

ORIGINAL ARTICLE

Discrimination between Surgical and Nonsurgical Nuclear Cataracts Based on ROC Analysis

Clemente Paz Filgueira^{1,2}, Roberto F. Sánchez^{1,2}, Elisa M. Colombo^{1,2},
Merixell Vilaseca³, Jaume Pujol³ and Luis A. Issolio^{1,2}

¹*Departamento de Luminotecnia, Luz y Visión, Facultad de Ciencias Exactas y Tecnología, Universidad Nacional de Tucumán, Tucumán, Argentina,* ²*Instituto de Investigación en Luz, Ambiente y Visión, CONICET-UNT, Tucumán, Argentina,* and ³*Center for Sensors, Instruments and Systems Development (CD6), Universitat Politècnica de Catalunya, Terrassa, Barcelona, Spain*

ABSTRACT

Purpose: The aim of this article is to propose a quantitative methodology for determining a criterion to discriminate the nonsurgical nuclear cataract from the surgical one taking into account objective measures of intraocular scattering in patients with good visual acuity (>0.6).

Methods: Two groups of subjects were taken into account: a control group and a group with nuclear cataracts. At a first stage, eyes belonging to the cataract group were classified into “nonsurgical” and “surgical” cataracts by ophthalmologists at their clinical settings. At a second stage a double-pass instrument was also used to determine the objective scatter index (OSI) at the laboratory. Receiver operating characteristic (ROC) curves were used to analyze OSI values to determine a value able to separate between nonsurgical and surgical cataracts.

Results: We obtained statistically significant differences among the control and both nuclear cataract groups ($p < 0.05$). ROC curves determined an OSI criterion level (of 2.1) to suggest surgery in nuclear cataracts with an area under curve of 0.83, i.e. with 80% of sensitivity and 80% of specificity.

Conclusions: ROC analysis allows separating both groups of nuclear cataract, and we determined a value of OSI in nuclear cataract quantification for surgery.

Keywords: Surgical nuclear cataract, ROC analysis, double-pass instrument, objective scattering index

INTRODUCTION

A cataract increases the intraocular diffusion, generating visual disturbances that can severely affect the daily performance of a person.¹ Some of the early cataract signs include poor night vision, glare, diplopia, contrast loss and reduction of the perceived brightness, and all of them can appear without generating a significant decrease in the visual acuity.² Patients with cataracts particularly complaint about bright light sources such as car headlights or sunlight, which produce halos around objects, reduce visibility and can derive in temporary blindness.

Because of this permanent discomfort for the patient, the practitioner needs to have a fast and clear diagnosis, confirming and objectively quantifying the intraocular scattering. Due to the fact that the unique existing treatment for cataract is surgery, the decision of when to deal with the operation is of great importance. For this purpose, ophthalmologists often determine through observation whether cataract development and visual performance reduction are advanced enough or not.

Meanwhile visual performance reduction is usually carried out by means of visual acuity and contrast sensitivity tests,^{3,4} biomicroscopy is mainly required

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Correspondence: Clemente Paz Filgueira, Departamento de Luminotecnia, Luz y Visión, Facultad de Ciencias Exactas y Tecnología, Universidad Nacional de Tucumán, Av. Independencia 1800, San Miguel de Tucumán, Tucumán, Argentina. Tel/Fax: +54 03814361936. E-mail: cpazfilgueira@herrera.unt.edu.ar

to accurately determine the cataract morphology through observation. By means of the analysis of slit-lamp images, it is possible to determine the cataract type and to establish a grade according to the Lens Opacities Classification System (LOCS) III.⁵ Although the diagnosis can often be made without dilating the pupil, the dilation is often useful in cases where pupils are small or when a nuclear cataract is suspected,⁶ and as it is known the use of mydriatics may induce closed-angle glaucoma. Moreover, the slit lamp is also very used in cataract diagnosis since it is a direct method that does not require the active subject participation, even though it must be taken into account that results might be influenced by the skill of the physician. To avoid this dependency and to assist the diagnose, Li and collaborators⁷ presented studies that attempted an automatic grading of nuclear cataracts from slit-lamp images and the development of computer-based systems to diagnose nuclear cataracts.⁸ On the other hand, Scheimpflug imaging, which is a tool for imaging the anterior ocular segment, can also be used to obtain quantitative information on the geometry of the crystalline lens.^{9,10} This technology has recently been shown as an objective and repeatable method for the assessment of lens density in nuclear cataracts as authors have reported a strong correlation between nuclear lens density and LOCS III.¹¹

Nevertheless, these systems based on the direct observation of the lens only assess the backscattered component of the complete intraocular scattered light. Therefore, the cataract grade provided by such systems does not take into account the forward scattering toward the retina, which is the one really affecting the visual capacity.¹

The retinal image analysis through a double-pass (DP) system¹² has recently arisen as a new tool that does not require the delivery of dilation drugs and might be suitable to assess the whole optical information of the eye, including the effect of higher-order aberrations and intraocular scattering.^{13,14} From this technique an objective scattering index (OSI) proposed by Artal *et al.*¹⁵ can be computed. This parameter takes into account the forward-scattered light and has been validated in several studies.^{16–18} Other studies have suggested the usefulness of this parameter in the clinical prediction of intraocular scattering,^{16,19,20} and it has been shown to be useful for grading nuclear, cortical and posterior subcapsular cataracts.^{15,21} Regarding aberrations, it has been shown that uncorrected defocus and astigmatism can strongly affect OSI,¹⁵ and to avoid this problem all measurements must be performed with the corrected refraction. When comparing DP images with those provided by spatially resolved methods like Hartmann–Shack wavefront sensor, it can be seen that in eyes with mild to high amount of scatter, wavefront sensors might overestimate image quality,

whereas the DP technique produces a more accurate description of the optical quality.¹⁴ Moreover, this DP technique has been successfully used in the evaluation of the ocular optical quality in patients with keratitis,²² uveitis²³ and dry eye²⁴ and after refractive surgery²⁵ among other studies.²⁶

As different cataract types produce different kinds of opacities that modify the backward- and forward-scattering balancing,¹ it is important to analyze each of them independently. In this study we analyzed eyes with nuclear cataracts, which are usually associated with aging. Therefore, it is very important to precisely assess their evolution and to obtain reliable information about when surgery is recommended. We compared the medical decision of operating a nuclear cataract based on the classical clinical evaluation and the OSI measurements. The goal was to introduce receiver operating characteristic (ROC)²⁷ analysis to determine a criterion level to differentiate between two cataract stages (nonsurgical cataracts [NSC] and surgical cataracts [SC] with good visual acuity). For this, we took the already-mentioned advantages of an objective system for measuring intraocular scattering as well as ROC curves, which are widely used in clinical and diagnostic medicine^{28,29} and biostatistics as assistance in making decisions.^{30,31}

MATERIALS AND METHODS

Subjects

Two different groups of patients were enrolled in the study: a cataract and a control group. The cataract group consisted of 10 subjects (20 eyes) with a mean age (\pm SD) of 68 ± 9 years old (ranging from 50 to 85). The control group included data from 26 observers (47 eyes) with a mean age of 34 ± 9 years old (ranging from 23 to 58).

The inclusion criterion in the cataract group considered those eyes that presented some opacity grade exclusively in the nucleus of the crystalline lens in a relative wide range regarding the level of scattering with a corrected visual acuity (CVA) higher than or equal to 0.6. On the other hand, the control group consisted of eyes without opacities in the crystalline lens and $CVA \geq 1$. Patients included in the study did not present ocular diseases other than the cataract itself at the moment of the experiment and had not suffered other ocular diseases previously (such as glaucoma, retinopathies and keratoconus). Patients who had been undergoing refractive surgery were also excluded.

Every patient was informed of the subject of the study, and a written informed consent was obtained, following the tenets of the Declaration of Helsinki.

Clinical Evaluation Procedure

The clinical evaluation of patients included a first stage performed by three ophthalmologists (WA, LP, EF) at their clinical setting. Examinations included autorefractometry; subjective manifest refraction; and determination of the noncorrected visual acuity (NCVA), the CVA and the stenopeic visual acuity. Observations through slit lamp were also carried out, which helped to determine the cataract type, its location in a lens scheme and its density according to LOCS III. From these data and having a previously agreed criterion, the practitioner had to separate between SC and NSC. The second stage was carried out at the laboratory of visual optics of the Universidad Nacional de Tucumán and included the intraocular scattering quantification using DP images and the corresponding computation of the OSI (see the next section for more information). Measurements were performed with the best refractive correction to avoid the influence of aberrations in the computation of the OSI, as discussed in Introduction.

DP Images Acquisition and Processing: Objective Scatter Index

As already mentioned, the system to quantify intraocular scattering was based on DP images. These images were recorded using a commercial instrument (the Optical Quality Analysis System, Visiometrics S.L., Terrassa, Spain),¹³ whose schematic layout is shown in Figure 1. The instrument acquires a retinal image that corresponds to a point-source object

(LD: laser diode; $\lambda=780\text{ nm}$) by means of a CCD camera (CCD1), after reflection on the retina and DP through the ocular media. The patient's refraction is internally corrected by the instrument using an optometer that consists of two lenses (L3, L4) and two mirrors (M2, M3), allowing the capturing of the DP images at the best focus. The entrance pupil has a fixed diameter of 2 mm. The instrument also has an artificial and variable exit pupil (ExP) controlled by a diaphragm wheel, whose image is formed on the patient's natural pupil plane. In this work we fixed the ExP at a value of 4 mm. Furthermore, near-infrared light is used in the DP system because it is more comfortable for the subject and provides retinal image quality estimates that are comparable to those obtained with visible light.³²

From each DP image, the OSI is calculated and provides an estimation of the amount of intraocular scattering.¹⁵ This parameter is computed as the ratio between the amount of light recorded inside an annular area between 12 and 20 min of arc and that recorded within 1 min of arc of the central peak. A similar methodological approach was proposed by Westheimer and Liang,³³ who measured an index of diffusion strongly tending to increase with the age. The choice of the angles from which OSI is computed is based on the results obtained in a previous study,¹⁵ in which authors found a maximum correlation between OSI values and a standard cataract gradation (LOCS III) using this configuration in patients with different grades of nuclear cataracts. In the present study, each OSI value was calculated by averaging six DP images that were acquired sequentially. Furthermore, the presented data are the average of five OSI determinations.

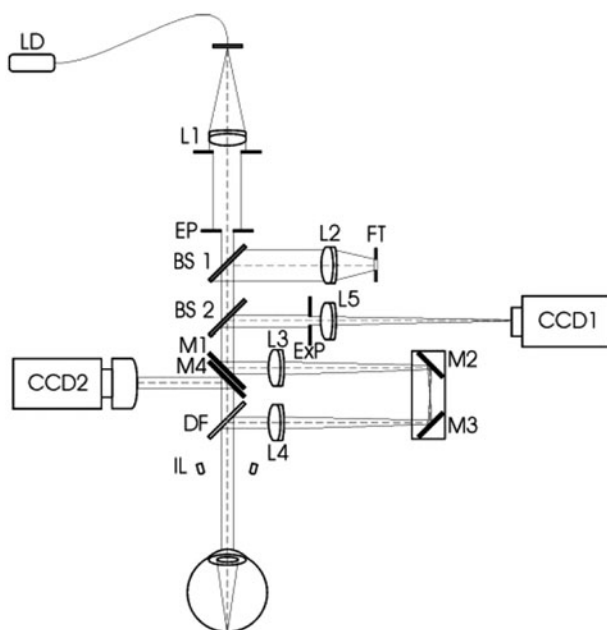


FIGURE 1. Schematic diagram of the DP instrument¹⁴.

Statistical Analysis

The data were analyzed using the Minitab Statistical Software[®] 16.1.0 (Minitab Inc., State College, PA). Comparisons were considered to be statistically significant for p values <0.05 (95% confidence interval). For testing data normality the Shapiro–Wilk test was used. Comparisons between the control group (CG) and the two cataract groups (NSC and SC) were performed by means of the Mann–Whitney nonparametric median test. ROC²⁷ curves were computed with MedCalc[®] 12.7.0.0 (MedCalc Software, Ostend, Belgium) to establish a separation criterion between NSC and SC groups. The ROC analysis is based on the ROC curves,³⁴ whose axes are sensitivity (power to identify positives) and specificity (power to identify negatives), which vary with the criterion level. The goal is to determine the optimum criterion level, i.e. the point in the curve where sensitivity and specificity are maximums.

TABLE 1. Sample size, age, CVA and OSI (objective scattering index) of the groups considered in this study.

Groups	Sample size (number of eyes)	Mean age (years)	CVA (mean)	OSI (median)
Control (C)	47	34	1.0	0.45
Nonsurgical cataract (NSC)	10	70	0.9	1.8
Surgical cataract (SC)	10	66	0.8	2.68

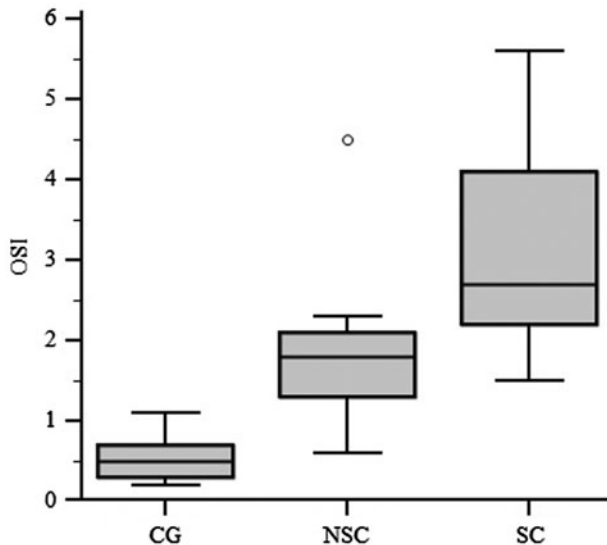


FIGURE 2. OSI values for the three groups: CG, NSC and SC groups. The box plots show five statistical descriptors: maximum, third quartile, median, first quartile and minimum.

RESULTS

Table 1 summarizes the sample size, age, CVA and OSI of each group considered in this study, i.e. the CG and the two cataract groups (NSC and SC). Figure 2 shows OSI data from eyes of the CG and the two cataract groups (NSC and SC) using box plots. The distribution of OSI in all the groups was asymmetric, and for this reason the median was considered for comparisons between them. It can be seen that SC group sampling generally presents OSI values higher than the NSC group, which in turn are higher than those of the CG.

The median corresponding to the CG was 0.45, while the medians were 1.80 and 2.68, respectively, for the NSC and SC groups. Furthermore, statistically significant differences could be established among the three groups ($p < 0.05$).

Considering that the OSI observed in the SC group was higher than that in the NSC group, a specific OSI value was objectively determined to discriminate, according to the medical criterion, between patients who should not undergo surgery and those who should undergo surgery. Figure 3 shows the probability density function of the NSC and SC groups. It can be seen that the curves cross each other at an OSI

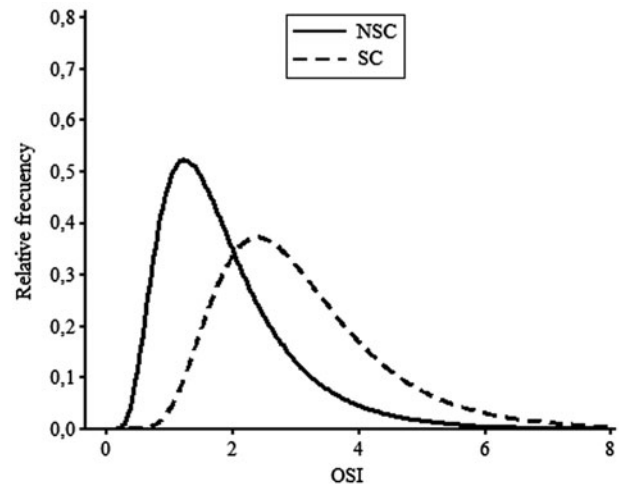


FIGURE 3. Probability density functions of the NSC and SC groups.

value close to 2, which is a first approximation to separate NSC and SC.

According to the aim of this article, ROC curves were used to look for an optimum criterion level between nonsurgical and surgical cataracts.

Figure 4 shows the ROC curve corresponding to OSI data from NSC and SC groups. The area under curve of the obtained ROC curve was of 0.830, which is a measure of the power of the test and represents, in this case, the probability for a randomly selected SC to have a higher OSI value than a randomly selected NSC. The optimum criterion level obtained was an OSI value of 2.1, which implies 80% of sensitivity and 80% of specificity. This criterion implies a predictive value of a positive (PV+), i.e. the probability of needing surgery with an OSI value higher than 2.1, of 80% and a predictive value of a negative (PV-), i.e. the probability of not needing surgery with an OSI value lower than 2.1, of 80%. Likewise, the analysis showed that OSI values higher than 2.1 are four times more likely to be found in SC than in another without this condition (LR+, positive likelihood ratio); similarly, an OSI value lower than 2.1 is four times more likely to be obtained in NSC than in one whose nuclear cataract is sufficiently developed to suggest the extraction and replacement of the crystalline lens (LR-, negative likelihood ratio). Figure 5 shows an interaction diagram between individual OSI values corresponding to all eyes analyzed and the criterion level proposed.

DISCUSSION

In this study we assessed the cataract grade through the OSI both in healthy subjects with normal vision and in patients with cataracts. At the first stage, experimented practitioners characterized the set of eyes with cataracts into two groups depending on whether they needed surgery or not. The obtained results showed OSI values increasing from normal

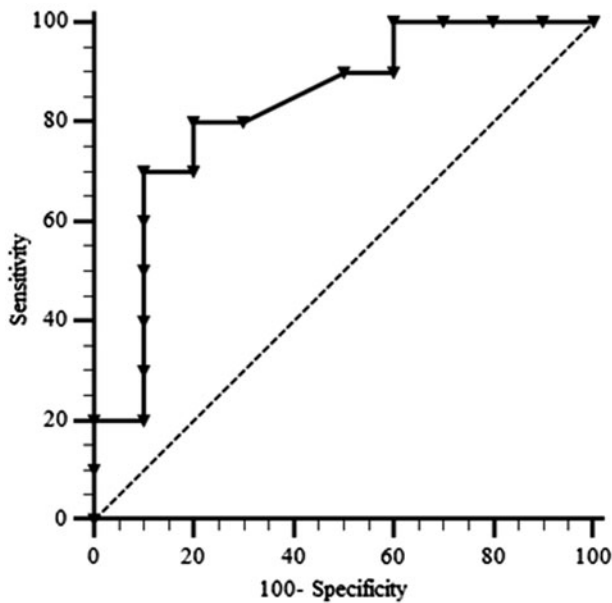


FIGURE 4. ROC curve for NSC and SC groups. As a reference, a curve with an area under curve of 0.5 has been plotted (dashed line).

eyes included in the CG to eyes with cataracts. Furthermore eyes classified as NSC presented lower OSI values than those of the SC group. These results fairly agree with previously performed studies in which nuclear cataracts were graded according to the degree of scatter¹⁵ as follows: values of OSI below 1 were considered normal eyes; OSI values between 1 and 3 were linked to old eyes or early cataracts; OSI values between 3 and 7 corresponded to mature cataracts that should undergo surgery and OSI values higher than 7 corresponded to eyes with severe cataracts. The CG median, i.e. without cataracts, was 0.45. This value is in the low range defined as normal in the previous classification. In turn, both cataract group medians (NSC and SC) were 1.80 and 2.68, respectively. Therefore the eyes belonging to the NSC group were located within the second group, described as old eyes or those with an early cataract. The eyes of the SC group are linked to OSI values placed in the boundary between the second group and the third one, corresponding to OSI values between 3 and 7 or, equivalently, mature cataracts that should undergo surgery. However, in this study we found that eyes with OSI values between 2 and 3 could also be candidates to undergo surgery. We identify two possible reasons to explain this difference in the surgical criterion level: first, in our study we limited the inclusion criteria to those eyes with $CVA > 0.6$, while Artal et al.¹⁵ do not declare restrictions in this respect. Second, the method used to determine an OSI value for discriminating between surgical and nonsurgical cataract is different because we used ROC curve analysis whereas Artal et al. did not.

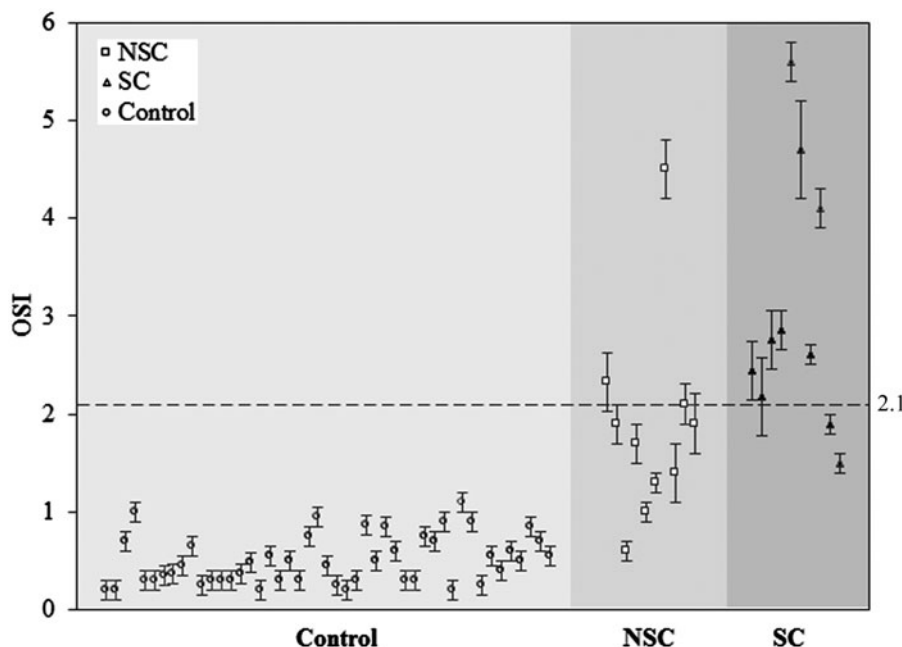


FIGURE 5. Interaction diagram between individual OSI values and the criterion level. Each individual value and error bar is the average and standard deviation of five measurements.

In this work we included subjects with CVA higher than or equal to 0.6. In cases where high opacity levels with significant decreased CVA are diagnosed, surgery is generally advised. But when there are opacities combined with good CVA, the decision becomes more difficult and practitioners need complementary tools to support what they decide. It is also relevant to study these cases considering the current trend to operate when the patient still has a CVA higher than 0.5.

On the other hand, taking advantage of the ROC analysis, our results showed that there is a correlation between the OSI parameter and the decision made by the practitioner. Therefore, it was possible to discriminate between NSC and SC by using the OSI parameter in most of the eyes; the limit value in the case of nuclear cataract approached 2.1. In this context, we showed that even in the early cataract range, the OSI measurement had enough sensitivity to separate between nonsurgical and surgical cases.

Therefore, this study demonstrates that in the case of nuclear cataract, the use of DP images might not only help in classifying cataract development but also serve as a criterion for proposing the surgery decision. Furthermore, this technique was performed without the need of pupil dilation, which should be highlighted regarding elderly people who are susceptible to have high intraocular pressure and the use of dilation drugs might increase it even more. Hence, DP instrument can be very useful in the daily ophthalmologic and optometric practice where dilation is often required to characterize cataract properly.

A recent study also presented grade outcomes not only in nuclear cases but also in cortical and posterior subcapsular cataracts, and it reported good percentages of agreement between OSI and LOCS III, revealing the OSI parameter as a complementary tool for the assessment of intraocular scattering.²¹ Therefore it would be desirable to analyze the criteria used in this study to limit the operable range in terms of OSI in other cataract morphologies, as it would be of great help in the diagnosis, particularly in cortical cataract, for which the dilation is always essential to make the diagnosis.

In conclusion, the main novelty of this work is the introduction of a statistical method widely used in several fields, which allows to establish a discrimination criterion between two populations that present overlapping. This tool consists of finding the value for which the diagnosis method has maximum sensitivity and specificity. In this way, the selected value was the one that better discriminated between NSC and SC, i.e. minimizing false-positive and false-negative cases. Implementing a robust and objective method for separating both groups is of great importance since up to now the unique cataract's therapy is lens replacement surgery. Therefore the methodology presented here might be a powerful

objective diagnosis tool supporting the practitioner's decision.

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DECLARATION OF INTEREST

Dr. Jaume Pujol is an investor for Visiometrics S.L. The other authors have no conflict of interest with the companies of instruments used in this study. The authors alone are responsible for the content and writing of the article.

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