

Master in Photonics

MASTER THESIS WORK

Measurement of the intraocular scattering using
different instruments and parameters.
Comparative study.

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Abstract. Intraocular scattering is the cause of most patient complaints that affect the normal daily activities when they have a cataract. This is the reason why it is important to evaluate when it is the right moment to perform cataract surgery. Nowadays, a variety of subjective methods for classifying opacity, which can allow a somehow standardized procedure, are used by ophthalmologists to diagnose cataracts. Procedures commonly used for this purpose are the visual acuity test, the cataract gradation by means of direct observation of the crystalline lens through a slit lamp, and the Lens Opacity Classification System III (LOCS III). The goal of this study is to perform clinical measurements of intraocular scattering by means of different available commercial instruments that have become common in clinical practice. Specifically, the instruments to be compared will be the C-Quant system, which allows performing a subjective psychophysical assessment, and the OQAS, which is based on the double-pass technique and is totally objective. In this study we analyzed 78 patients with cataracts of different degree and type. The scattering results obtained by means of both instruments and parameters were compared by means of a statistical analysis. The results of the study show that both instruments are good predicting methods of the gradation of different types of cataracts in the clinical practice, although the OSI parameter has shown more statistically significant results. Nevertheless, future studies in this field should focus on a larger number of patients with cortical and subcapsular cataracts in order to find better conclusions.

Keywords: Intraocular scattering, optical quality of the eye, double-pass technique, cataract

1. Introduction

The crystalline lens is one of the most important optical surfaces in the human eye and it should have a good optical quality in order to provide the best possible retinal image and make focusing objects at different distances possible. As time goes by, the lens starts becoming opaque due to the cataracts, increasing the amount of scattered light in the eye, reducing the visual acuity (VA) and causing a degradation of the retinal image quality. For this reason, when a cataract appears it must be extracted. However, so far there has been no agreement on the most adequate technique to predict the visual disturbances associated with a gradation of cataracts. There are several subjective procedures commonly employed by the ophthalmologists to evaluate cataracts. One of these methods is the classical visual acuity test LogMAR (Logarithm of the Minimum Angle of Resolution), but it is not a complete method to predict cataracts due to the different illumination conditions during the test and the daily activities. A second one is the slit-lamp examination, which consists of the direct observation of the lens by means of the slit-lamp from which a first gradation of the state of every cataractous eye is assessed. In this examination, 0 is a clear lens, 1 mild cataract, 2 moderate cataract and 4 severe cataract. The third one is The Lens Opacities Classification System III (LOCSIII), which is one

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of the most representative methods in research [1]. Although the analysis considers different aspects like color, grade of opacification or cataract type, the final decision strongly depends on the subjective criterion of the ophthalmologist and depends on the type of cataract. These two last methods might increase the difficulty of a direct interpretation.

Moreover, other commercial and more specific approaches such as C-Quant instrument (Oculus GmbH, Wetzlar-Dutenhofen, Germany) measure, in an accurate and subjective way, the amount of straylight on the retina caused by light scattering in a patient's eye through a psychophysical assessment, and quantify the absolute intraocular scattering by means of the value as $\log(s)$ [2-3]. In recent years, a new optical method has been introduced: the Optical Quality Analysis System (OQAS, Visiometrics SL, Spain), which is based on the double-pass technique (DP) [4]. It has been shown to be a useful tool to analyze the optical quality of the eye for discriminating healthy eyes from early abnormal ones [5] and to quantify intraocular scattering by means of the OSI parameter (Objective Scatter Index) [6]. Furthermore this system has been used to evaluate the optical quality of eyes in several situations, such as in patients implanted with monofocal [7] [8] and multifocal IOLs, or after refractive surgery [9-11].

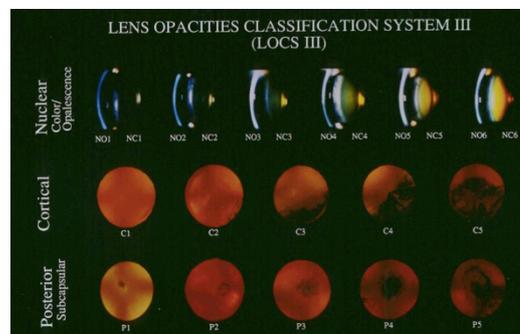
The purpose of this study is to compare the analysis of the intraocular scattered light in cataractous patients by means of different available commercial instruments, namely, the C-Quant system, which provides an absolute intraocular scattering value ($\log(s)$), and OQAS, which uses the OSI parameter obtained from the retinal image quality. In addition, we will compare these results with those obtained using more conventional subjective procedures such as the LOCS III gradation.

2. Subjective Methods

There are a variety of subjective methods for classifying cataracts that may allow a somehow standardized procedure by ophthalmologists. The most representative ones are the slit-lamp examination (figure 1a), which is the direct observation of the lens, and the LOCS III (figure 1b). This subjective gradation of cataracts is based on the direct observation of the cataract with a slit-lamp or biomicroscope.



(a)



(b)

Figure 1. (a) Slit-lamp. (b) The LOCS III standardized chart showing graded nuclear opalescence/nuclear color in the top row, cortical cataract in the middle row, and posterior subcapsular cataract in the bottom row.

The classification evaluates four features: nuclear opalescence (NO), nuclear color (NC), cortical cataract (C), and posterior subcapsular cataract (P). Nuclear opalescence (NO) and nuclear colour (NC) are graded on a decimal scale from 1 to 6, based on a set of six standardized photographs (figure 1b). Cortical cataract (C) and posterior subcapsular cataract (P) are graded on a decimal scale from 1 to 5, based on a set of five standardized photographs each [13]. Nuclear and cortical cataracts are often diagnosed as CN. In general, the prevalence of nuclear and cortical cataracts is more common than posterior subcapsular ones in the population [14].

Another relevant test is LogMAR, which is used to justify the reduction of vision that is affecting the daily life of the patient. It consists of a back-illuminated test with a chart, which has been designed using high contrast lettering. In clinical research, it is more common than

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Snellen test due to right reliability in patients with a reduced VA. In addition, another test to detect cataracts is CSV-1000E (VectorVision, Greenville OH, USA). It allows finding de values of the contrast sensitivity (CS) at different spatial frequencies at different contrasts and provides the contrast sensitivity the function (CSF). It is the most worldwide used test (figure 2) and consists of four rows with tests of different spatial frequencies (3, 6, 12 and 18 cycles/degree) and contrasts measured in mesopic conditions [15]. The human contrast sensitivity function shows a typical band-pass shape peaking at around 4 cycles per degree with sensitivity dropping off at either side of the peak. This shows that the human visual system is able to detect gratings of 4 cycles per degree at a lower contrast than at any other spatial frequency.

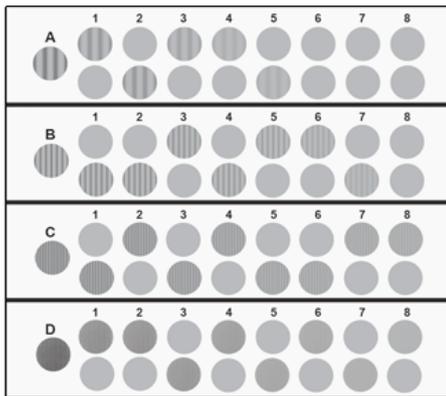


Figure 2. CSV-1000LV test

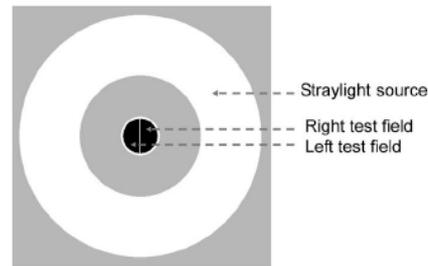


Figure 3. Stimulus layout for the compensation comparison method

3. Compensation Comparison Method: C-Quant

C-Quant (Oculus GmbH, Wetzlar, Germany) is a commercial instrument to evaluate intraocular scattering. It is called the “compensation comparison” method and is based on direct compensation Method [16]. In the C-Quant, the light is presented in one of the two test field halves (randomly chosen), whereas no compensation light is present in the other test field half (figure 3) [17]. As a result, two flickers, which differ in modulation depth, are perceived: one results from straylight only (the response is recorded as 1), while the other is a combination of straylight and compensation light (the response is recorded as a 0), flickering in counter phase with this straylight. Simplified, the procedure runs as follows: during the test, a series of limited duration stimuli that differ in the amount of compensation light are presented in test field 1. The patient’s task is a forced-choice comparison between the two half fields to decide which half flickers more intensely. The subject’s responses are recorded by means of two push buttons, representing the left and right test fields. Using the psychophysical model for this flicker comparison task, a psychometric curve is fitted to the subject’s responses and provides the straylight parameter ($\log(s)$) [17]. In addition, it has Esd value, which proves to be an efficient tool to detect unreliable measurements. Esd is the expected standard deviation of the individual measurement value in case of repeated measurements [18]. If $Esd < 0.08$ and $Q > 1$, the reliability of the result is considered to be good or if $Esd < 0.08$ and $Q > 0.5$, the reliability is considered to be acceptable, but a warning is given if $Esd > 0.08$ or $Q < 0.5$.

4. Double-pass System (OQAS)

Optical Quality Analysis System OQAS (Visiometrics S.L., Terrassa, Barcelona) is a clinical instrument based on the double-pass technique. It was developed by the Centre for Sensors, Instruments and Systems Development (CD6) of the Technical University of Catalunya (UPC) in collaboration with the Laboratorio de Óptica de la Universidad de Murcia (LOUM). The OQAS consists of an optical head and laser equipment, a computer workstation and a custom designed software. It allows measuring the joint effect of high-order optical aberrations and scattered light, thus providing complete information on the optical quality of the patient’s eye in the clinical practice. This system is based on an unequal pupil configuration with a 2 mm diameter in the entrance pupil and a variable diameter for the exit pupil. In this study, the

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diameter of the exit pupil used was set to 4 mm for the whole procedure. The main parts are shown in a schematic representation of the instrument (Figure 3). An infrared diode laser ($\lambda = 780 \text{ nm}$) coupled to an optical fiber is collimated (CL) and, the light after passing the entrance pupil (P1) enters the eye. After reflection in the retina and double-pass through the ocular media, the light is reflected in a beam splitter and goes through the exit pupil (P2) to be recorded in a digital camera. We obtained DP images of every eye at best focus, corrected internally by the instrument by an optometer, which ranges from -8D to +6D. External cylindrical lenses are required for astigmatism $>0.50 \text{ D}$.

From the double-pass image, OQAS computes the Modulation Transfer Function (MTF), which represents the loss of contrast as a function of the spatial frequency. The system also provides other parameters related to the MTF function that account for the eye's optical quality, such as the OQAS values (OVs) at contrasts of 100%, 20% and 9%. Furthermore, the system allows the objective evaluation of the intraocular scattered light by means of the OSI parameter. It is based on the analysis of the intensity distribution in the outer parts of the DP image and it is defined as the ratio between the integrated light in the periphery and in the surroundings of the central peak of the DP image. In the particular, the central area selected was a circle of a radius of 1 minute of arc, while the peripheral zone was a ring set between 12 and 20 minutes of arc. The standard software program, provided with the OQAS system, incorporates the option of manually modifying the energy of the laser to obtain the best retinal images in the eye that we used for mature cataracts, which was used in several eyes during the process. Artal et al. [6] established the following classification according to the OSI value: below 1 correspond to normal eyes with low amounts of scattering, between 1 and 3 corresponds to older eyes with associated scatter of an early cataract, between 3 and 7 corresponds to developed cataracts that should undergo surgery, and higher than 7 to eyes with severe cataracts with large amount of intraocular scattering.

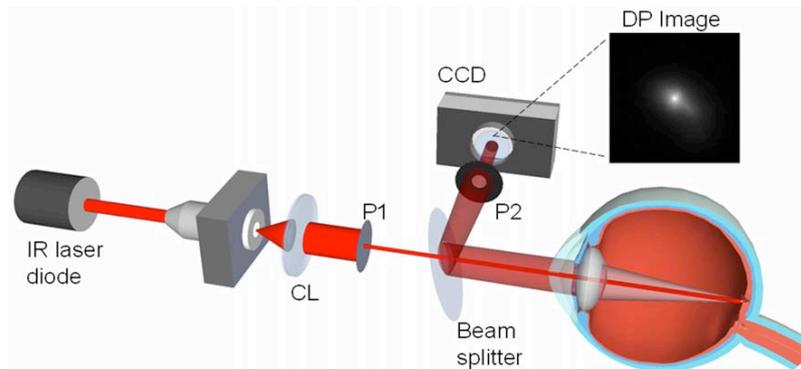


Figure 3. Schematic representation of the double-pass method.

5. Patients and Methods

This study included the analysis of 103 eyes with different types and grades of cataracts, 24 patients were excluded taking into account the criteria for inclusion for each test. Finally, 78 eyes of 52 patients were included in the study (37 right eyes, and 41 left eyes), 41 female and 37 male between 47 and 85 years (average \pm standard deviation (sd): 68.24 ± 8.3 years). Patients' examination was performed in the Hospital de Terrassa under supervision of two ophthalmologists (Dr. Assad, and Dra. Almudí), and an optometrist (J.C. Ondategui). All subjects gave their written informed consent after receiving a written and verbal explanation of the nature of the study following the tenets of the Declaration of Helsinki.

Inclusion criteria for the group of cataract patients were subjects with no history of ocular pathology (except cataracts) or surgery, the spherical refractive error was automatically measured and corrected by the double-pass system by means of a motorized optometer within a range of -8.00 to +6.00 D external cylindrical lenses are required for astigmatism $>0.50 \text{ D}$. Retinal image quality was measured by means of the OQAS for a 4 mm artificial pupil with the subject's retinal image optimally focused.

The best spectacle-corrected visual acuity LogMAR of the eyes ranged from -0.20 to 1.25

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(average±sd: 0.17±0.27), spherical manifest refractive error ranged from -8.00 to +5.75D and the cylinder from 0.00 to 3.00D. The grade and type of cataract was: 24 eyes of nuclear cataract (30.4%), 27 of mixed nuclear (34.2%), 9 eyes of cortical (11.4%) and 18 of posterior subcapsular (24.1%).

Patients were analysed with the following protocol:

- Patient's medical history (age, AV, refractive error and pathologies)
- AV LogMAR at 3 meters with the refractive error corrected
- Measurement of the CSF (CSV-1000, VectorVision, Greenville OH, USA).
- Determination of the OSI parameter by means of the OQAS system.
- Determination of the log(s) by means the C-quant
- Dilution of the pupil with a drop of Colircusí Tropicamida 5ml, *Alcon Cusí, S.A.* (each ml contains 10 mg of Tropicamida) every 10 minutes with a maximum of 3 drops.
- Classification the degree of opacification using the LOCS III classification system

6. Statistical analysis

Statistical analysis was performed using SPSS IBM statistics 20 for Macintosh. The results were expressed as the mean ± the standard deviation (SD). A *p* value less than 0.05 were considered to be statistically significant.

The ANOVA test was used to evaluate the normal distribution of all variables. Balanced analysis of variance was used to analyze the influence on the results of sphere, cylinder, eye, sex, and age.

7. Results

The OSI, log(s), LogMAR and SC parameters were obtained for the 78 eyes included in the study, which were also classified into the different grades and types of cataracts using the LOCS III system. For nuclear cataracts and mixed nuclear cataracts the eyes were classified according to the opalescence grade in groups NO2-NO6 and according to nuclear color in groups NC2-NC6. For cortical cataracts, they were classified into C2-C4 groups, and for posterior subcapsular cataracts, into P2-P4. Table 1 shows the distribution of the number of eyes classified into every group.

Table 1. Distribution of the number of eyes classified according the groups

	n	Nuclear Opalescence					Nuclear Colour				
		NO2	NO3	NO4	NO5	NO6	NC2	NC3	NC4	NC5	NC6
Nuclear Cataract	24	2	4	13	5	0	2	6	8	7	1
Mixed Cataract	27	3	5	13	5	1	1	9	9	6	2
Cortical Cataract						Posterior Subcapsular Cataract					
	n	C1	C2	C3		n	P1	P2	P3		
	9	4	3	2		18	7	6	5		

Figure 4 shows the correlation between log(s) and OSI values for all types of cataract, (a) all OSI values are included, and (b) when OSI values >8 are removed. When we considering all types of cataract, the Pearson correlation between log(s) and OSI is statistically significant ($r=0.339$ and $p=0.002$), but inconsistencies appear when a high degree of cataract and OSI is high. When such values are removed, a better correlation ($r=0.559$ and $p<0.001$) is obtained.

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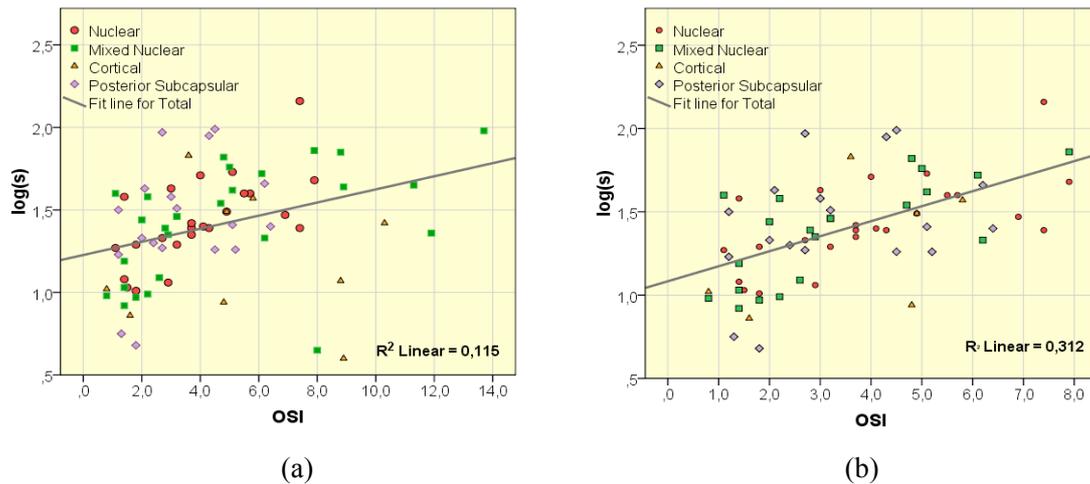


Figure 4. OSI values and log(s), and linear regression: (a) taking into account all analyzed eyes, (b) taking into account the eyes with OSI values <8.

Figure 5 shows the comparison between the average OSI and s values for each group, being $s = \exp(\log(s))$.

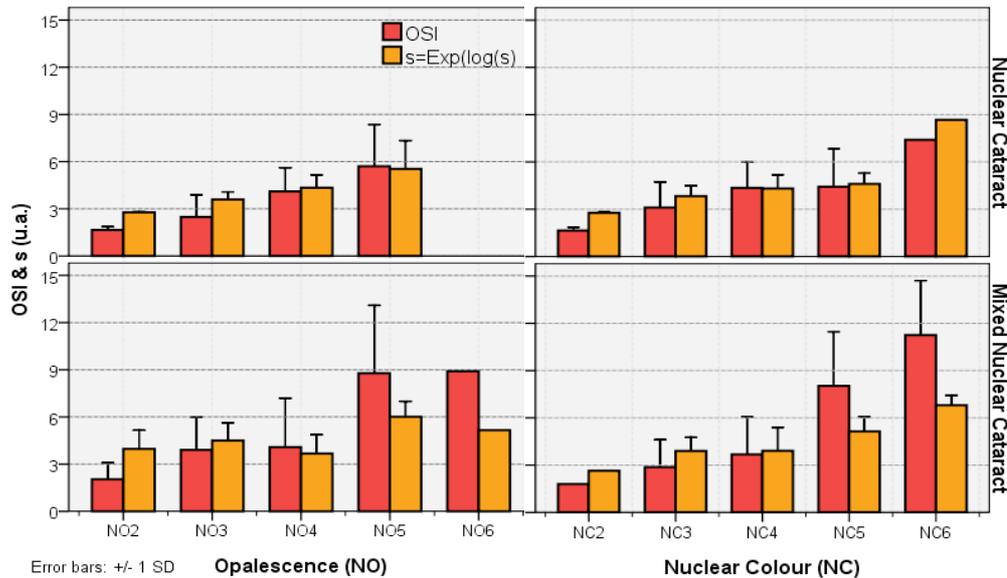


Figure 5. Average OSI values and s values for the different degrees of cataracts according opalescence (NO) and Nuclear Color (NC).

For nuclear cataracts, the average OSI values \pm sd for each opalescent group (NO): 1.65 ± 0.21 for the NO2 group, 2.48 ± 1.42 for the NO3 group, 4.11 ± 1.51 for the NO4 group and 5.70 ± 2.66 for the NO5 group. For the same groups, the average values of log(s) are: 1.02 ± 0.01 for the NO2 group, 1.27 ± 0.14 for the NO3 group, 1.45 ± 0.19 for the NO4 group and 1.68 ± 0.28 for the NO5 group. As for the Nuclear Color (NC) in the nuclear cataract, the average values of OSI are: 1.65 ± 0.21 for the NC2 group, 3.10 ± 1.64 for the NC3 group, 4.35 ± 1.64 for the NC4 group, 4.43 ± 2.41 for the NC5 group, and 7.40 for the NC6 group. For the same groups, the average values of log(s) are: 1.02 ± 0.01 for the NC2 group, 1.33 ± 0.17 for the NC3 group, 1.44 ± 0.21 for the NC4 group, 1.52 ± 0.15 for the NO5 group, and 2.16 for NC6 group.

For mixed nuclear cataracts, the average OSI values \pm sd are: 2.03 ± 1.07 for the NO2 group, 3.90 ± 2.09 for the NO3 group, 4.08 ± 3.12 for the NO4 group, 8.78 ± 4.32 for the NO5 group, and 8.90 for the NO6 group. For the same groups, the average values of log(s) are: 1.34 ± 0.33 for the NO2 group, 1.48 ± 0.25 for the NO3 group, 1.25 ± 0.33 for the NO4 group, 1.78 ± 0.16 for the NO5 group, and 1.64 for the NO6 group. As for the NC in mixed nuclear cataracts, the average

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values of OSI are: 1.80 for the NC2 group, 2.87±1.75 for the NC3 group, 3.68±3.38 for the NC4 group, 8.03±3.43 for the NC5 group, and 11.25±3.46 for the NC6 group. For the same groups, the average values of log(s) are: 0.97 for the NC2 group, 1.34±0.23 for the NC3 group, 1.30±0.40 for the NC4 group, 1.62±0.19 for the NO5 group, and 1.92±0.09 for NC6 group.

Figure 6 shows the correlation between log(s) and OSI values separate in nuclear cataract group and mixed nuclear cataract group, both show statistically significant Pearson correlation ($r=0.654$ and $p=0.001$) for nuclear cataract group (left), and $r=0.707$ ($p<0.001$) for mixed nuclear cataract group (right).

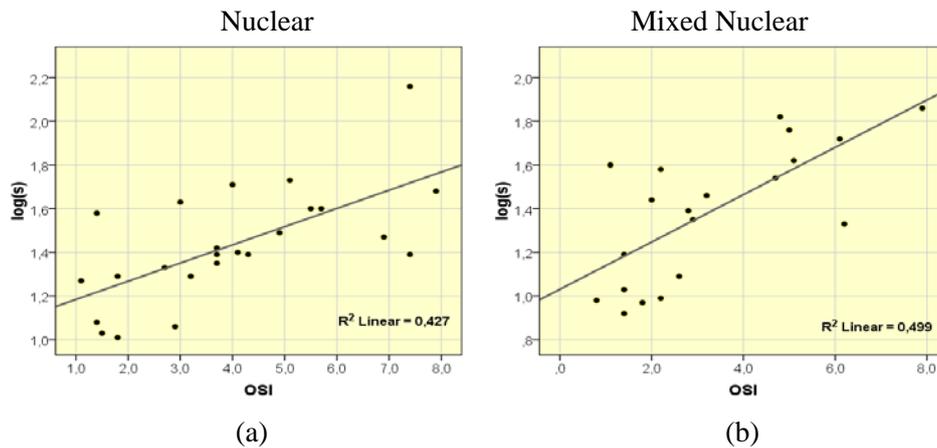


Figure 6. OSI values and log(s), and linear regression for nuclear cataract (a), and mixed nuclear cataract (b).

Table 2 shows the correlation among different parameters that assess scattering (CS, LogMAR, log(s), and OSI) for the nuclear cataract and mixed nuclear cataract. A good correlations are obtained between log(s), OSI, and CS 3 c/deg for all type the nuclear cataract (NO and NC). Regarding mixed nuclear cataracts, there are a significant correlations between NO and NC and log(s), OSI and LogMAR. In addition, the C gradation correlates statistically not only with all the mentioned parameters but also to all the CS frequencies except with log(s).

Table 2. Pearson correlation r between CS (3, 6, 12, and 18 c/deg), LogMAR, log(s), and OSI, in NO and NC groups for the Nuclear cataract (up) and Mixed Nuclear (bottom), * is statistically significant (95%). ** is statistically significant (99%). In brackets, p values.

Cataract	LOCS III		CS				LogMAR	log(s)	OSI
			3 c/deg	6 c/deg	12 c/deg	18 c/deg			
Nuclear	NO	r	-0.456*	-0.308	-0.264	-0.120	0.419	0.685**	0.596*
		(p)	(0.025)	(0.143)	(0.213)	(0.575)	(0.052)	(0.000)	(0.002)
	NC	r	-0.405*	-0.224	-0.192	-0.042	0.118	0.688**	0.500*
		(p)	(0.050)	(0.292)	(0.370)	(0.844)	(0.600)	(0.000)	(0.013)
Mixed Nuclear	NO	r	-0.209	-0.199	-0.119	-0.076	0.531*	0.274	0.532*
		(p)	(0.296)	(0.321)	(0.555)	(0.707)	(0.005)	(0.167)	(0.004)
	NC	r	-0.118	-0.203	-0.180	-0.033	0.690**	0.534*	0.717**
		(p)	(0.556)	(0.310)	(0.370)	(0.870)	(0.000)	(0.004)	(0.000)
	C	r	-0.392*	-0.440*	-0.384*	-0.440*	0.505*	0.069	0.673**
		(p)	(0.043)	(0.021)	(0.048)	(0.022)	(0.008)	(0.731)	(0.000)

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Figure 7 shows the average OSI and s values for different degrees of cortical and posterior subcapsular cataracts. For the cortical cataracts, the average values of OSI±sd are: 2.70±1.83 for the C1 group, 8.00±2.79 for the C2 group, and 7.35±2.19 for the C3 group. For the same groups, the average values of log(s) are: 1.16±0.45 for the C1 group, 1.33±0.23 for the C2 group, and 1.09±0.69 for the C3 group.

For the posterior subcapsular cataract group, the average values of OSI±sd are: 2.36±1.35 for the P2 group, 3.28±1.82 for the P3 group, and 4.72±1.10 for the P4 group. For the same groups, the average values of log(s) are: 1.27±0.45 for the P2 group, 1.52±0.35 for the P3 group, and 1.54±0.32 for the P4 group.

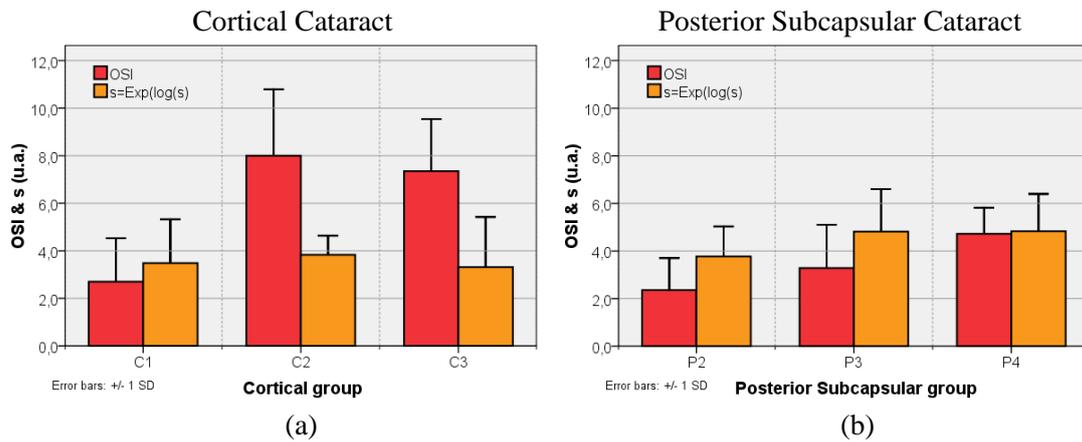


Figure 7. Average OSI and s values for the different degrees of cataracts, cortical groups (a) and posterior subcapsular groups (b).

Figure 8 shows the correlation between OSI and log(s) for cortical and posterior subcapsular cataract. There is no statistically significant Pearson correlation for both cortical cataracts group ($r=0.524$ and $p=0.286$) (left), and for posterior subcapsular cataract group ($r=0.359$ and $p=0.144$) (right).

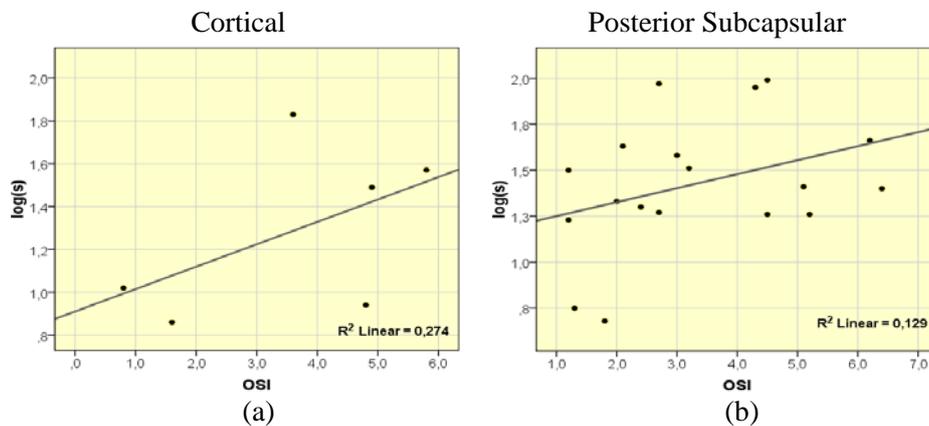


Figure 8. No significant correlation between OSI and log(s) for cortical cataract (a) and posterior subcapsular cataract.

Table 3 shows the differences among groups when CS, LogMAR VA, log(s), and OSI are compared with cortical and posterior subcapsular by LOCSIII are shown Table 3. For cortical cataracts 12 c/deg CS is significant, whereas for posterior subcapsular ones, LogMAR and OSI parameters are so.

Table 3. Pearson correlation r values between CS (3 c/deg, 6 c/deg, 12 c/deg, and 18 c/deg), LogMAR, log(s), and OSI, in cortical and posterior subcapsular cataracts types. In brackets, p values. * is statistically significant (95%).

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Cataract	LOCS III		CS				LogMAR	log(s)	OSI
			3 c/deg	6 c/deg	12 c/deg	18 c/deg			
Cortical	C	r	-0.348	-0.326	-0.702*	-0.279	0.573	-0.030	0.676*
		(p)	(0,359)	(0,392)	(0,035)	(0,467)	(0,107)	(0,938)	(0,045)
Posterior Subcaps.	P	r	0,331	0,100	0,267	0,330	0,485*	0,326	0,575*
		(p)	(0,180)	(0,693)	(0,284)	(0,181)	(0,041)	(0,186)	(0,013)

Contrast sensitivity gets worse with each LOCS III gradation for all types of cataracts but the impact is not uniform with gradation (Figure 9). Graphic (c) shows the impact is more uniform for cortical groups, where deterioration is similar for every frequency. For the rest of groups, such deterioration responds in a more chaotic way depending on spatial frequency. Graphics (a) and (c) show how the first stages in nuclear cataracts present less CS deterioration than in cortical and posterior subcapsular ones.

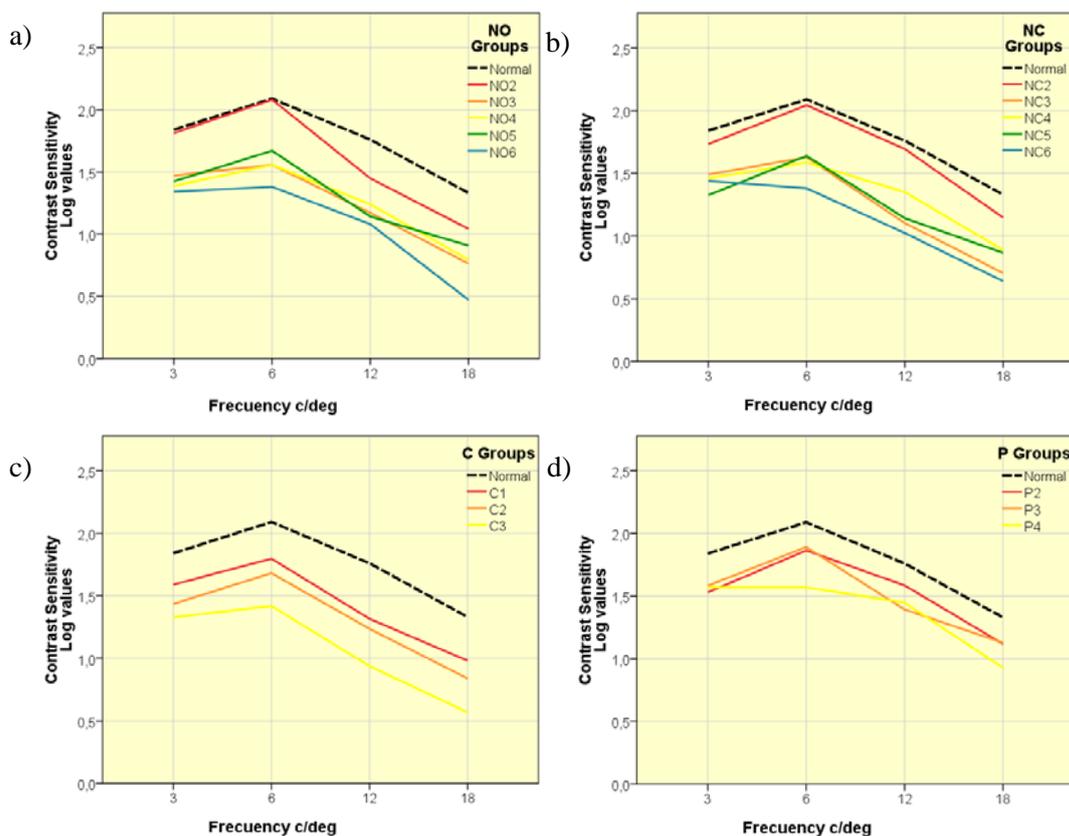


Figure 9. Contrast Sensitivity for different groups of degrees of cataracts obtained by LOCS III.

8. Conclusions

In this study the measurement of intraocular scattering by means of different available commercial instruments C-Quant system (subjective instrument) and the OQAS (objective instrument) were performed. The scattering results obtained by log(s) and OSI parameters were compared by means of a statistical analysis. In general, we obtained a good correlation between them for all degree and type of cataracts. However, for a high degree of cataracts and high OSI values are not so good but get better when the OSI values < 8 are removed. Instead, if different kinds of cataracts are treated separately, we found good correlations for nuclear cataracts and mixed cataracts groups, but no statistically significant differences can be observed for cortical

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and posterior subcapsular groups. In the case of the cortical group, the number of patients is not large enough in order to extract conclusions of the results.

Finally, it should be noted that contrast sensitivity decreases with cataract degree, but it does not seem a good predictor of cataract gradation either, as it depends on the type of cataract and on the frequency. The most affected type of cataract, even in early stages, is the subcapsular one. The results of the study show that both instruments are good predicting methods of the gradation of different types of cataracts in the clinical practice, although the OSI parameter has shown more statistically significant results. Nevertheless, future studies in this field should focus on a larger number of patients with cortical and subcapsular cataracts in order to find better conclusions.

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