Determination of central corneal clearance in scleral lenses with an optical biometer and agreement with subjective evaluation

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ABSTRACT

Purpose: To compare three methods to measure central corneal clearance (CCC) during scleral lens wear: subjective (slit lamp), image processed (ImageJ) and with an optic biometer. The optic biometer technique was validated in comparison to an OCT in the first part of the study.

Methods: Twenty-two eyes (11 subjects) with healthy corneas were recruited. Three measures of OCT with scleral lens and ten measurements of axial length (AL) with IOLMaster with and without lens were performed. For the second part, 61 eyes (35 subjects) enrolled in a clinical study were selected. Measurements of CCC were done with IOLMaster, SlitLamp and ImageJ.

Results: The measurements of CCC indirectly obtained with IOLMaster had a strong correlation with AS-OCT measurements (r = 0.981), showing a mean difference of 122.18 ± 46.05 μm (higher with IOLMaster). Regarding the second part, measurements of CCC were 238.66 ± 95.94 μm, 250.16 ± 124.31 μm and 263.15 ± 90.60 μm, for the IOLMaster, SlitLamp and ImageJ, respectively. The correlations were higher for ImageJ vs Subjective measure (r = 0.891) than for IOL vs Subjective (r = 0.748) and IOL vs ImageJ (r = 0.745). Analysis of differences and correlations between SlitLamp and ImageJ through time showed a mean difference of -32.28 ± 89.95 μm (r = 0.683) at V1month, 12.53 ± 59.46 μm (r = 0.850) at V6months and 11.57 ± 32.95 μm (r = 0.940) at V12months.

Conclusions: It is possible to measure CCC with IOLMaster, considering AL measured with and without lens and lens thickness. The three methods tested have good correspondence, showing that IOLMaster and ImageJ could be objective techniques to measure CCC. Also, it is possible to improve the agreement of subjective measures when compared to objective measures trough time.

1. Introduction

Modern scleral lenses (ScCLs) are large diameter lenses that have their resting point beyond the corneal borders. They have recently gained more interest among practitioners around the world and are one of the first and best visual correction options for eyes that are unsuccessful with conventional contact lens modalities. Evolutions in lens materials, production techniques and improved knowledge on anterior ocular surface anatomy, boosted the indications of scleral lens fitting, varying from severely irregular corneas to normal/ healthy corneas [1–3].

Fitting scleral lenses can be a challenge, especially for a practitioner with limited knowledge and practice on scleral lenses (Macedo-de-Araújo R, Poster presented at GSLS 2018, Las Vegas). Knowledge on the

several aspects regarding all the anterior ocular surface anatomy characteristics (both corneal, corneo-scleral and scleral geometries), different scleral lens designs and fitting characteristics are topics that must be mastered by practitioners. Regarding the fitting characteristics, one must be aware of several aspects. First, as these lenses land exclusively on the conjunctiva tissue underlying the sclera, practitioners need to fully understand its complex anatomy and geometry [4–6]. This will aid to find the lens landing zone that will be close to the overall scleral shape of the eye being fitted in order to prevent some common scleral lens problem, which can be a challenge for a novel practitioner [7]. Second, as the first aim of these lenses is to bridge the entire cornea and limbus avoiding touching these structures, the scleral lens sagittal height is another important feature. Scleral lenses need to be inserted with liquid - preferably unpreserved saline solutions - that will fill the
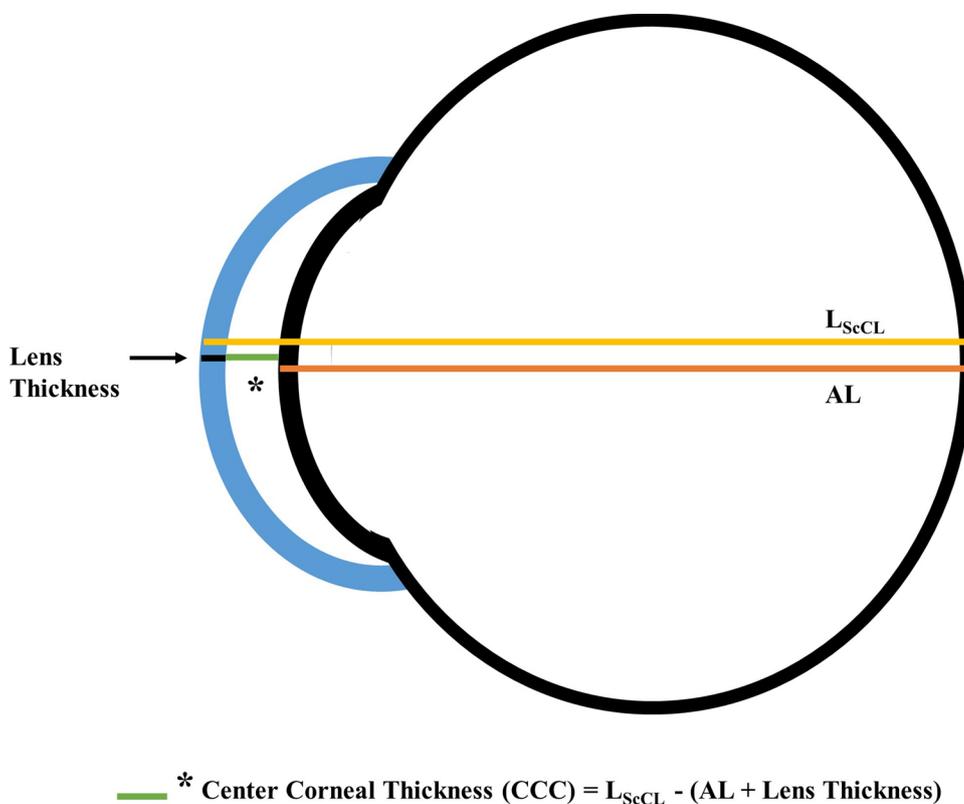
Fig. 1. Schematic image showing the relationship between the measurements taken with IOLMaster. L_{ScCL} is the distance between pigmented epithelium of the retina and the anterior surface of the scleral lens. AL is the distance between the retinal pigmented epithelium and the anterior surface of the cornea (measurement taken after removing the lens). As the value of clearance is normally the distance between the front corneal surface and the back surface of the scleral lens, the lens thickness must be subtracted.

* Center Corneal Thickness (CCC) = L_{ScCL} - (AL + Lens Thickness)

space between the front corneal surface and the back surface of the lens – the central corneal clearance (CCC). Finding or achieve this best postlens tear fluid thickness or clearance is one of the most difficult challenges during scleral lens fitting process [8,9]. In one hand, scleral lenses should not touch any part of the corneal or limbal area [10]. In the other hand, this CCC should not be very high because of the hypoxia effects [9,11–15]. In addition, it is known that the postlens tear fluid thickness decreases through time, phenomena called *settling,* making the measurement of this an important issue [16–19]. Objective and subjective methods are available to measure this cornea-lens separation. Subjective methods are dependent on practitioner experience and skills and comprise direct evaluations with slit lamp. If the postlens fluid is dyed before insertion, practitioners can observe the overall fitting and check for areas of corneal or limbal touch. To observe and estimate the thickness of CCC with biomicroscopy, an optic section can be used and compared to central contact lens thickness or central corneal thickness, if known [16,20]. Anterior segment optical coherence tomography (AS-OCT) is an objective method that has been widely used in different studies to measure clearance [16,17,21,22] and corneal swelling [21,23]. However, despite their accuracy and precision, this kind of instruments have a considerable cost and not all practitioners can have easily access to them [24], so it is important to find the accuracy of others methodologies to assess CCC. One must take into account that to have a more precise measurement of CCC, more sophisticated equipment may be needed – like OCT, built-in camera in the slit lamp or other equipment.

The present study has been designed to investigate if other clinically available instruments and techniques could be used to have an objective measure of the on-eye cornea-lens separation. Three techniques were compared – a subjective technique (with slit lamp), image processing technique with Image J, and an indirect measure with an optic biometer. The Part I of the present study was conducted in order to validate an optic biometer to measure CCC in the sample of the present study.

2. Methods

2.1. Part I – validation of two methods for CCC measurement

2.1.1. The use of an optic biometer for CCC measurement

The aim of the first part of the study was to validate an optical biometer to measure cornea-lens separation. This allowed the authors to use this device in the second part of the study. Measurements were performed in 22 healthy eyes of 11 subjects (10 women) with a mean age of 25.51 ± 4.70 years and spherical equivalent of -0.02 ± 1.00 D. Subjects used two different plano scleral lenses from the same manufacturer (Procornea, Eerbeek, the Netherlands), one different in each eye. Both diameter and parameters regarding the landing zone of the lens were the same for the two ScCL selected (16.4 mm) and same radii of curvature (8.20 mm). The sagittal height of the two lenses differed in 100μm: one lens (ScCL1) with 4673 μm and the other with (ScCL2) 4773 μm (values provided by the manufacturer). They were applied randomly in left or right eye in the same subject. The cornea-lens separation (clearance) was measured indirectly with the axial length of the naked eye (AL) and eye with ScCL (Length - L_{ScCL}) measurement with the optical biometer IOLMaster (Zeiss, Germany) and directly with AS-OCT RS-3000 (NIDEK, USA). The AL was recorded 10 times before scleral lens insertion. The remain measurements were performed up to 20 min after lens insertion to avoid any edema response or warpage. The L_{ScCL} was also recorded with IOLMaster 10 times for each eye and the average was calculated. AS-OCT measurements were recorded 3 times for each eye, and the CCC measurements were performed with the same methodology described in previous works – the image was magnified using the software of the instrument and the measurements were obtained along the central location [25–27]. CCC was measured by the same operator from the anterior corneal surface to the posterior curve of the scleral lens. Later, the values of the two instruments were compared. A simple calculation was made to obtain the value of CCC with IOL: CCC = L_{ScCL} – (AL + Lens Thickness) (Fig. 1), being 402 μm the central lens thickness. The results showed that both measurements were

strongly correlated (r = 0.981, p < 0.001) with a mean difference of 122.18 ± 46.05 μm (higher with IOLMaster). The results of this validation will be used on Section 2.2.

2.1.2. The use of ImageJ for CCC measurement

To validate the technique to measure CCC with an image processing software, 13 pictures of scleral lenses on-eye were randomly selected. All these pictures (that were randomly selected from the database) were taken with the build-in camera on the slit lamp (CSL990 Elite 5x Digital Video, CSO, Italy) during scleral lens evaluations at different appointments during a clinical trial at Clinical & Experimental Optometry Research Laboratory (CEORLab, University of Minho, Portugal). Posteriorly, these pictures were evaluated with Image J 1.52a software (National Institutes of Health, Bethesda, Maryland, USA) in order to validate this technique to measure CCC. Images were analyzed in a random order. Measurements of cornea-lens separation and lens thickness were repeated 3 times (not consecutively) for each image (intra-session). All these measurements were randomly repeated 2 more times in 2 different days (inter-session) by the same observer and applying the same criteria.

2.2. Part II – comparison of three methods to measure CCC

The aim of this second study was to compare three methods for CCC measurement: an optic biometer (IOLMaster), a subjective measure (Slit-Lamp) and using an image processing program (Digital Image). Sixty-one eyes of 35 subjects (20 female) enrolled in the clinical trial at CEORLab were randomly selected and voluntarily participated in this study. The ages of the participants ranged between 16 and 60 years with an average age of 35 ± 8 years. As the sample participating in the clinical trial was divided into two groups according to corneal condition, the subjects recruited to this study were from the two groups: 52 eyes of 30 patients with irregular corneas due to different etiologies (Group I) and 9 eyes of 5 patients with normal corneas (Group II) whose motivation and inclusion criteria to enroll the study was having moderate-to-high refractive errors (myopia ≥ 6.00D, astigmatism ≥ 4.00D and/or hyperopia ≥ 4.00D).

The lenses fitted were manufactured by Procornea (Eerbeek, The Netherlands) using Boston XO material (hexafocon A). The overall diameter of the lenses used by the subjects of the present study was 16.4 mm. All lenses were fitted by the same practitioner/ examiner following the manufacturer's instructions. Subjects of the present study were already enrolled in a clinical study and fitted with scleral lenses and had several evaluations through the follow-up period (lens dispense visit, and appointments of 1, 3, 6 and 12 months). The measurements of the present study were performed at 6 months visit (6 months after lens dispense visit). The subjects came to the visit with their scleral lenses on-eye for more than 90 min of lens wear (mean wearing time: 208 ± 147 min). The fitting of the lenses – and respectively the CCC - was evaluated with slit lamp (CSL990 Elite 5x Digital Video, CSO, Italy). CCC value was obtained by comparing the thickness of cornea-lens separation to the known value of lens thickness (provided by the manufacturer for all the lenses). The same routine was used in all appointments to subjectively measure CCC – an optic section showing the total lens thickness, post lens tear film reservoir thickness and cornea with 16x magnification and the slit lamp and biomicroscope set at 60 degrees from each other. Pictures of each fitting were taken over a period of about 1-year with the video imaging system build-in the slit lamp with the same technique described above. The Digital Image analysis was performed more than 4 months after the acquisition of the pictures at 6-month appointment with ImageJ with the previously validated methodology (Section 2.1.2). All the images were coded and no information of the patient was present at the time of examination, in order to mask the observer. Six repeated measures of lens thickness and six repeated measurements of cornea-lens separation (CCC) were performed by tracing a line between the front and back surface of the lens

and the back surface of the lens and the anterior surface of the cornea, respectively. This way, the program can determine the number of pixels within both areas measured. As the observer knew the lens thickness (in microns) provided by the manufacture for each one of the lenses analyzed, a simple conversion of the CCC from pixel to micrometers was done. Previous studies already used this software to measure clearance [20] and turbidity of post-lens tear film [21].

Similarly to the protocol followed in the Part I of the present study, measurements of CCC were also been indirectly obtained with IOLMaster. Again, measurements were performed with the lens on-eye (L_{ScCL}) and later after lens removal (AL) (Fig. 1). Taking into account the results of Part I, the CCC value was calculated by:

$$CCC = L_{ScCL} - (AL + Lens\ thickness) - 122\ \mu m$$

2.2.1. Learning process of subjective CCC measurement vs ImageJ

The aim of this last part of the study was to evaluate the learning process or improvement in the skills of the practitioner to measure CCC subjectively with slit lamp (comparing with ImageJ measurements). Sample was the same from section 2.2. Data from visits of 1 month (V1m), 6 months (V6m) and 12 months (V12 m) were analyzed. Slit lamp examination was also performed and pictures from each visit were analyzed with ImageJ. CCC was recorded with the same techniques described on Section 2.1.2 and 2.2.

2.3. Statistical analysis

Statistical analysis was conducted using SPSS v.25.0 (SPSS, Inc, Chicago, Illinois, USA). Normality of data distribution was assessed with the Shapiro-Wilk test in different groups of subjects analyzed. The values presented are the mean and standard deviations (mean ± SD). Differences between the different techniques and between the same technique within subjects through time (dependent samples) were estimated with Friedman test or ANOVA for repeated measurements, depending on the sample distribution. For pairwise comparisons between techniques and within the same subjects through time, the differences were estimated with Wilcoxon signed-rank test if the sample was no-normally distributed or with paired sample *t*-test if it was normally distributed. Correlations between instruments were assessed with Spearman's rho. The level of statistical significance was set at p < 0.05.

3. Results

3.1. Part I - validation of two methods for CCC measurement

3.1.1. The use of an optic biometer for CCC measurement

The mean CCC values measured were 441.18 ± 197.54 μm and 319.00 ± 168.72 μm, for IOLMaster and AS-OCT, respectively. This result shows that measurements performed with IOLMaster are, on average, 122.18 ± 46.05 μm higher than measurements performed with AS-OCT (Fig. 2A). Despite these differences, the measurements of CCC indirectly obtained with the optic biometer had a positive and strong correlation with the measurements done with AS-OCT (Fig. 2B: r = 0.981, p < 0.001). In addition, the differences between the measurements of the two devices were very similar in the two scleral lenses used: in the ScCL1 the mean difference between instruments was 120.52 ± 52.20 μm and in ScCL2 the mean difference between instruments was 123.85 ± 41.49 μm.

3.1.2. The use of ImageJ for CCC measurement

Fig. 3A and B represents the differences intra- and inter-session in the measurement of lens thickness (LT) (A) and CCC (B) with ImageJ. There were no statistical significant differences between the three measurements of LT and CCC performed at each day except for the
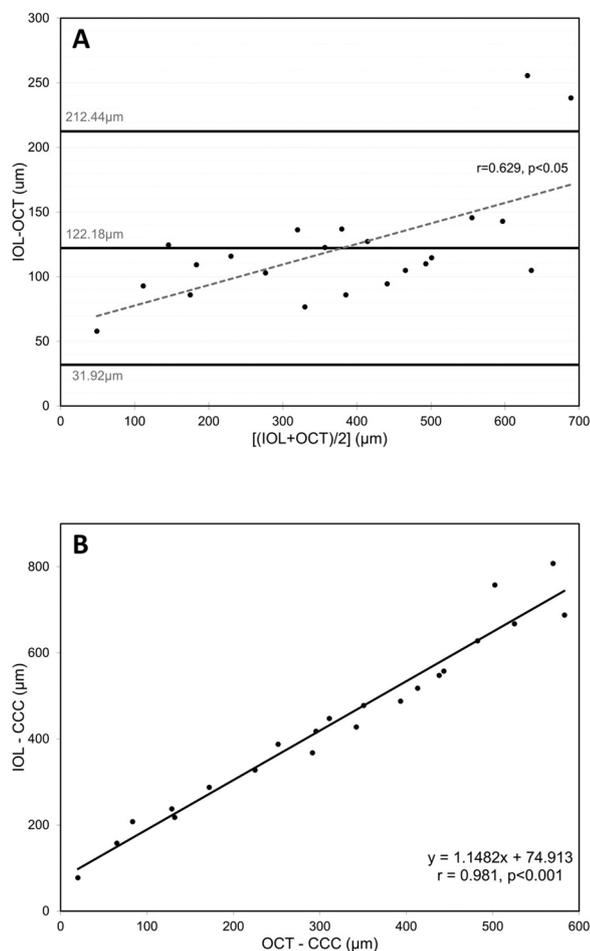
Fig. 2. (A) Bland-Altman plot of CCC measurements obtained from IOLMaster and AS-OCT. 95 per cent limits of agreement are shown as two darker horizontal lines above and below the mean difference value (mean difference ± 1.96SD). **(B)** Correlation of clearance measurements obtain with OCT and IOLMaster.

measurements of lens thickness at first day (p < 0.05, Friedman test), between measurement 1 and measurement 3 (p = 0.01, Wilcoxon). The maximum standard deviation between 3 consecutive measures in the same picture was 4.36, meaning that 95% of the measurements performed had less than 8 μm of variability. There were no statistical significant differences between inter-session measurements (p > 0,05).

3.2. Part II - comparison of three methods to measure CCC

Measurements of CCC at 6 months visit were 238.66 ± 95.94 μm, 250.16 ± 124.31 μm and 263.15 ± 90.60 μm, for the IOLMaster, Subjective measure (Slit Lamp) and Image J processed, respectively. Fig. 4 shows the boxplots for the three methods. Comparisons between the three techniques did not demonstrated significant variations between the measurements obtained (p > 0.05, Friedman test). However, pairwise comparisons showed a statistical significant difference between the measurements performed with IOLMaster and Image J (p = 0.010, Wilcoxon).

Fig. 5 represents the Bland-Altman analysis between IOL, Slit Lamp and ImageJ. The average difference between IOLMaster and Slit Lamp was -12 ± 83 μm (p > 0.05, range: −242 min to 158max μm) meaning that Slit Lamp recordings are slightly higher than IOLMaster on average (Fig. 5A). For lower CCC values, measurements performed with Slit Lamp are underestimated when compared to IOL, but this trend is reversed as higher CCC are assessed. The average difference between IOLMaster and ImageJ was -25 ± 62 μm (range: -188 to

90 μm, p = 0.01), with the ImageJ measurements being higher on average (Fig. 5B). Lastly, the mean difference between ImageJ and Slit Lamp measurements was 13 ± 59 μm (range: -149 to 138 μm, p > 0.05), with the Slit Lamp giving lower values on average (Fig. 5C). Slit Lamp underestimates the CCC values when the cornea-lens separation is lower, but tends to overestimate this value with increasing cornea-lens separation.

The correlations were higher for Image J vs Subjective measure (r = 0.891, p < 0.001) than for IOL vs Subjective (r = 0.748, p < 0.001) and IOL vs ImageJ (r = 0.745, p < 0.001).

3.2.1. Learning process of subjective CCC measurement vs ImageJ

Table 1 shows the mean difference in clearance measurements performed with two techniques (slit lamp and Image J) through time – V1m, V6m and V12 m. A greater difference between both measurements is observed at V1m, being the subjective measures (slit lamp) overestimated (more positive) than the Image J processed images. However, in the remain visits, measurements performed with ImageJ were higher (mean difference of -32.28 ± 89.95 μm at V1m, 12.53 ± 59.46 μm at V6m and 11.57 ± 33.23 μm at V12 m). The correlations between both measurements were statistical significant (p < 0.001) in all the visits, with increasing correlations through time (r = 0.683, r = 0.850 and r = 0.940, respectively).

Fig. 6 shows the Bland-Altmann analysis between ImageJ and Slit Lamp for the different visits (V1m, V6m and V12 m). Notice that the average difference between both measurements tends to decrease with the increasing experience of the practitioner, as well as the 95% limits of agreement.

4. Discussion

Over the last few years many advances have been made on scleral lens field. However, specific limitations continue in the fitting process, namely when practitioners do not have advanced instrumentation like AS-OCT available. Although there is lack of consensus on the amount of desired corneal clearance of an ideal fit [28], it is accepted that these lenses shouldn't touch the corneal surface neither have a great cornea-lens separation because of the potentially induced hypoxic stress into the corneal tissue. Moreover, practitioners need to account on lens settling at the initial fit, as these lenses land on the bulbar conjunctiva that is a soft and compressible tissue that will cause the lens to sink, decreasing CCC overtime [29]. All these details make extremely important to accurately estimate the CCC. The present study intended to compare three different approaches to measure CCC *in situ*, including the clinical subjective evaluation. In the first part of the study, a method to measure central corneal clearance (CCC) using an optic biometer (IOLMaster) was suggested.

At the first part of the study, measurements of CCC with IOLMaster and AS-OCT in 22 healthy eyes were compared. To measure axial length (AL), IOLMaster takes the measurements from the anterior tear layer above corneal epithelium and the retinal pigmented epithelium. With a scleral lens on-eye, the authors hypothesize that the measurement is performed from the anterior surface of the lens and the retinal pigmented epithelium. Because of that, having the L_{ScCL} and subtracting the AL and lens thickness (402 μm in the present study) to it, the authors believe that the final result is the CCC. In fact, the CCC measured with IOLMaster waspositively and strongly correlated with the measurements made with AS-OCT (Fig. 2B: r = 0.981, p < 0.001). However, the mean difference in the measurements with these two devices was of 122.18 ± 46.05 μm (higher with IOLMaster). The mean differences between devices with the two lenses analyzed were very similar (121 μm for ScCL1 and 124 μm for ScCL2). The authors hypothesize that this difference could be related to small deviations to the center with the two instruments (differences in measurement position) and differences between acquisitions systems of both instruments. To the author's knowledge, this was the first study that evaluated the
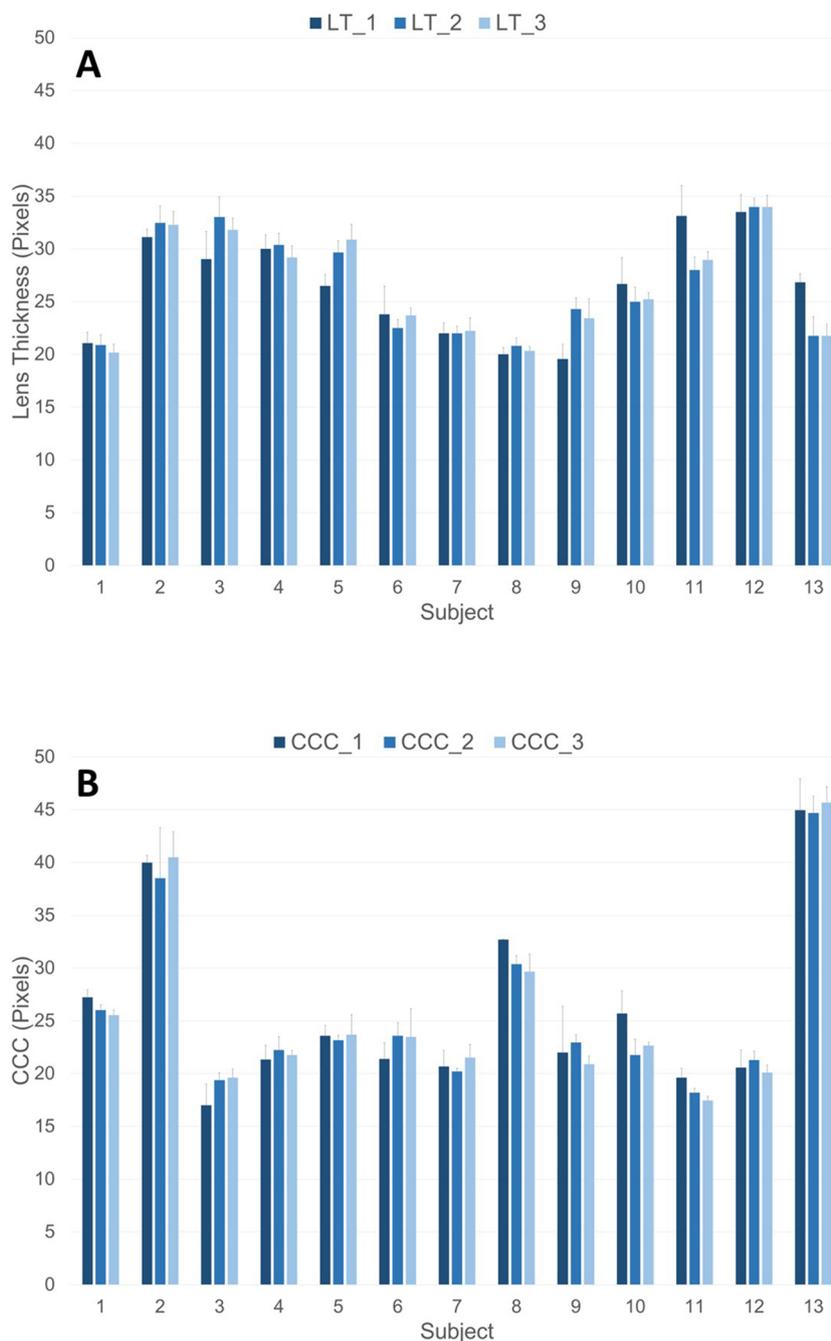
Fig. 3. Differences intra- and inter-session in the measurement of lens thickness (LT – **A**) and clearance (CCC - **B**). Each bar represents the Mean ± SD of the three repeated measures in the same session (intra-session). LT_1, LT_2, LT_3, CCC_1, CCC_2, CCC_3 represent the measurements performed at each different day at day 1, day 2 and day 3, respectively (inter-session).

viability of an optic biometer to measure CCC, and further studies may be needed to clarify the systematic differences in the measurements performed with these two devices and/or build new devices based on optic biometry technique to measure CCC. The authors consider that this methodology should be reproduced in a larger sample and with different and masked observers (in order to introduce the inter-observer analysis), in order to validate this methodology to use it in the clinical practice. With the results of this first part the authors conclude that the CCC value measured with IOLMaster can be obtained by:

$$CCC = L_{ScCL} - (AL + Lens\ thickness) - 122\ \mu m$$

and this was the calculation used at IOLMaster measurements in the second part of the study.

In the second part of the study, three techniques for CCC measurement were evaluated: an optic biometer (IOLMaster), a subjective measure (Slit-Lamp) and using an image processing program (Digital Image - where photos recorded during slit lamp evaluation of scleral lens fitting were posteriorly analyzed with ImageJ software). To guarantee that the digital image technique was reliable to use in the present analysis, 13 photos of scleral lens fitting were randomly selected and measured in the same session and repeated in three different days. In order to use it in a clinical setting, it is mandatory to reproduce it in a larger sample and design the study to add the inter-observer reliability. For the purpose of the present study, the authors conclude that there were no statistical significant differences between the measurements made in the same session (intra-session) neither at the different days
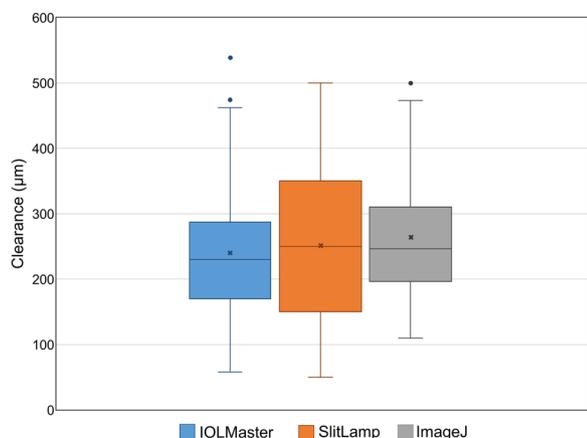
Fig. 4. Box and whiskers plot comparing the CCC measurements with IOLMaster, subjective method (slit lamp) and Image J processed. It is represented the median value and the 95% confidence interval, as well as the maximum and minimum values.

(inter-session) (Fig. 3A and B).

The slit lamp is the most used tool to measure CCC - regarding SCOPE study results, Jennifer Harthan et al [30] found that the great majority of the 989 practitioners that answered the survey rely on slit lamp (97.3%) and topography (88.7%), but only 47.5% rely on AS-OCT in the scleral lens fitting process. It is important to emphasize that the great majority of the respondents are based in the United States (72%), so future studies are needed to target more practitioners who are fitting scleral lenses outside the United States [31]. So, slit lamp seems to be the most used device to assess scleral lens fitting, and consequently the CCC. However, this is a subjective technique that is somewhat dependent on practitioner experience and skills. In fact, there is no gold-standard method for CCC measurement, and no limits of agreement are established as clinically acceptable between measurements to consider methods interchangeable when comparing different techniques. The 95% limits of agreement in the present study were between -175 and 151 (IOLMaster vs SlitLamp), -147 to 98 (IOLMaster vs ImageJ) and -130 to 103 (SlitLamp vs ImageJ). The average CCC measured with the three techniques were very similar between them: IOLMaster measurements were on average 12 ± 83 and 25 ± 62 μm lower than the measurements with slit lamp and Image J, respectively, and Image J measurements were 13 ± 59 μm higher than those performed with slit lamp. The only statistically significant difference was found between IOLMaster and ImageJ (p = 0.01, Wilcoxon), however the authors assume that this has no clinical relevance (25 μm).

There are few studies comparing subjective measures using central lens thickness as biometric ruler and AS-OCT. Fuller et al [24] concluded that neophyte clinicians tend to overestimate the central clearance when compared to AS-OCT measures, with differences between both measurements of 115 μm (right eye) and 49 μm (left eye). In the present study it was found that measurements performed with slit lamp

Table 1
Differences in CCC between subjective measure (with slit lamp) and image processed measure (with ImageJ) at 1, 6 and 12 months visit.

	V1m	V6m	V12m
Image J	290 ± 94.50	257.14 ± 80.07	240.05 ± 87.75
Slit Lamp	322.71 ± 123.44	242.71 ± 105.48	228.47 ± 96.95
Difference	−32.28 ± 89.95	12.53 ± 59.46	11.57 ± 33.23
	(p = 0.009)*	(p = 0.089)*	(p = 0.012)*

* Wilcoxon.

are overestimated (on average) when compared to objective techniques, like IOLMaster or ImageJ (Fig. 5A and B). However, it was possible to further conclude that for small CCC values, the measurements performed with Slit Lamp are lower than those recorded with IOL-Master or ImageJ, and that this tendency is reversed as the CCC values became higher. This has an important clinical consequence – if a subject has been fitted in a scleral lens with a lower CCC, the practitioner tends to underestimate the value and will take an action to augment the sagittal height of the lens for preventing the lens from touching the cornea. On the other hand, if the subject was fitted with a higher CCC value, the practitioner tends to overestimate the value and will decrease the lens sagittal height to avoid hypoxia problems. One should think that this bias can be decreased as the fitter gains more experience, however there is some controversy about this. Yeung and Sorbara [20] concluded that, independently of the experience of the observers, there was an overestimation of clearance by an average of 103 μm when compared to AS-OCT measurement, with high correlations (r > 0.79). In the same study, when comparing the estimated clearance with the digital clearance (measured with an image processing software), an average overestimation of 27 μm was encountered, again, with high correlations between both measurements. Along with this, they also concluded that the increasing experience with ScCL fitting did not improve the correlation between measurements (subjective and AS-OCT), but the advanced fitters had significantly less inter-observer variability compared with the neophyte group (less SD). However, they were independent samples and were grouped according to the number of scleral lens fittings done in the past. In the present study, the conclusions drawn from Fig. 6 and Table 1 are for the same practitioner – is the learning curve of the practitioner over the follow-up visits. The practitioner began to fit scleral lens without previous experience, but followed 95 consecutive subjects during a follow-up of 12 months – the authors consider that at the end of 3 months following such a large sample, the practitioner was considered experienced. As the clinician gained more experience, it was possible to reduce the average difference between the subjective measures of CCC made with Slit Lamp and the objective measures recorded with ImageJ as well as to narrow the intervals of agreement. In addition, and according to Yeung and Sorbara [20], the overall standard deviation also decreased between V1m and V12 m, meaning that there was also a reduction in the variability of the differences. It is also observed on Figs. 6 A, B and C, where a reduction in the 95% confidence intervals is observed. Also, the
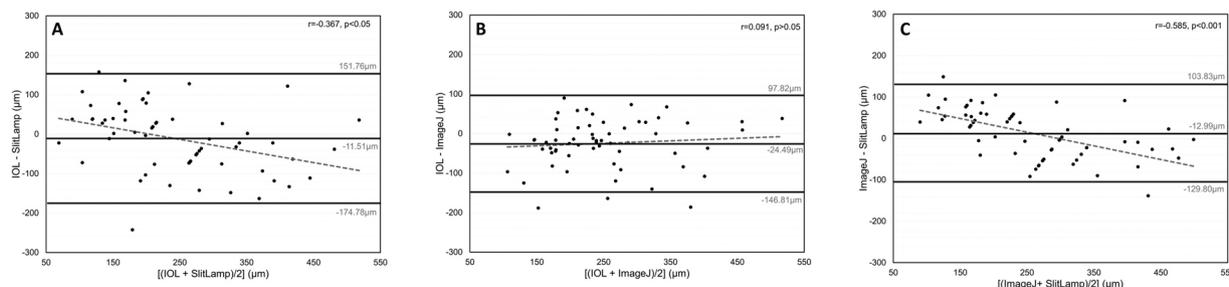

Fig. 5. Bland-Altman plot of CCC measurements obtained from IOLMaster and SlitLamp (**A**), IOLMaster and ImageJ (**B**) and SlitLamp and ImageJ (**C**). 95 per cent limits of agreement are shown as two darker horizontal lines above and below the mean difference value (mean difference ± 1.96SD).
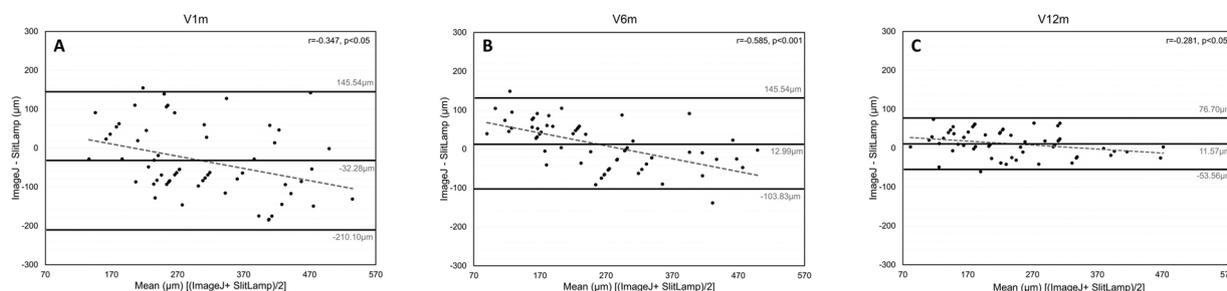
Fig. 6. Bland-Altman plot of clearance measurements obtained from ImageJ and SlitLamp at the different follow-up visits: 1 month visit (V1m – **A**), 6 months visit (V6m – **B**) and 12 months visit (V12 m - **C**). 95 per cent limits of agreement are shown as two darker horizontal lines above and below the mean difference value (mean difference ± 1.96SD).

correlations between both measurements were higher at V12 m than V6m and V1m (r = 0.94, r = 0.85 and r = 0.683, respectively), meaning that there was an improvement in agreement between techniques with the increasing expertise of the fitter.

Measuring CCC with IOLMaster and with image processing software (like the one used in the present study) could be time-consuming and difficult to implement in the clinical practice. For the first one, it is necessary to take measurements with the lens on eye and later after removing the lens and perform a calculation to have the CCC value. For the second technique, it is required to have a photography acquisition system, preferably incorporated into the slit lamp, and then export the image and perform the measurements (both lens thickness and CCC) with the image processing software. As measurements with Image J are given in pixels it is necessary to convert it to microns, which is a simple calculation if the observer knows the central contact lens thickness or other neighbor feature in the image as a "ground-truth". However, both techniques can have significant importance in the investigation fields, where objective measures are preferred to subjective ones to avoid inter-subject variability.

Nowadays, there is no "true" objective measure of CCC. In three of the four methods used in the present study, the observer needs to take an action to have the CCC value: with AS-OCT it is needed to use the calipers within the software, the same way in the ImageJ. The only device that don't need the observer/ practitioner to make an action or manipulate the pictures was the IOLMaster. However, this last technique has some limitations, as both measurements with and without lenses are needed, followed by a calculation. Also, the authors assume that this device was not developed with the purpose of CCC measurement and has an important difference (122 μm) when compared with AS-OCT, although with very strong correlation between the measurements of both devices. The authors agree that the development of an optic biometer technique or a software development to measure CCC will have great value.

In summary, central corneal clearance (CCC) can be measured with IOLMaster. The practitioner needs to account on lens thickness and on the systematic error (122 μm) found between IOLMaster and AS-OCT measurements. Also, there was a good correlation between the measurements performed with IOLMaster, ImageJ and with slit lamp, making it possible to measure CCC with these three devices. The present study confirms that it is possible to improve the agreement of subjective measures when compared with objective measures with the increasing experience of the practitioner.

Acknowledgments

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