Master in Photonics

MASTER THESIS WORK

TEAR FILM QUALITY EVALUATION WITH INTRAOCULAR SCATTERING MEASUREMENTS

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Tear film quality evaluation with intraocular scattering measurements.

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Abstract. A new objective method to diagnose and classify dry eye patients has been carried out in this study. Tear film quality was objectively evaluated by means of a double-pass system in patients with healthy eyes, with some tear deficiency and dry eye patients. Intraocular scattering present in those eyes was studied by analyzing a new parameter called Objective Scatter Index (OSI) obtained with the Optical Quality Analysis System (OQAS), a device based on the double-pass technique. Several complementary subjective clinical exams commonly used to evaluate tear film quality were also performed on patients (dry eye questionnaire, Non-Invasive Break-Up Time (NIBUT), Phenol Red Thread Test and Visual Acuity) in order to correlate them with the OSI parameter. Correlations between OSI and dry eye questionnaire and NIBUT showed that there exists a trend that could help to classify more accurately patients affected by some tear problem.

Keywords: Optical quality, tear film, dry eye, intraocular scattering, double-pass system.

1. Introduction
One of the several parameters that describe an optical instrument is its optical quality. The measurement of it is based on a very simple principle: to analyze the image that is formed through the device at the image plane of it. However, if the goal is to measure the optical quality of a human eye, the procedure becomes more difficult because the image plane is the patient’s retina. Retinal image quality is basically determined by two factors, eye’s aberrations and intraocular scattering\(^1\). The classical solution to obtain information of these factors is to apply psychophysical methods that need active patient’s participation but, fortunately, new objective measurement techniques have appeared to characterize them. For example, clinical instruments built on the Hartmann-Shack wavefront sensor or, newest ones, on the double-pass technique. Both techniques differ in that wavefront sensors can only measure aberrations by means of the estimated wavefront function, while the double-pass technique can measure both, aberrations and, particularly, intraocular scattering\(^2\). This scattering is caused by the interaction of light with molecules or particles that locally change refractive index. The result of it is to randomly modify the direction of light and generate a blurred retinal image. In young eyes, without pathologies, the contribution of this factor to eye’s optical quality and hence patient’s vision, is not important because it is mainly affected by ocular aberrations due to imperfections of optic surfaces, such in size as in position or refractive index. Even so, intraocular scattering becomes important in cases of eyes with incipient or developed cataracts\(^3\).

As it was mentioned above, new technological progress allow to apply objective measurement techniques based on the formation of a point-source image on the retina and the analysis of the
light reflected by it that travels out of the eye. Specifically, the double-pass technique\textsuperscript{4}, which consists of generating an image of a point-source object on patient’s retina and capturing the reflected light after double pass through the ocular media, has been shown as the only method that objectively measures intraocular scattering. This technique was proposed half a century ago as a means of estimating retinal image quality\textsuperscript{5}. Later, the method incorporated various technical innovations\textsuperscript{4} and was shown to provide accurate estimations of eye’s image quality.

Several authors have focused their studies on the double-pass technique to analyze retinal image quality in different situations such as in the normal population as a function of age\textsuperscript{6}, in contact lenses wearers\textsuperscript{7,8}, in LASIK patients\textsuperscript{2}, in cataract patients\textsuperscript{10} and in patients implanted with monofocal\textsuperscript{2,10} and multifocal\textsuperscript{11} intraocular lenses (IOL’s). Retinal image quality is conditioned by every ocular medium which are cornea, aqueous humor, crystalline lens, vitreous humor, retina, etc., but there is another medium that determines retinal image quality and usually is forgotten: tear film. Tear film is a continuous film that covers the outer surface of the cornea, filling in the irregularities of corneal epithelium to convert it into a “perfect” optical surface (as a polished optical surface) and guarantees correct vision. Furthermore, tear film eliminates substances that do not belong to the eye, hydrates, oxygenates and also nurtures the cornea and facilitates the physiological corneal dehydration needed to avoid the formation of edema and, as a consequence, to maintain corneal transparency\textsuperscript{18}. Unfortunately, almost 10-30\% of the population\textsuperscript{13,14} suffer some tear alteration related to dry eye or some of its symptoms (burning, stinging, itching, pain, sensitivity to light, redness, blurry vision, stringy mucus, and/or a feeling that there is a speck of dirt in the eyes)\textsuperscript{13}. Dry eye pathology is defined as a deficiency in tear production or as excessive tear film evaporation that hurts eye surface\textsuperscript{13}. Fortunately, recent preliminary studies\textsuperscript{15} confirm that any irregularity in tear film can cause an increase of intraocular scattering and hence retinal image is deteriorated. There are several methods that allow the quantification of tear film quality, for instance, Schirmer test (small strips of filter paper are placed inside the lower eyelid of each eye during 5 minutes; the eyes are closed. It quantifies the amount of tear), Break-Up Time test, (BUT; tear film is observed under the slit lamp, yellow filter and with a colorant –fluorescein- which is instillated to enhance the contrast. The patient avoids blinking until tiny dry spots develop), Non-Invasive Break-Up Time test, (NIBUT; some bright rings are projected on the cornea by a keratoscope, for instance, and they must keep sharp, while the patient avoids blinking, until tear film is broken) and Phenol Red Thread test (yellow cotton threads are placed inside the lower eyelid of each eye during 15 seconds; the eyes can be closed or not. It quantifies the amount of tear, too). The inconvenience of these methods is that most of them are invasive (Schirmer test, BUT, Phenol Red Test) and therefore the quantification of tear film quality can be erroneous because when the eye detects something that not corresponds to itself, it starts to segregate tear in order to expel the foreign body, so that this “extra” tear is measured at the same time that normal tear and hence this is not an accurate result. Moreover, many of them need the physician or the optometrist subjective observation and evaluation (NIBUT, for instance), so the final results can differ among them. The method that we purpose is absolutely non-invasive and objective; the eye is not touched in any moment and the measurement is carried out by a double-pass clinical based device.

In this study we evaluate the retinal image quality as a function of time with a double-pass system in patients with deficient tear film, taking into account that tear film variations can mainly cause fluctuations in time of intraocular scattering. Our aim is to develop a new double-pass method to objectively estimate and quantify tear film quality by means of the measurement of intraocular diffuse light and consequently, to distinguish among patients with healthy tear and patients affected by dry eye or some kind of tear deficiency.

2. Experimental set up
The double-pass system used in this study is called Optical Quality Analysis System (OQAS)\textsuperscript{16} and was developed by the Centre de Desenvolupament de Sensors, Instrumentació i Sistemes (CD6, Terrassa) in collaboration with the Laboratorio de Óptica de la Universidad de Murcia (LOUM). This instrument is produced and commercialized by Visiometrics S.L., spin-off of the CD6.
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The OQAS (Figure 1) records the retinal image corresponding to a point-source object in near-infrared light, consisting of a laser diode (LD; \( \lambda = 780 \text{ nm} \); Power = 5\( \mu \text{W} \)) coupled to an optical fiber and to a spatial filter (composed by a microscope objective and a pinhole), after reflection on the retina and a double pass through the ocular media. Near-infrared light (IL) is used to illuminate patient’s eye because it is more comfortable for the subject and provides retinal image quality estimates that are comparable to those obtained with visible light\(^{17}\).

![Figure 1. Double-pass experimental setup (Optical Quality Analysis System [OQAS, Visiometrics S.L.]). Red line: First step; Green line: Second step; Blue line: Manual pupil alignment.](image)

This technique is divided in two steps: First, laser beam heads for the eye and second, the retina of the human eye reflects the laser light and a CCD camera captures it. First step: laser beam, which is collimated by lens L1, travels towards entrance pupil (EP) and two beam splitters (BS1, BS2). Next, the beam is reflected by mirror 1 (M1) and passes through a motorized optometer (Badal’s system. It is used to measure the subject’s defocus correction) that consists of two lenses (L3, L4) with a focal length of 100 mm and two mirrors (M2, M3). The distance between lenses is variable; this fact allows the modification of the optical path and hence patient’s spherical refraction is corrected. After the optometer, a dichroic filter (DF) reflects the laser beam and it is focalised on the patient’s retina by the eye’s optics. Second step: approximately 3% of the light that reaches the retina is reflected by itself and returns through the dichroic filter, mechanical optometer and mirror 1 until beam splitter 2 (BS2), which turns the beam 45° and send it to the exit pupil (ExP) of the system. Finally, CCD1, a video camera with a pixel size of 8.4 \( \mu \text{m} \), records the double-pass image. The exit pupil of the instrument is an artificial and variable diaphragm controlled by a diaphragm wheel, whose image is formed on the patient’s natural pupil plane; it will be the effective exit pupil if it is smaller than the pupil of the eye. In this study, the optical quality measurements were performed using a double-pass asymmetrical configuration in order to capture all asymmetries present in the retinal image and a pupil diameter of 4 mm\(^{18}\), which is a standard value used in real clinical studies. On the other hand, pupil alignment is controlled with an additional video camera (CCD2). Infrared LEDs illuminate the eye. The light reflected by the outer surface of the eye is transmitted for the dichroic filter and reflected in mirror 4 (M4). After that, CCD2, which is
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focalised on the conjugate plane of entrance and exit pupils, captures the image. The optics of the system is placed on a bolster that can be vertically and horizontally moved to align the instrument with the patient’s eye.

Moreover, a fixation test (FT) helps the subject during the measurements. It is illuminated with white light; this light is collimated by lens (L2), it crosses beam splitter BS1 and BS2, is reflected in mirror 1, and passes through the Badal’s system and the dichroic filter until the subject’s retina. This fixation test is useful to minimize eye movements and accommodative fluctuations.

In general terms, the commercial version of the system acquires six double-pass images for each measurement, calculates the mean of them, and generates a final double-pass image, which can be considered equivalent to the Point Spread Function (PSF) of an optical system. However, the double-pass image is obtained by double pass of the light through the ocular media and not using a single pass as usual; from the profile of the double-pass image, the optical quality of the eye might be assessed: the lower the width of the profile the better optical quality of the patient’s eye. The system also calculates the Modulation Transfer Function (MTF), which can be directly computed from the PSF by doing a Fourier Transform. The MTF function is widely used to completely determine the quality of an optical system, and represents the loss of contrast produced by the eye’s optics as a function of the spatial frequency. It means, in visual terms, the patient’s capacity to discriminate details of a scene, without taking into account the neurological process that occurs after retinal image formation. In addition, the latest version of this instrument incorporates a new parameter called Objective Scatter Index (OSI), which objectively quantifies intraocular scattering. The OSI parameter is obtained by analyzing the peripheral region of the double-pass image (Figure 2), which is mainly affected by scattered light (basically, aberrations only alter the central part of the retinal image).

![Figure 2. OSI parameter is obtained by analyzing the peripheral region of the double-pass image. Left: Double-pass image; Right: Profile of a double-pass image and region of analysis of OSI.](image)

However, in this study the software of the OQAS system has been modified in order to measure the OSI parameter of the patient’s eye along 20 seconds and therefore, to study scattering variations over time as a consequence of tear film quality changes. During this time, a double-pass image is acquired every 0.5 seconds, obtaining, therefore, 40 retinal images and also 40 OSI values. After that, a graphic of OSI as a function of time is generated; thanks to that we can observe how intraocular scattering changes while the patient does not blink.

3. Methods

In this research, a clinical study has been carried out in order to obtain a practical and reliable method to assess tear film quality by means of a double-pass system.

26 patients are included in this study: a control group of 9 patients (18 eyes) with healthy tear film, a group of 7 patients (14 eyes) which reported some tear deficiency or alteration such as discomfort, and a group of 10 patients (19 eyes) with a clinical diagnosis of dry eye made by the physician. Patients with tear deficiency suffer some of the dry eye symptoms at a low degree of severity, at a specific time of the day and/or when they perform a specific task; patients
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diagnosed by dry eye suffer always/very often all or some of dry eye symptoms at a medium or high degree of severity. The tear deficiency and dry eye patients selected for this study did not have any other eye pathology or general disease that could also alter the eye's optical quality. The patients’ examination was performed at the Hospital Universitari Mútua de Terrassa under supervision of Dr. A. Salvador and Dr. M. J. Romero and at the Centre Universitari de la Visió (CUV) in Terrassa, under the supervision of optometrist J. C. Ondategui

The established protocol of measurement to be performed over patients included the following clinical exams: patient’s anamnesis (medical history), dry eye questionnaire, subjective manifest refraction, visual acuity measurement with (BSCVA, Best Spectacle Corrected Visual Acuity) and without correction (UCVA, Uncorrected Visual Acuity) measured using a standard logMAR test at 3 meters, Phenol Red Thread (PRT) test and Non-Invasive Break-Up Time test (NIBUT) and Objective Scatter Index (OSI) with OQAS.

Dry eye questionnaire is a subjective test on which the patient punctuates the severity of seven dry eye symptoms (0 = symptom not present; 10 = acute symptom). Then, the mean punctuation is assessed to know the dry eye subjective degree according to each patient. Moreover, this test contains two more questions; artificial tear use and daily administration frequency (Figure 3).

The last two tests (PRT and NIBUT) quantify the amount of tear of each subject and evaluate tear quality, respectively. Every test was chosen with the purpose of minimizing, as far as possible, any induced change in tear film of the patient, and therefore, to avoid distortions that could affect posterior OQAS measurements. PRT consists of hanging over each lower eyelid a yellow cotton thread that becomes red when it is wetted by tear during 15s. Therefore, the result of this test is the length (in mm) of the wet portion of the thread that becomes red. Values related to problems of tear quantity are those which are lower than 10mm (in 15 seconds); values higher than 10mm (without contact lenses) are considered normals. On the other hand, NIBUT is performed by using a Placido’s disk (Klein Keratoscope, KEELER, England), an instrument for examining the front surface of the cornea. It is composed of a pattern of alternately black and white concentric rings reflected by the cornea and seen through a lens mounted in an aperture at the centre of the pattern. During this test, the patient must maintain opened the examined eye, without blinking, while the examiner observes the white reflected rings until they become blurred; this means that tear film has broken. Therefore, NIBUT is the time (in seconds) since the patient does not blink until tear film is broken. NIBUT test values below 10 second correspond to eyes affected by some problem about tear quality; in return, values over this value can be considered normal.
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Finally, tear film quality was also analyzed with OQAS. In order to perform optical quality measurements with OQAS, patient’s refraction must be previously corrected: spherical refraction is corrected by the device itself by means of the Badal system and one of the options of the software, called objective refraction, which finds the best focus of the double-pass image; before that, astigmatic refraction must be manually corrected by an outer astigmatic lens. As it was mentioned above, the OSI parameter provided by OQAS during 20 seconds was selected in order to assess tear film quality of patients, since it quantifies the intraocular scattering present in the eye. After some preliminary measurements, we concluded that the valid acquisition range along which the OSI parameter should be analyzed would be between the first retinal image captured after blink and the image recorded before next blink. During this period, it can be assured that the recorded variations in the retinal image and the corresponding OSI values are basically caused by tear film changes. Therefore, the patient was asked to keep the eye open until he/she would need to blink during the measurement. In addition, the eye that was not being measured was kept closed in order to avoid the stimulation of the tear glands and the production of “extra” tear on the non-measured eye, which could affect its posterior measurement because of the abnormal amount of tear.

4. Results

Patients demographics (age, gender), manifest subjective refraction (sphere, cylinder and spherical equivalent) as well as logMAR visual acuity (BSCVA, UCVA) for the three groups of patients are given in Table 1. The mean, standard deviation, and corresponding ranges for these parameters are detailed.

Table 1. Patients demographics, manifest refractive error of eyes and visual acuity (LogMAR) belonging to the control group (healthy eyes), the tear deficiency group and the dry eye group.

<table>
<thead>
<tr>
<th></th>
<th>Healthy eyes</th>
<th>Tear deficiency eyes</th>
<th>Dry eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>21.0 ± 1.3 (19 to 23)</td>
<td>33.3 ± 14.6 (22 to 60)</td>
<td>53.6 ± 17.4 (22 to 75)</td>
</tr>
<tr>
<td>Gender</td>
<td>M 3</td>
<td>F 6</td>
<td>F 0</td>
</tr>
<tr>
<td>Sphere (D)</td>
<td>-1.97 ± 1.56 (-4 to 0)</td>
<td>0.79 ± 3.07 (-2.75 to 6)</td>
<td>0.75 ± 1.99 (-1.75 to 4.5)</td>
</tr>
<tr>
<td>Cylinder (D)</td>
<td>-0.09 ± 0.20 (-0.75 to 0)</td>
<td>-1.05 ± 1.41 (-5 to 0)</td>
<td>-0.75 ± 0.80 (-2.75 to 0)</td>
</tr>
<tr>
<td>SE (D)</td>
<td>-2.01 ± 1.59 (-4 to 0)</td>
<td>0.26 ± 2.67 (-3.5 to 4.875)</td>
<td>0.38 ± 1.79 (-2 to 3.125)</td>
</tr>
<tr>
<td>BSCVA</td>
<td>-0.11 ± 0.12 (0.26 to -0.26)</td>
<td>-0.12 ± 0.12 (0.14 to -0.3)</td>
<td>0.01 ± 0.10 (0.18 to -0.2)</td>
</tr>
<tr>
<td>UCVA</td>
<td>0.18 ± 0.42 (0.96 to -0.2)</td>
<td>0.33 ± 0.46 (1 to -0.22)</td>
<td>0.53 ± 0.36 (1.08 to -0.04)</td>
</tr>
</tbody>
</table>

(D = Diopters; SE = Spherical Equivalent)

Figures 4, 5 and 6 show some representative examples of double-pass data corresponding to patients with healthy tear (control group), patients with tear deficiency and dry eye patients, respectively. Every figure shows the evolution of the double-pass images included in the range of time in which the patient did not blink (valid acquisition range). Moreover, a graph of the evolution of OSI parameter along time is also shown. The corresponding averaged OSI and the standard deviation are also reported.

The OSI evolution over time for all patients belonging to the three examined groups is represented in Figure 7.

Table 2 shows the mean, the standard deviation and corresponding ranges for the averaged OSI value along the valid acquisition range (OSI Mean), the standard deviation of the OSI parameter along the valid acquisition range (OSI Dev), NIBUT, Phenol Red Thread test and dry eye questionnaire for the three groups of analyzed patients.
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**Figure 4.** Sequence of double-pass images and OSI evolution of two representative cases of patients belonging to the control group (with healthy tear film). The averaged OSI and the corresponding standard deviation are also reported.

**Figure 5.** Sequence of double-pass images and OSI evolution of two representative cases of patients with tear film deficiency. The averaged OSI and the corresponding standard deviation are also reported.

**Figure 6.** Sequence of double-pass images and OSI evolution of two representative cases of patients with dry eye syndrome. The averaged OSI and the corresponding standard deviation are also reported.
As a means of determining the statistical significance of the results obtained in terms of OSI among the three groups of patients, a statistical analysis T-test type was performed over the data. P values lower than 0.05 were considered statistically significant. Tables 3 and 4 provide the P values obtained for the OSI Mean and OSI Dev parameters. The results related to OSI Mean parameter showed that groups which present significant differences between them are the

Table 2. Dry eye questionnaire, NIBUT, Phenol Red Thread test, OSI Mean and OSI Dev of eyes belonging to the control group (healthy eyes), the tear deficiency group and the dry eye group.

<table>
<thead>
<tr>
<th></th>
<th>Healthy eyes</th>
<th>Tear deficiency eyes</th>
<th>Dry eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± standard deviation (range)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dry Eye Quest.</td>
<td>0.33 ± 0.60 (0 to 1.71)</td>
<td>3.22 ± 1.22 (1 to 5.29)</td>
<td>4.14 ± 2.38 (1.71 to 7.29)</td>
</tr>
<tr>
<td>NIBUT (s)</td>
<td>14.61 ± 5.67 (6 to 27)</td>
<td>12.43 ± 9.52 (5 to 37)</td>
<td>6.32 ± 1.89 (3 to 10)</td>
</tr>
<tr>
<td>Phenol (mm)</td>
<td>21.72 ± 5.28 (15 to 32)</td>
<td>17.64 ± 3.13 (12 to 22)</td>
<td>19.16 ± 5.81 (9 to 26)</td>
</tr>
<tr>
<td>OSI Mean</td>
<td>0.49 ± 0.22 (0.18 to 0.92)</td>
<td>0.73 ± 0.58 (0.18 to 1.80)</td>
<td>1.40 ± 0.80 (0.47 to 3.37)</td>
</tr>
<tr>
<td>OSI Dev</td>
<td>0.12 ± 0.10 (0.04 to 0.39)</td>
<td>0.13 ± 0.08 (0.05 to 0.35)</td>
<td>0.33 ± 0.37 (0.06 to 1.73)</td>
</tr>
</tbody>
</table>

Table 3. T-test statistics of OSI Mean

<table>
<thead>
<tr>
<th>OSI Mean – P value</th>
<th>Healthy eyes</th>
<th>Tear deficiency eyes</th>
<th>Dry eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy eyes</td>
<td>-</td>
<td>0.166</td>
<td>7.380e-5</td>
</tr>
<tr>
<td>Tear deficiency eyes</td>
<td>-</td>
<td>-</td>
<td>0.013</td>
</tr>
<tr>
<td>Dry eyes</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
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### Table 4. T-test statistics of OSI Dev

<table>
<thead>
<tr>
<th>OSI Dev – P value</th>
<th>Healthy eyes</th>
<th>Tear deficiency eyes</th>
<th>Dry eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy eyes</td>
<td>-</td>
<td>0.963</td>
<td>0.026</td>
</tr>
<tr>
<td>Tear deficiency eyes</td>
<td>-</td>
<td>-</td>
<td>0.049</td>
</tr>
<tr>
<td>Dry eyes</td>
<td>-</td>
<td>-</td>
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</tr>
</tbody>
</table>

control group and the dry eye group (P<0.01) as well as the tear deficiency group and the dry eye group (P<0.05). On the other hand, the control group and tear deficiency group did not present significant differences (P=0.17). The same behaviour is found for the statistics of OSI Dev; in this case, the groups which present significant statistical differences are also the control group and dry eye group (P<0.05) and the tear deficiency group and dry eye group (P<0.05). Once again, the control group and tear deficiency group did not report significant differences.

Figure 8 shows the correlation found between OSI Mean and OSI Dev and the dry eye questionnaire. The two upper graphs include all patients and in the lower ones the patients are classified by groups (healthy eyes - green, tear deficiency eyes - yellow, dry eyes - red) depending on the ophthalmologist diagnostic. Furthermore, OSI parameters have been correlated with more standard tests used to assess tear film quality. Figure 9 shows the correlations of OSI Mean and OSI Dev and the NIBUT test, which gives information of the tear film quality. Finally, the correlation of the OSI parameters and the results of the Phenol Red Thread test, which quantifies the amount of tear, are given in table 10. Finally, figures 11 and 12 show two graphs in which the patients are ordered in function of OSI Mean and OSI Dev individual values and classified depending on the group to which they belong to, by means of the colour code.

### 5. Discussion

As it can be seen in figures 4 to 6, healthy eyes are related to low OSI values over time, patients with tear film deficiency are related to moderate OSI values, while dry eye patients have high OSI values. Furthermore, dry eye patients seem to have larger variations of this parameter than healthy eyes over time.

Again, in Figure 7 dry eye patients (represented in red) seem to be associated with higher values, and healthy tear film eyes (green) with lower ones. However, patients with some tear film deficiency (yellow) overlap among patients of the other two groups, mainly with patients with healthy tear film.

The behaviour described above can be better understood with the numerical analysis of table 2, in which the averaged OSI Mean and OSI Dev parameters are reported. The results obtained state that the averaged OSI Mean is higher in dry eye patients, meanwhile this parameter is intermediate in patients with some tear deficiency and lower in eyes belonging to the control group. Moreover, the averaged OSI Dev parameter is also high for dry eye patients, while in the other two groups is lower and has a similar value. However, the results of the statistical analysis performed (Tables 3 and 4) suggest that there are no statistically significant differences between healthy eyes and tear deficiency eyes in terms of both OSI Mean and OSI Dev, although the comparison among all the other groups present clear differences. This correlates with the trend shown in figure 7, where many of the OSI profiles corresponding to patients with tear film deficiency overlap with the profiles found for eyes of the control group.

Therefore, it can be concluded that these two parameters (OSI Mean and OSI Dev) could be used in order to clinically decide whether an eye should be diagnosed as dry eye or not, and to make a more objective classification of the dry eye syndrome. As shown in the results section, in order to determine the efficiency of the OSI Mean and OSI Dev parameters for the evaluation of the dry eye syndrome, these parameters have been correlated with the dry eye questionnaire, the NIBUT test and the Phenol Red Thread test (Figures 8, 9 and 10).
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Figure 8. OSI Mean and OSI Dev versus dry eye questionnaire punctuation. Upper graphs include all analyzed patients; lower graphs classify patients into tear film groups: green (control group, healthy eyes); orange (tear deficiency group); red (dry eye group).

Having in mind the degree of correlation generally managed in clinical ophthalmological or medical studies, which tends to be very low in comparison to other areas (where do not obtain \( R^2 \) values higher than \( 0.3 \text{-} 0.4 \)), it can be stated that certain correlation (\( R^2 = 0.2396 \)) exists between OSI Mean and the dry eye questionnaire punctuation. On the other hand, the correlation found between OSI Dev and the dry eye questionnaire is much lower (\( R^2 = 0.1283 \)). With this analysis, it can be concluded that dry eye questionnaire punctuations lower than 2 points are normally associated to normal eyes, while higher punctuations are related to eyes with tear problems. In spite of the fact that the correlations are not high, certain trend between OSI Mean and the patient’s subjective perception of dry eye exists as it is shown in Figure 8. It should be remarked that dry eye questionnaire punctuation strongly depends on the subjective perception of the patient analyzed, and that could vary a lot among patients. Therefore, this could be the reason why not better correlations are found between this parameter and the OSI values, which are clearly more objective.

On the other hand, a slight parallelism between OSI Mean parameter and NIBUT has also been detected by observing the correlations shown in Figure 9. High values of NIBUT are often associated to better tear film quality and, usually, to low OSI Mean values. For this correlation, \( R^2 \) is equal to 0.1767. However, there is practically no correlation between OSI Dev and NIBUT (\( R^2 = 0.0636 \)). Therefore, it can be stated that there exist a slight correlation between tear film quality obtained by means of NIBUT test and tear film quality measured with OQAS by means of the intraocular scattering, in particular by applying OSI Mean parameter (OSI Dev does not provide accurate results in this case). At this point, it must be remarked again that NIBUT is a parameter which depends on the subjective evaluation of the clinician or physician, and its value can suffer variations among evaluators. Therefore, the mismatches found between NIBUT values and OSI could be partially attributed to this.

Finally, it can be seen that correlations between Phenol Red Thread values, which inform of the amount of tear, and OSI Mean and OSI Dev parameters do not exist (Figure 10). For this reason, it can be concluded that measurements of tear film carried out by OQAS do not provide information about the amount of tear in the examined eye because this measurement is related to the patient’s tear film quality. In this study tear film quality is mostly reported by means of the dry eye questionnaire and the NIBUT test. Moreover, almost all patients analyzed have Phenol Red Thread test values over 10 mm and hence, they do not suffer a great lack of tear but they have bad tear film quality.
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Figure 9. OSI Mean and OSI Dev versus NIBUT test. Upper graphs include all analyzed patients; lower graphs classify patients into tear film groups: green (control group, healthy eyes); orange (tear deficiency group); red (dry eye group).

Figure 10. OSI Mean and OSI Dev versus Phenol Red Thread test. Upper graphs include all analyzed patients; lower graphs classify patients into tear film groups: green (control group, healthy eyes); orange (tear deficiency group); red (dry eye group).

Figures 11 and 12 show two graphs in which the patients are ordered as a function of OSI Mean and OSI Dev parameters magnitude and classified depending on the group to which they belong to, by means of the colour code. As it can be observed, dry eye patients are mainly placed at the right side of both graphs while healthy eyes are at the left side. Tear deficiency eyes are dispersed along all the range of patients.

As it can be observed in figures 11 and 12, where patients are ordered as a function of OSI Mean and OSI Dev, respectively, that even the described correlations were not very good, the dry eye patients are mainly placed at the right side of both graphs while eyes with healthy tear
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film are located at the left side. Eyes with some tear deficiency are dispersed along all the range of patients. This is an expected behaviour, since the OSI measurement (OSI Mean and OSI Dev) do not provide a solution to classify patients with weak symptoms of tear film from healthy eyes, as it was seen before. However, it is a useful tool to decide whether or not an eye should be diagnosed as dry eye or not.

6. Conclusions
In this study, we evaluated tear film quality along time with a new double-pass based objective procedure in three groups of population: 9 patients with healthy eyes, 7 patients with some tear deficiency and 10 patients affected by dry eye.

Optical quality was assessed using OQAS, a clinical instrument based on the double-pass technique. The eye’s optical quality was analyzed by using the OSI parameter (Objective Scatter Index) provided by OQAS, which quantifies the intraocular scattering. The tear film quality was analyzed by means of the averaged OSI over time (OSI Mean) and its variation in terms of standard deviation (OSI Dev).

The main results show that OSI parameter has a different behaviour regarding the tear film quality of the eye analyzed. Healthy eyes present OSI parameter values between 0 and 1 (OSI Mean = 0.49 ± 0.22) and they are very constant over time (very low OSI Dev value = 0.12 ± 0.10) while patients diagnosed with dry eye show higher OSI Mean values (1.40 ± 0.80) and more variability of this parameter (higher OSI Dev value = 0.33 ± 0.37).

As it has been proved, OSI parameter is more related to tear quality, assessed by means of a dry eye questionnaire and the NIBUT test, than to the amount of tear which can not be measured by OQAS. For that reason, there not exists any correlation between OSI parameter and Phenol Red Thread test.

In conclusion, the results obtained by OQAS (OSI) can help to diagnose dry eye pathology and to establish a new objective classification with advantages to more standard test used nowadays, such as dry eye questionnaire and NIBUT tests. Furthermore, thanks to this new methodology, patients affected by some tear deficiencies can be considered closer to dry eye pathology or more closer to normal eyes classification. Although the correlations obtained in this study between OSI parameters and these tests show that some trends can be established among them.

Future work is oriented to increase the number of analyzed eyes of each group of patients in order to clarify the results, improving correlations and establishing OSI ranges that could be linked with different dry eye levels. Because of that, after the delivery of this MSc thesis, more patients are being analyzed.
References


