**Research Article** Vol. 8, No. 3 | 1 Mar 2017 | BIOMEDICAL OPTICS EXPRESS 1889

Biomedical Optics EXPRESS

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

**GRZEGORZ ŁABUZ,[1,2,*] ELENI PAPADATOU,[3] FERNANDO VARGAS-MARTÍN,[2] NORBERTO LÓPEZ-GIL,[2] NICOLAAS J. REUS,[4] and THOMAS J. T. P VAN DEN BERG[5]**

[1]*Rotterdam Ophthalmic Institute, Rotterdam, Netherlands*
[2]*Facultad de Óptica y Optometría, Universidad de Murcia, Murcia, Spain*
[3]*Optomety Research Group, Facultad de Física, Universidad de Valencia, Valencia, Spain*
[4]*Department of Ophthalmology, Amphia Hospital, Breda, Netherlands*
[5]*Neth. Inst. Neurosc., Royal Netherlands Academy of Arts and Sciences, Amsterdam, Netherlands*
**g.labuz@hotmail.com*

**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.

**OCIS codes:** (290.2648) Stray light; (330.5370) Physiological optics; (290.5820) Scattering measurements; (330.4460) Ophthalmic optics and devices; (170.1610) Clinical applications

## References and links

1. N. Mamalis, J. Brubaker, D. Davis, L. Espandar, and L. Werner, "Complications of foldable intraocular lenses requiring explantation or secondary intervention--2007 survey update," J. Cataract Refract. Surg. **34**(9), 1584–1591 (2008).
2. J. J. Vos, "Disability glare - a state of the art report," Commission International de l'Eclairage Journal **3**, 39–53 (1984).
3. G. Labuz, N. J. Reus, and T. J. van den Berg, "Straylight from glistenings in intraocular lenses: an in-vitro study," J. Cataract Refract. Surg. in press.
4. M. van der Mooren, L. Franssen, and P. Piers, "Effects of glistenings in intraocular lenses," Biomed. Opt. Express **4**(8), 1294–1304 (2013).
5. M. van der Mooren, R. Steinert, F. Tyson, M. J. Langeslag, and P. A. Piers, "Explanted multifocal intraocular lenses," J. Cataract Refract. Surg. **41**(4), 873–877 (2015).
6. L. Werner, J. C. Stover, J. Schwiegerling, and K. K. Das, "Effects of Intraocular Lens Opacification on Light Scatter, Stray Light, and Overall Optical Quality/Performance," Invest. Ophthalmol. Vis. Sci. **57**(7), 3239–3247 (2016).
7. K. K. Das, J. C. Stover, J. Schwiegerling, and M. Karakelle, "Technique for measuring forward light scatter in intraocular lenses," J. Cataract Refract. Surg. **39**(5), 770–778 (2013).
8. L. Werner, J. C. Stover, J. Schwiegerling, and K. K. Das, "Light scattering, straylight, and optical quality in hydrophobic acrylic intraocular lenses with subsurface nanoglistenings," J. Cataract Refract. Surg. **42**(1), 148–156 (2016).
9. T. Van den Berg, L. Franssen, and J. Coppens, "Ocular media clarity and straylight," Encyclopedia of the Eye **3**, 173–183 (2010).
10. L. Franssen, J. E. Coppens, and T. J. van den Berg, "Compensation comparison method for assessment of retinal straylight," Invest. Ophthalmol. Vis. Sci. **47**(2), 768–776 (2006).
11. G. Łabuz, F. Vargas-Martín, T. J. van den Berg, and N. López-Gil, "Method for in vitro assessment of straylight from intraocular lenses," Biomed. Opt. Express **6**(11), 4457–4464 (2015).
12. T. J. van den Berg, "Analysis of intraocular straylight, especially in relation to age," Optom. Vis. Sci. **72**(2), 52–59 (1995).

#280857 https://doi.org/10.1364/BOE.8.001889
Journal © 2017 Received 7 Dec 2016; revised 17 Feb 2017; accepted 17 Feb 2017; published 27 Feb 2017

13. T. J. van den Berg and H. Spekreijse, "Light scattering model for donor lenses as a function of depth," Vision Res. **39**(8), 1437–1445 (1999).
14. J. J. Vos and T. J. Van Den Berg, "Report on disability glare," CIE collection **135**, 1–9 (1999).
15. H. C. van de Hulst, *Light Scattering by Small Particles* (Dover Publications, New York, 1981).
16. T. J. van den Berg and K. E. Tan, "Light transmittance of the human cornea from 320 to 700 nm for different ages," Vision Res. **34**(11), 1453–1456 (1994).
17. J. W. McLaren, W. M. Bourne, and S. V. Patel, "Standardization of corneal haze measurement in confocal microscopy," Invest. Ophthalmol. Vis. Sci. **51**(11), 5610–5616 (2010).
18. G. C. de Wit, L. Franssen, J. E. Coppens, and T. J. van den Berg, "Simulating the straylight effects of cataracts," J. Cataract Refract. Surg. **32**(2), 294–300 (2006).
19. H. Matsushima, Y. Katsuki, K. Mukai, M. Nagata, and T. Senoo, "Observation of whitening by cryo-focused ion beam scanning electron microscopy," J. Cataract Refract. Surg. **37**(4), 788–789 (2011).
20. M. J. Langeslag, M. van der Mooren, G. H. Beiko, and P. A. Piers, "Impact of intraocular lens material and design on light scatter: In vitro study," J. Cataract Refract. Surg. **40**(12), 2120–2127 (2014).

## 1. 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 ($<\lambda$) particles in IOLs, by means of their spectral light-scattering characteristics.

## 2. Methods

### 2.1 Straylight measurements

Straylight was assessed using a commercial straylight meter (C-Quant) adapted for *in vitro* evaluation of light scattering from IOLs. 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 (Fig. 1). A test field (Fig. 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 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].

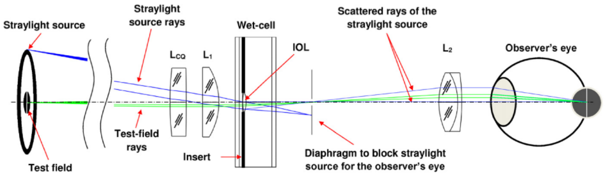

Fig. 1. Schematic illustration of the C-Quant adaptation (not to scale). $L_{CQ}$=lens of the C-Quant, IOL=intraocular lens, L=lens.

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

$$S_{IOL} = 10\hat{}\log(S_{set-up+IOL}) - 10\hat{}\log(S_{set-up})[deg^2/sr] \tag{1}$$

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 $2\sqrt{2}$. 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].

### *2.2 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 ($\lambda^{-4}$) [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 $L_2$ (Fig. 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.

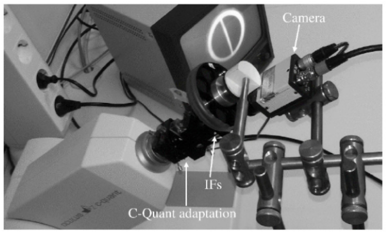

Fig. 2. Complete set-up for assessment of straylight-wavelength dependence of intraocular lenses.

### *2.3 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].

### *2.4 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.

## 3. 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 Fig. 3.

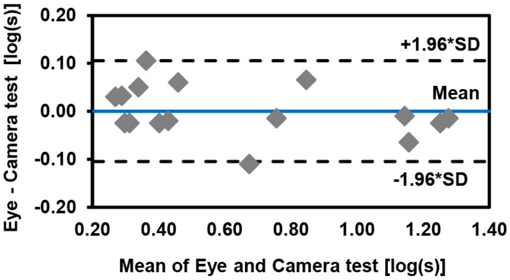

Fig. 3. Comparison between straylight measured with the observer's eye looking at the camera projection ("Camera test") and with the observer's eye looking directly through the C-Quant adaptation ("Eye test").

Figure 4 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.

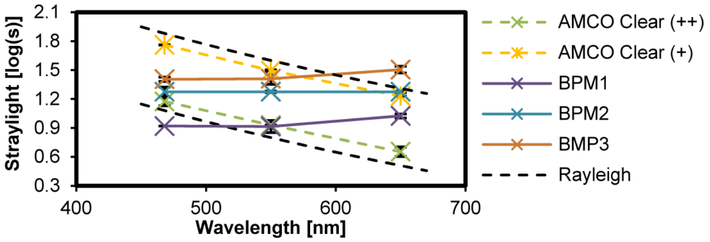

Fig. 4. Validation of the set-up for detection of submicron particles. Straylight of AMCO Clear and Black Pro Mist (BPM) filters was measured with interference filters of 468, 550 and 650 nm. The “+” and “++” signs refer to different dilutions of AMCO Clear. Error bars = standard deviation.

Straylight results of the studied lenses obtained at 2.5° and 7.0° angle are presented in Fig. 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 20y old crystalline lens. The remaining 6 lenses showed increased straylight levels close to that of an aged lens (70y).

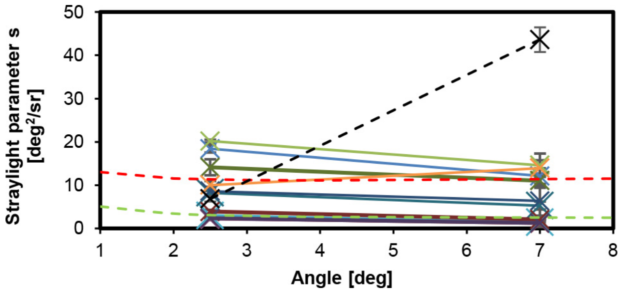

Fig. 5. Straylight of the studied IOLs at 2.5° and 7.0° scatter angle. The dashed green and red line indicate straylight levels of the normal crystalline lens at age 20 and 70, respectively. For comparison, results of AMCO Clear are also presented (dashed black line). Error bars = standard deviation.

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 (Fig. 6).

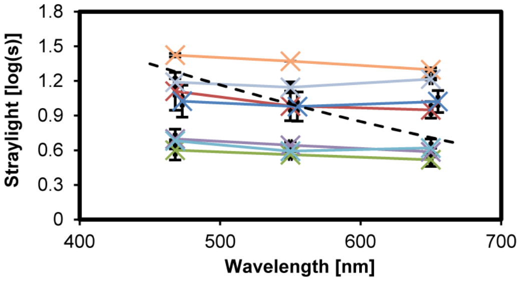

Fig. 6. Analysis of straylight-wavelength dependency of IOLs. Straylight was measured at 7.0° scatter angle. The dashed black line corresponds to Rayleigh-type scatter ($\lambda^{-4}$). Error bars = standard deviation.

## 4. 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 $\lambda^{-4}$ law (Fig. 4). As expected, the BPM filters did not show spectral effects. Figure 3 indicates that the C-Quant adaptation and procedure give 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. 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:

$$s = \theta^{2} \text{x PSF}(\theta) \left[ \text{deg}^{2} / \text{sr} \right] \qquad (2)$$

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 $\theta^2$ 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 (Fig. 5), but no Rayleigh-type dependence on wavelength (Fig. 6). Although (weak) wavelength dependency can be seen in some of the IOLs studied (Fig. 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 (<λ) 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.

## Funding

AGEYE project (608049), Marie Curie Initial Training Network (FP7-PEOPLE-2013-ITN), granted by the European Commission, Brussels, Belgium.