lens only in 3 lenses with glistenings.

Straylight of 14% of the studied IOLs was seriously increased, closely corresponding to debilitating straylight elevation reported in 10% of the pseudophakic patients (Chapter 3). As IOL degeneration was found in all lenses with seriously increased straylight, this study points to the lens degeneration as a potential reason for straylight elevation in pseudophakia. It was reported in Chapter 3 that only 6% of the pseudophakic eyes show a straylight level that is below the level of that of the young eye. In the study of Chapter 7 however, straylight of 41% of the IOLs was very low. Hence, straylight originating from IOLs may be responsible for straylight elevation in some, but not all pseudophakic eyes. Other potential sources of light scattering in the pseudophakic eye must be a subject of future studies.

This study shows that IOL opacification due to material degradation/alteration is a significant contributor to ocular straylight, but lens abnormalities differ in their straylight effects.

Surface deposits and snowflake-like degeneration yield more straylight than glistenings that appear (*in vivo*) in the eye. These findings may help clinicians to better understand patient symptoms associated with IOL degeneration, and improve the decision-making process before explantation of an opacified lens.

Multifocal contact lenses most often involve a multi-zonal design to provide near and distance vision for presbyopic patients.[48-50] As a lens consists of several areas that differ in refractive power, abrupt changes in the lens power profile have been considered as a potential source of light scattering.[48] Moreover, glare related symptoms have often been reported in association with the use of multifocal contact lenses.[51] However, straylight of multifocal contact lenses has never been reported. To address this issue, we measured straylight of volunteers fitted with 4 multifocal contact lenses with different optical designs. This is presented in **Chapter 8**. Straylight was measured after pupil dilation because glare complaints are most important in night vision conditions. We found that straylight increases by an average of 0.06 log(s) following insertion of the multifocal contact lenses. However, a significant difference was found between the studied lens groups. With only one lens type straylight was significantly higher; 0.11 ±0.07 log(s) more than that of the naked eye (the control). *In vitro* evaluation of the contact lenses with a slit lamp (using reverse illumination) did not demonstrate increased light scattering from transition zones. Bulk scattering, however, was revealed in the lens group that showed the highest straylight.

This study showed that jumps in the power profile do not contribute to straylight, contradicting earlier suggestions.[48] Although one of the 4 multifocal lens designs showed increased straylight, this may be related to material properties as uniform scattering was observed in slit-lamp images only in this lens. Straylight was measured in a natural and dilated pupil showing a significant straylight increase following pupil dilation. Therefore, the results of this study may raise awareness of eye care providers of increased glare sensitivity after pupil dilation, and that some contact lens materials may cause significant straylight increase.

In **Chapter 9**, we propose a new method for *in vitro* straylight measurements from IOLs. It works based on a psychophysical approach implemented in a clinical device (C-Quant, Oculus),[52, 53] which was adapted for assessment of the IOLs. The C-Quant adaptation consists of several optical components to project an image of a C-Quant test field that can be seen by an observer who performs the test. A diaphragm, which is placed behind the IOL, blocks the light of the straylight source form the observer's eye, thus only straylight of the IOL is measured. The observer's eye is used as an optical detector. The proposed method was validated by 3 observers with commercial scattering filters, and proved independent of straylight of the eye, as a good agreement between the 3 observers was found. The C-Quant adaptation was also tested with different types of IOLs, including multifocal and monofocal lenses, and proved effective in measuring straylight of all types of IOLs.

Chapter 10 provides a further modification to the C-Quant adaptation that enables to differentiate between large and small particles scattering in IOLs. It takes advantage of straylight-wavelength dependence in case of small particles, which is defined by Rayleigh scattering theory.[20] To this end, interference filters were introduced into the experimental set-up to measure straylight at 3 wavelengths. A camera was used to amplify the intensity of the image of the C-Quant test, because the 10 nm bandwidth of the interference filters reduces intensity considerably. The observer performed the test based on camera projection. This method was validated using scattering filters (large particles) and a turbidity standard (submicron particles).[54, 55] In this study, 11 IOLs were tested that were either routinely explanted from pseudophakic patients or removed from pseudophakic donor eyes. Straylight of the included lenses was measured at 2 scatter angles, to study their straylight-angular dependence. Straylight-wavelength dependence of the turbidity standard measured with the proposed methodology agrees well with Rayleigh theory. As expected, straylight of the scattering filters did not change much with the wavelength. The spectral and 2-angle analysis showed that large particles can be considered the major source of light scattering in the studied IOLs.

Chapter 9 and 10 introduce a relatively simple and effective method for straylight assessment of IOLs. The use of a clinical instrument may increase the accessibility of *in vitro* straylight measurements for clinicians, whereas it has previously been solely restricted to an optical laboratory. A potential application could be to test brand-new IOLs before implantation. Another advantage of the proposed methodology is that *in vitro* and *in vivo* straylight results can be directly compared, and that could be of importance when, *e.g.* an IOL is explanted due to patient dissatisfaction.

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SUMMARY IN DUTCH - SAMENVATTING

Vele studies hebben laten zien dat na implantatie van monofocale of multifocale lenzen het visuele strooilicht fenomeen sterker is dan men zou kunnen verwachten.[1-17] Verhoogd strooilicht geeft typisch klachten van verblinding en is het onderwerp van dit proefschrift. Het hier gerapporteerde onderzoek aan strooilicht bij intraoculaire lenzen (IOLs) kan nieuw licht werpen op mogelijke oorzaken van strooilichtverhoging bij pseudofakie. Een nieuwe methode voor de bepaling van lichtverstrooiing door IOLs wordt voorgesteld en gevalideerd.

Een literatuuroverzicht van studies naar strooilicht in pseudofake ogen (zonder comorbiditeit) wordt gepresenteerd in **Hoofdstuk 3**. Een norm voor strooilicht in pseudofakie wordt voorgesteld, die afgeleid is van 13 studies (1.533 ogen), als volgt:

$$\text{Strooilicht} = 0{,}0044 \times \text{leeftijd} + 0{,}89\ [\log(s)],$$

Waarbij s de strooilicht parameter is. Deze norm wordt vergeleken met de fake referentie en daaruit blijkt dat de wijze waarop strooilicht van de leeftijd afhangt verschillend is voor fake en pseudofake ogen. Voor oudere fake ogen neemt strooilicht gemiddeld met 0,15 log eenheden per decade toe,[1] terwijl voor pseudofake ogen de toename gemiddeld 0,044 log eenheden per decade is. Deze bevinding maakt duidelijk dat het gebruik van de fake referentie in strooilicht studies bij pseudofake patiënten[2, 4, 6, 16, 18] niet juist is. De hier voorgestelde pseudofake norm zou in zulke studies gebruikt moeten worden.

Gemiddeld wordt een strooilichtverhoging van een factor 2 gevonden wanneer pseudofake ogen worden vergeleken met de normale waarde van log(s)=0,9 voor het jonge oog.[1] Dit wordt bevestigd in Hoofdstuk 3, want daar wordt een gemiddelde strooilicht waarde van log(s)=1,21 gevonden, gebaseerd op 1.869 strooilichtwaardes uit 16 studies. Drie studies maken een vergelijking tussen preoperatieve en postoperatieve strooilichtwaardes mogelijk. Daarbij blijkt dat de strooilichtverbetering door de operatie niet alleen van de preoperatieve strooilichtwaarde afhangt, maar ook van de leeftijd. In Hoofdstuk 3 wordt een model voorgesteld om de strooilichtverbetering te voorspellen, gebaseerd op de resultaten van 558 ogen uit deze 3 studies:

$$\text{Strooilichtverbetering} = 1{,}04 \times \text{preop strooilicht} - 0{,}006 \times \text{leeftijd} - 0{,}84\ [\log(s)]$$

Dit model voorspelt dat bij jongere patiënten (<70 jaar oud) postoperatieve verbetering gemiddeld gesproken alleen bereikt kan worden als de preoperatieve strooilichtwaarde hoger is dan de leeftijdsafhankelijke normaalwaarde. Het model geeft een *break-even* *point* (BEP) voor strooilichtverbetering dat loopt van 1,06 log(s) voor de leeftijdsgroep van 40 tot 50 jaar, tot 1,29 log(s) voor de leeftijdsgroep van 80 tot 90 jaar. Omdat dit verloop overeenkomt met de pseudofake norm, kan geconcludeerd worden dat die norm tevens gebruikt kan worden als criterium voor postoperatieve strooilichtverbetering. De analyse van pre- en postoperatieve gegevens laat zien dat 18% van de pseudofake patiënten in de betreffende studies een verslechtering van hun strooilichtwaarde na de operatie laten zien. Toepassing van de pseudofake norm in de klinische praktijk kan een verbetering betekenen van het besluitvormingsproces en een vermindering van het aantal patiënten dat na de operatie een verslechtering van het strooilicht ervaart. De norm kan tevens gebruikt worden als algemene referentie voor beoordeling van postoperatieve resultaten.

Hoofdstuk 4 doet verslag van postoperatieve visuele resultaten (met een focus op strooilicht) bij 2 groepen patiënten die behandeld werden met 2 verschillende diffractieve multifocale intraoculaire lenzen (SeeLens MF, van Hanita versus Restor SN6AD1 van Alcon). Postoperatieve verte-gecorrigeerde gezichtsscherpte in logMAR was -0.03 ±0.06 en -0.02 ±0.08, respectievelijk voor de SeeLens en Restor groep. Postoperatieve refractie was +0.01 ±0.43 D in de SeeLens groep en +0.06 ±0.35 D in de Restor groep. Alhoewel postoperatieve gezichtsscherpte en refractie niet significant verschillen, word wel een significant verschil in strooilicht gevonden. Postoperatief strooilicht is hoger in de Restor groep (1.17 ±0.14 log[s]) dan in de SeeLens groep (1.10 ±0.19 log[s]) (p=0.003). Hierbij dient genoteerd te worden dat dit relatief goede ogen zijn omdat de meeste gevallen refractieve procedures betreffen. Na leeftijdscorrectie is het gemiddelde verschil 0.06 log(s) (p=0.03). Een strooilichtverbetering van 0.08 ±0.18 log(s) wordt gevonden in de SeeLens group, terwijl die in de Restor groep 0.01 ±0.21 log(s) is.

Moderne multifocale lenzen geven als regel goede visuele resultaten, met name wat betreft gezichtsscherpte en refractie. Als verschillende modellen IOL met elkaar vergeleken worden, worden maar kleine verschillen gevonden.[8, 17, 19] Hoofdstuk 4 toont echter dat er wel verschillen in strooilicht gevonden kunnen worden, dus toch een verschil in kwaliteit van visuele functie. Alhoewel de SeeLens en Restor IOLs zeer vergelijkbaar zijn in optisch ontwerp (beide zijn geapodiseerde diffractieve lenzen) is het strooilicht verschillend, met de laagste waarde in de SeeLens groep. Als verklaring wordt voorgesteld het verschil in materiaal eigenschappen (hydrofoob versus hydrofiel) dan wel het verschil in fabricageproces (spuitgieten versus draaibank frezen).

In **Hoofdstuk 5** wordt door middel van een literatuur studie verder onderzoek gedaan naar mogelijke strooilicht effecten bij multifocale IOLs. Tien studies worden besproken die in totaal 9 verschillend multifocale IOL modellen betreffen. De gemiddelde strooilichtwaarde is 1,18 ±0,19 log(s) bij 822 ogen. Statistische analyse toont dat patiënten met hydrofobe IOLs meer strooilicht hebben dan patiënten met hydrofiele IOLs. Het verschil is gemiddeld 0,08 log eenheden. Een vergelijking tussen verschillende optische ontwerpen brengt geen verschillen in strooilicht aan het zicht, als althans gecorrigeerd wordt voor het verschil in materiaal (hydrofoob versus hydrofiel), waarmee het belang van materiaal karakteristieken voor strooilicht wordt onderstreept. IOLs die voorzien zijn van een blauw/violet reducerend filter tonen gemiddeld 0,04 log eenheden minder strooilicht, maar dit verschil is niet statistisch significant.

Voor monofocale IOLs is in een betrekkelijk kleine studie al eerder gevonden dat strooilicht verhoogd is ingeval van hydrofobe IOLs.[18] De huidige studie toont dat hetzelfde gevonden wordt voor multifocale IOLs. Een verklaring kan gezocht worden in het verschil in het aantal glistenings (microvacuolen) in de 2 materialen. Bovendien zou het verschil in brekingsindex een rol kunnen spelen. Hydrofiele IOLs hebben een lagere brekingsindex. Daardoor vermindert het verschil in brekingsindex tussen het IOL materiaal en de vloeistof (kamerwater) dat zich in de microvacuole bevindt en daardoor vermindert ook de lichtverstrooiing door de microvacuole.[20] Dit alles wijst erop dat het type materiaal dat voor de IOL gebruikt wordt een belangrijke factor kan zijn voor het postoperatieve strooilicht resultaat.

Verscheidene studies hebben gezocht naar verschillen in lichtverstrooiing tussen lenzen van verschillend ontwerp.[2-6, 8, 9, 14, 15, 17] Alhoewel verwacht zou kunnen worden dat multifocaliteit meer strooilicht geeft, hebben vergelijkende studies aan monofocale versus multifocale lenzen geen eensluidend beeld gegeven. Slechts 2 van 5 klinische studies rapporteren een significant verschil in strooilicht tussen monofocale en multifocale IOLs.[2-4, 9, 14] De discrepantie in resultaten zou mogelijk verklaard kunnen worden uit het verschil in materialen voor de IOLs, zoals dat volgens dit hoofdstuk het strooilicht kan beïnvloeden. Er moet echter ook een andere reden overwogen worden, namelijk potentiële selectie bias. Kandidaten voor multifocale lenzen moeten als regel aan striktere criteria voldoen dan kandidaten voor monofocale lenzen. In Hoofdstuk 5 wordt inderdaad gerapporteerd dat de variatie in postoperatief strooilicht kleiner is na implantatie van een multifocale IOL, als dat vergeleken wordt met de variatie die gevonden wordt in de algemene pseudofake populatie (0,18 versus 0,21 log eenheden). Alhoewel dit verschil klein is zou het effect een rol kunnen spelen als monofocale en multifocale IOLs worden vergeleken.

Verschillende studies hebben getest of geel kleuring van IOLs verblindingsgevoeligheid tegengaat, maar de resultaten zijn onduidelijk.[21, 22] Het literatuuroverzicht gepresenteerd in Hoofdstuk 5 toont dat patiënten geïmplanteerd met IOLs die blauw/violet licht reduceren gemiddeld minder strooilicht ervaren dan patiënten geïmplanteerd met standaard IOLs. Het ontbreekt echter aan voldoende gegevens om deze bevinding helder te interpreteren.[23] De conclusie lijkt gerechtvaardigd dat blauw/violet reductie geen belangrijke verbetering van postoperatieve verblindingsgevoeligheid oplevert.

In de literatuur is vaak de vraag gesteld of glistenings belangrijk zijn voor de visuele functie.[24] **Hoofdstuk 6** geeft een antwoord op deze vraag door de lichtverstrooiing aan glistenings kwantitatief te bepalen en in visueel strooilicht uit te drukken. In 7 IOLs van Acrysof materiaal werden glistenings geïnduceerd met een laboratorium methode. Strooilicht werd bepaald bij verschillende niveaus van glistening inductie, om de relatie tussen strooilicht en de hoeveelheid glistenings, zoals die in de kliniek gezien wordt, vast te stellen. De glistening hoeveelheid wordt uitgedrukt in het aantal per mm^2 pupiloppervlak (wij hadden waarden van 114 tot 12.386 mm^{-2}) zowel als in de fractie van het pupiloppervlak dat met de microvacuolen bezet is (bij ons 1,4% tot 26,9%). Deze fractie wordt "surface portion" genoemd en berekend als (gemiddeld frontaal oppervlak van de microvacuole x het aantal glistenings per mm^2 pupiloppervlak). Het strooilicht liep van 0,24 tot 1,80 log(s). Voor beide grootheden blijkt de relatie tussen glistening hoeveelheid en strooilicht bij goede benadering proportioneel te zijn. In Hoofdstuk 6 wordt een model voorgesteld om in de kliniek het effect van glistenings op de strooilichtwaarde uit te kunnen rekenen, uitgaande van beide grootheden, als volgt:

Strooilicht parameter s = 0,0046 x aantal glistenings per mm^2 [$graden^2$/ steradiaal]

Strooilicht parameter s = 215 x surface portion [$graden^2$/ steradiaal]

Dit model wordt in hoofdstuk 6 vergeleken met de theorie van Mie voor lichtverstrooiing.[20] Bij de gevonden gemiddelde diameter van 5 micrometer wordt een zeer goede overeenstemming geconstateerd tussen de Mie berekening en de meetresultaten.

Hoofdstuk 6 is belangrijk om vast te stellen hoe op fysische gronden begrepen kan worden dat glistenings nauwelijks effect kunnen hebben op gezichtsscherpte en contrast gevoeligheid, terwijl glistenings wel visueel belangrijk kunnen zijn door hun strooilichteffect. Het voorgestelde model geeft een nauwkeurige schatting van het strooilichteffect van glistenings, en kan gebruikt worden in de kliniek, als directe analyse van IOLs met glistenings niet mogelijk is. Hoofdstuk 6 geeft ook uitleg hoe schijnbare tegenstrijdigheden in de literatuur begrepen kunnen worden. Interpretatieproblemen zijn in belangrijke mate veroorzaakt door het gebruik van diverse graderingssystemen. Verschillende subjectieve graderingssystemen blijken onvoldoende gedefinieerd te zijn om betekenisvolle vergelijking mogelijk te maken.[25-35] Er zijn ook meer kwantitatieve graderingssystemen voorgesteld.[36-41] Echter, in verschillende studies wordt het werkelijke nummer in de belangrijke hoogste graad slechts aangeduid als "meer dan" een bepaald aantal (b.v. meer dan 50 of 200 per mm^2). Een dergelijke gradering is van toepassing op 19% van de gerapporteerde gevallen. Als we deze gradering vergelijken met de resultaten van Hoofdstuk 6 wordt duidelijk dat een kans gemist is.

De beperkingen van de graderingsmethodes kunnen vermeden worden door een exacte kwantitatieve benadering zoals voorgesteld door Colin en Orignac.[27] Dit zou een nauwkeurige vergelijking tussen verschillende studiecentra mogelijk maken waarbij ons model goede diensten zou kunnen bewijzen. In de discussie van Hoofdstuk 6 wordt voor het beperkte aantal studies waarvoor enige schatting gegeven kan worden, gevonden dat de resultaten goed overeenstemmen met het voorgestelde model. Er zijn ongeveer 2.500 glistenings per mm^2 nodig om de strooilichtwaarde voor de normale 70-jarige ooglens te bereiken. Hiermee wordt duidelijk dat alleen bij zeer grote hoeveelheden glistenings visueel storende strooilicht effecten te verwachten zijn die kunnen leiden tot klachten van de patiënt.

In **Hoofdstuk 7** worden resultaten gepresenteerd van strooilichtmetingen en microscopische waarnemingen aan 74 IOLs die eerder waren verkregen uit pseudofake ogen van hoornvliesdonoren. Slechts 41% van deze lenzen blijkt lage strooilichtwaardes te hebben. Geen van deze lenzen heeft een waarde in de buurt van de strooilichtwaarde voor een cataracteuze lens, maar in 14% van de gevallen is er wel sprake van een aanzienlijke strooilichtverhoging, met waardes hoger dan die voor een 70-jarige normale ooglens. Waarnemingen met de spleetlamp en lichtmicroscopie laten verschillende mogelijke oorzaken van strooilicht zien, waaronder "snowflake-like degeneration",[42] "surface deposits",[43] en glistenings.[24] Strooilicht is verhoogd bij de IOLs die deze afwijkingen vertonen, maar de mate waarin strooilicht verhoogd is verschilt in afhankelijkheid van het type afwijking en het type IOL. In totaal 8 typen IOL werden geïdentificeerd (61 van de 74 IOLs). De "snowflake-like deposits" en de "surface deposits" lijken belangrijk te zijn voor lichtverstrooiing, want dit zijn de afwijkingen die voorkomen in de 2 typen IOLs met de hoogste strooilichtwaardes. In 3 van de 8 typen IOLs komen glistenings voor, maar deze typen laten veel lagere strooilichtwaardes zien dan de twee typen met "snowflake-like degereration" en "surface deposits". Slechts 3 lenzen met glistenings laten strooilichtwaardes zien die hoger zijn dan typisch is voor een 70 jaar oude normale ooglens.

In 14% van de bestudeerde IOLs blijkt strooilicht aanzienlijk verhoogd te zijn, in overeenstemming met het getal van 10% bij pseudofakie zoals gevonden in de literatuurstudie van Hoofdstuk 3. Aangezien in alle lenzen met aanzienlijk verhoogd strooilicht een vorm van degeneratie van de IOL gevonden wordt, maakt deze studie duidelijk dat IOL degeneratie een mogelijke reden is waarom strooilicht in pseudofakie vaak verhoogd is. In Hoofdstuk 3 wordt gevonden dat slechts 6% van alle pseudofake ogen een strooilichtwaarde heeft die lager ligt dan die van een jong gezond oog. In Hoofdstuk 7 wordt echter gevonden dat in 41% van de IOLs strooilicht heel laag is. Geconcludeerd moet dus worden dat degeneratie van IOLs slechts een gedeeltelijke verklaring kan zijn voor de strooilichtverhoging in pseudofake ogen. Nader onderzoek is nodig om andere mogelijke oorzaken te vinden.

Hoofdstuk 7 maakt duidelijk dat veranderingen en degeneratie van het materiaal waaruit de IOL bestaat belangrijk kan bijdragen aan strooilicht, maar dat de verschillende afwijkingen verschillen in hun strooilichteffecten. "Surface deposits" en "snowflake-like degeneration" geven meer strooilicht dan glistenings zoals die *in vivo* in ogen gevonden worden. Deze bevindingen kunnen behulpzaam zijn voor clinici om beter de symptomen van de patiënt te begrijpen die geassocieerd zijn met degeneratie van de IOL, en een ondersteuning van de beslissing om tot explantatie van een opake lens over te gaan.

In **Hoofdstuk 8** wordt onderzoek beschreven naar strooilichteffecten bij multifocale contactlenzen. Bij multifocale contactlenzen wordt meestal met een zogenaamd multi-zone ontwerp gelijktijdig verte en nabij gezichtsscherpte mogelijk gemaakt voor presbyope patiënten.[44-46] de lens bevat dan verschillende deelgebieden die verschillen in brekende kracht. De (abrupte) overgangen tussen deze gebieden worden verondersteld een potentiele bron van lichtverstrooiing te zijn.[44] Vaak is geconstateerd dat multifocale contactlenzen verblindingsklachten geven.[47] Strooilicht bij gebruik van multifocale contactlenzen is echter nog nooit onderzocht. Wij maten strooilicht bij vrijwilligers die 4 verschillende soorten multifocale contactlenzen aangepast kregen, met verschillende optische ontwerpen. Strooilicht werd gemeten met farmacologisch verwijde pupillen omdat de verblindingsklachten vooral 's nachts, als de pupillen fysiologisch verwijd zijn, optreden. Hoofdstuk 8 laat zien dat de multifocale contactlenzen gemiddeld een strooilichtverhoging van 0,06 log eenheden veroorzaken ten opzichte van het oog zonder contactlens. Er wordt echter gevonden dat er significante verschillen tussen de verschillende contactlenzen bestaan. Een van de 4 onderzochte soorten lens geeft een verhoging van 0,11±0,07 log eenheden ten opzichte van het oog zonder contactlens. De contactlenzen werden met een microscoop onderzocht onder spleetlamp belichting met geïnverteerde stralengang. Daarbij bleken de transities tussen de verschillende zones geen sterke lichtverstrooiing te geven. Echter, de lenzen van de groep met de hoogste strooilichtwaarde lieten lichtverstrooiing in de bulk van het materiaal zien.

De studie van Hoofdstuk 8 geeft een sterke aanwijzing dat de sprongen in de brekende kracht tussen de verschillende zones geen belangrijke bronnen van strooilicht zijn, in tegenstelling tot wat in de literatuur verondersteld wordt. [44] Een van de 4 onderzochte soorten contactlens laat een duidelijke strooilichtverhoging zien, maar onderzoek met een spleetlamp laat zien dat de bulk van het materiaal licht verstrooit. Een andere bevinding is dat pupilverwijding (zonder contactlens) ook strooilichtverhoging geeft. De studie maakt duidelijk dat pupilverwijding tot versterkte verblindingsgevoeligheid leidt, iets waar oogartsen en optometristen hun voordeel mee kunnen doen.

In **Hoofdstuk 9** wordt een nieuwe methode voorgesteld om *in vitro* lichtverstrooiing aan IOLs te meten. De methode is gebaseerd op een adaptatie van het klinische toestel voor *in vivo* strooilichtmeting bij patiënten (C-Quant van Oculus).[48, 49] De adaptatie van de C-Quant bestaat uit enige optische componenten waarmee het C-Quant testveld na passage door de te testen IOL wordt geprojecteerd voor het oog van een onderzoeker. Het oog van de onderzoeker ziet echter alleen het centrale bipartite deel van het testveld omdat de strooilicht inducerende ring wordt geblokkeerd middels een diafragma. Op deze manier beïnvloed alleen de IOL het bipartite veld met strooilicht, en niet het oog van de onderzoeker. Zo wordt het oog van de onderzoeker zuiver als optische detector gebruikt. De methode is gevalideerd met 3 onderzoekers, gebruikmakend van filters met geijkte verstrooiingswaardes. De methode is ook gebruikt om lichtverstrooiing in verschillend soorten IOLs te meten, waaronder monofocale zowel als multifocale IOLs.

Hoofdstuk 10 beschrijft een verdere uitwerking van de methode van Hoofdstuk 9, bedoeld om ook spectraal opgelost te kunnen meten. Dit is interessant omdat daarmee iets gezegd kan worden over de effectieve grootte van de licht verstrooiende deeltjes. In geval van heel kleine deeltjes is de lichtverstrooiing zeer sterk van de golflengte afhankelijk (Rayleigh verstrooiing, het blauw van de hemel).[20] In geval van heel grote deeltjes is er vrijwel geen golflengte-afhankelijkheid (het wit van de wolken). Het licht van de C-Quant wordt door interferentiefilters geleid. Vanwege hun geringe bandbreedte van 10nm neemt de intensiteit van het beschikbare licht sterk af, en is lichtversterking nodig om de test te kunnen uitvoeren. Daartoe wordt een camera gebruikt die het bipartite testveld op een monitor projecteert. De onderzoeker kijkt dus niet rechtstreeks naar het geprojecteerde bipartite veld, maar naar de monitor. Ook deze methode is gevalideerd met licht verstrooiende filters, waarbij zowel Rayleigh verstrooiing (met een commerciële verstrooiingsstandaard) als grote-deeltjes-verstrooiing getest is.[50, 51] In deze studie zijn tevens 11 IOLs onderzocht die afkomstig zijn van humane ogen (deels geëxplanteerd bij patiënten, deels uit donor ogen). Bovendien is de strooilichtwaarde bij 2 verschillende verstrooiingshoeken gemeten (Hoofdstuk 6), want de hoekafhankelijkheid van verstrooiing geeft ook een indicatie van de deeltjesgrootte. De spectrale, zowel als de hoek-opgeloste analyse laten zien dat bij de bestudeerde IOLs grote deeltjes overheersen bij de lichtverstrooiing.

Hoofdstukken 9 en 10 introduceren een relatief eenvoudige en effectieve methode voor strooilicht-bepaling bij IOLs. Het gebruik van een klinisch beschikbaar instrument maakt de methode toegankelijk voor breed gebruik, terwijl voorheen *in vitro* strooilichtmeting alleen in gespecialiseerde laboratoria mogelijk was. Een mogelijke toepassing is het testen van IOLs voorafgaande aan implantatie. Een voordeel van de voorgestelde methode is dat de strooilichtwaarde zoals die functioneel in de klinische routine bepaald wordt, direct vergelijkbaar is met de strooilichtwaarde die met de voorgestelde *in vitro* methodes verkregen wordt. Een dergelijke directe vergelijking kan b.v. voorkomen als de IOL geëxplanteerd wordt van een patiënt met strooilichtklachten.

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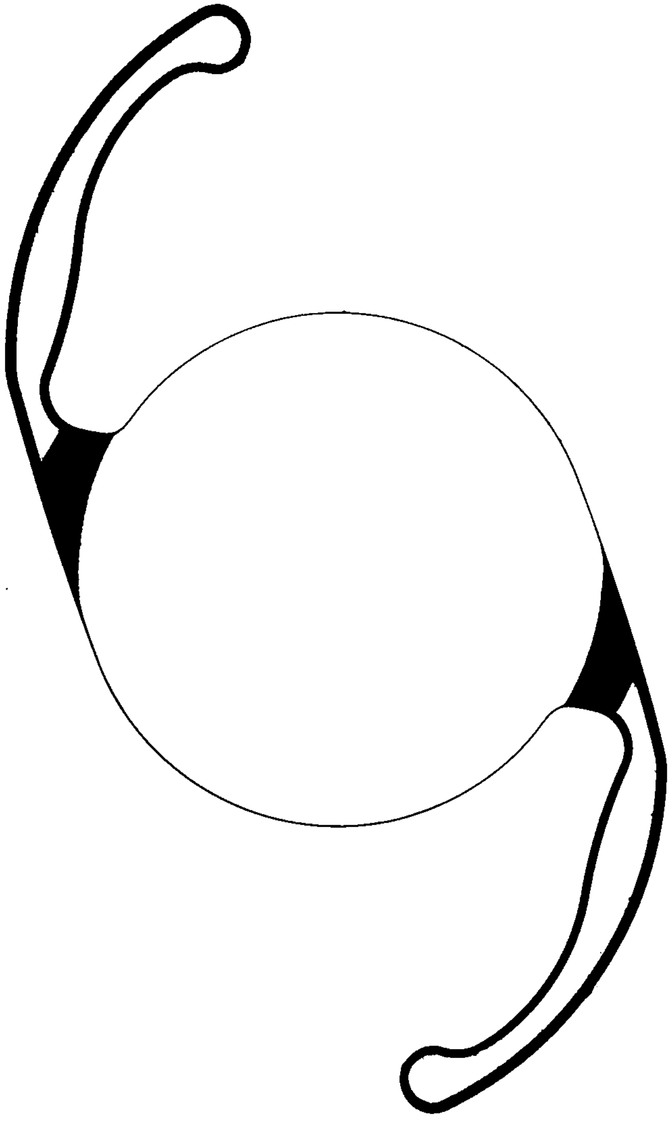

Appendix

ABBREVIATIONS

BC	Base curvature
BEP	Break-even point
BPM	Black Pro Mist
BSS	Balanced slat solution
CC	Compensation comparison
CCD	Charge-coupled device
CDVA	Corrected distance visual acuity
CI	Confidence interval
CIE	Commission Internationale de l'Eclairage
CS	Contrast sensitivity
CT	Center thickens
CW	Content of water
DA	Total diameter
DC	Direct compensation
Deg.	Degree
D/N	Distance/Near
ESD	Expected standard deviation
FU	Follow-up
GS	Grading system
IOL	Intraocular lens
L	lens
logMAR	Logarithm of the minimum angle of resolution
log(s)	Logarithm of the straylight parameter
Mo	Month
n	Refractive index
Nd:YAG	Neodymium-doped Yttrium Aluminum Garnet
p	Significance level
PCO	Posterior capsule opacification
PMMA	Polymethylmethacrylate
PSF	Point spread function
R^2	Coefficient of determination
RGB	Rigid gas permeable
RI	Refractive index
RLE	Refractive lens exchange
RMSD	Repeated-measures standard deviation
s	Straylight parameter
SD	Standard deviation

sr	Steradian
VA	Visual acuity
y	Year
θ	Scatter angle
λ	wavelenght

PHD PORTFOLIO

PhD student: Grzegorz Łabuz	Promotor: Prof. dr. Jan C. van Meurs
Institution: Rotterdam Ophthalmic Institute (ROI)	Co-promotors: Dr. Thomas J.T.P. van den Berg,
PhD period: Apr 2014 – Apr 2017	Dr. Nicolaas J. Reus

1. PhD training

	Year	Workload (Hours/ECT)
General courses		
- Fourier analysis for vision science. University of Murcia, L. Thibos (Indiana University School of Optometry, USA)	2014-2015	5 ECTS
- Advanced clinical contactology. University of Murcia, D. López- Alcón	2014	4 ECTS
- Aging of the visual system. University of Murcia, N. López-Gil	2014	4 ECTS
- Ocular pathology of the anterior and posterior segment of the eye. University of Murcia, E. Usón-González	2015	
- Advances in refractive and cataract surgery. University of Murcia, R. Pérez-Cambrodí	2015	4 ECTS
- Applied statistics for optometrists. University of Murcia, J. Sánchez-Meca	2015	4 ECTS
- Biomedical English Writing and Communication, Erasmus MC	2016	3 ECTS
- Scientific Integrity, Erasmus MC	2016	0.3 ECTS
Specific courses (e.g. Research school, Medical Training)		
- Introduction to Zemax. Dr. Ian Wallhead (Anncar Optics, Spain)	2015	32 hours
- Straylight seminar. Rich N. Pfisterer (Laser 2000 GmbH, Germany)	2016	24 hours
Seminars and workshops		
- Weekly scientific seminars, University of Murcia	2014-2015	2 hours
- Weekly scientific seminars, ROI	2014-2017	1 hour
(Inter)national conferences		
- VPO, Wroclaw, Poland	2014	
- XXXII ESCRS, London, UK	2014	
- OC'15 Ageing Eye, Valencia, Spain (oral presentation)	2015	30 hours
- ARVO, Denver, USA (poster presentation)	2015	40 hours
- II International meeting of Lexum Academy, Krakow, Poland (oral presentation)	2015	30 hours
- XXXIII ESCRS, Barcelona, Spain (oral/poster presentation)	2015	70 hours
- OC'16 Ageing Eye, Murcia, Spain (oral presentation)	2016	30 hours
- ARVO, Seattle, USA (oral presentation, 2nd author of the presented poster)	2016	90 hours
- WAEH, Rotterdam, the Netherlands (poster)	2016	10 hours
- VPO, Antwerp, Belgium (oral presentation)	2016	40 hours
- XXXIV ESCRS. Copenhagen, Denmark (2 oral presentations)	2016	90 hours
- Scientific seminar, University of Murcia (3 oral presentations)	2014-2015	12 hours
- Scientific seminar, ROI (3 oral presentations)	2014-2017	12 hours

LIST OF PUBLICATIONS

1. Łabuz G, Reus NJ, van den Berg TJTP. Ocular straylight in the normal pseudophakic eye. J Cataract Refract Surg. 2015 Jul;41(7):1406-15.
2. Lapid-Gortzak R, Łabuz G van der Meulen I, van der Linden JW, Mourits MP, van den Berg TJTP. Straylight Measurements in Two Different Apodized Diffractive Multifocal Intraocular Lenses. J Refract Surg. 2015 Nov;31(11):746-51.
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4. Łabuz G, Reus NJ, van den Berg TJTP. Comparison of ocular straylight after implantation of various multifocal intraocular lenses. J Cataract Refract Surg. 2016 Apr;42(4):618-25.
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8. Łabuz G, Reus NJ, van den Berg TJTP. Light scattering levels from intraocular lenses extracted from donor eyes. J Cataract Refract Surg. (in press).

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ABOUT THE AUTHOR

Grzegorz was born on November 20, 1985 in Zlotoryja (Poland). After completing a study of Optical Engineering at the Faculty of Fundamental Problems of Technology (Wroclaw University of Technology) in 2010, he received a master's degree in Optometry at the same faculty in 2012. In 2010 he also started a 4-year professional career as a clinical optometrist, first at the SPEKTRUM eye clinic, and later at the LEXUM (Optegra) eye clinics. To pursue a scientific career, he moved to the Netherlands in 2014 to join the international Ageye project (Marie Curie Initial Training Network) to conduct research on "Intraocular scattering through different optical designs" at the Rotterdam Ophthalmic Institute, and to obtain a PhD degree. During his PhD study he did a secondment at the University of Murcia, which was also part of the Ageye network, where he received hands-on training in optics, and obtained a master's degree in Advanced Optometry and Vision Science. After completing his 3-year PhD project in 2017, he started a new position at the David J Apple International Laboratory for Ocular Pathology at the University of Heidelberg to continue the intraocular lens research.