

## SOPTI Meeting Abstracts 2022

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# SOPTI Meeting 2022: Abstracts

The 27th National Conference of the Italian Optometric Association (SOPTI) was held in Bologna on May 29–30, 2022. This year the conference title was “*Technical procedures for good clinical practice in Optometry*” and was arranged in 3 sessions: presbyopia management, contact lenses and paediatric optometry. Two keynote speakers were invited during the conference: Dr Shehzad Naroo (Reader at Aston University, UK) and Dr Mohammed Jalie (past head of the Applied Optics department at the City & Islington College and current visiting lecturer at Ulster University).

The abstracts from accepted posters and free papers are presented here.

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## Visual performance and adaptation with DIMS (Defocus Incorporated Multiple Segments) ophthalmic lenses

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### Abstract

The aim of this study was to compare the visual performances between the single vision spectacle lenses usually worn and the DIMS ophthalmic lenses for the management of myopic progression. Also, to assess the grade of fit after seven days of wearing the DIMS lenses.

The study was carried out on 15 myopic students aged between 22 and 32, treated with DIMS lenses. The inclusion criteria were myopia  $\leq -4.00D$ , astigmatism  $\leq -1.00D$ , habitual use of glasses, normal binocular vision. The visual functions compared between the two lenses were: visual acuity at high (HLVA) and low luminance (LLVA), contrast sensitivity (CS), all at far. At near: reading visual acuity (AV Radner), critical print size (CPS) and reading speed. All tests were carried out, first with the lenses usually worn, then immediately after delivering the glasses with DIMS lenses and again after a week of wearing.

The measurements were carried out with Vision Chart (CSO, Italy), for HVLA, LLVA, CS; with Radner test, for near AV, read speed and critical print size. The Pelli Robson test was used for the measure of the contrast sensitivity.

As for far vision, the differences detected were statistically significant ( $p < 0.05$ ) only for HLVA, not significant for LLVA and CS. However, all have negligible values from a clinical point of view. See the first three lines of Table 1.

Monofocal	DIMS	ODDS	p-value	t-test	p-value Wilcoxon	Adaptation
HLVA	-0.14±0.06	-0.17±0.04	-0.02±0.05		0.049	-0.16±0.04
LLVA	0.01±0.09	0.01±0.07	0.00±0.10		0.909	0.01±0.07
CS	0.01±0.00	0.01±0.00	0.00±0.00		0.472	0.01±0.00
AV Radner	-0.03±0.05	-0.05±0.06	-0.02±0.08		0.183	-0.06±0.06
CPS	0.17±0.07	0.15±0.11	-0.02±0.10	0.424		0.13±0.08
VEL Radner	215.07±24.5	224.6±32.0	9.5±15.8	0.035		225.7±29.5

The Radner test did not reveal statistically significant differences ( $p > 0.05$ ) for reading acuity and CPS. There was a significant difference in reading speed, but clinically the difference is negligible. See the last three lines of Table 1. See Figure 1 for

results of the Radner test for the three measurement conditions.

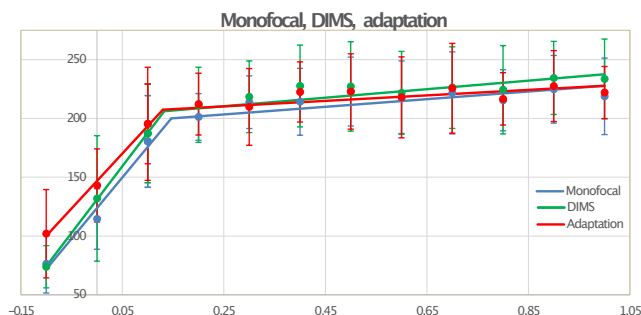


Figure 1: Results of the Radner test with single vision lenses and with DIMS lenses, just after delivering and after a week of wearing.

As for the adaptation during the week of wearing, it was found that the symptoms were mild or absent and the adaptation was complete in less than a week in most of the subjects.

To our knowledge this is the first study in which reading speed with DIMS lenses has been measured. From the data collected in the analysed sample, no significant deterioration in visual performance was shown with DIMS ophthalmic lenses for the control of myopic progression. According to our sample, a certain number of subjects need a short period of adaptation. A limitation of the study relates to the age of the subjects, all were adults. However, it is to be expected that the lenses can be well tolerated by children, who have greater adaptability and lower demands for high visual performance in comparison with adults.

## Correlation between corneal and refractive astigmatism with power vectors

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### Abstract

This work aimed to investigate the correlation between corneal and refractive astigmatism. Along with the WTR and the ATR types of astigmatism, the oblique astigmatism was considered, unlike previous literature (Javal, 1890).

A sample of 62 eyes was analysed, estimating the corneal astigmatism by the Allergan Humphrey auto keratometer model 420 (autoker), and the refractive astigmatism by an optometric exam. The subjects' ametropia ranged from -11.00 D to +8.00 D with astigmatism ranging from 0.75 D to 5.00 D.

Subjects affected by corneal ectasia and those with an astigmatism less or equal than 0.50 D were excluded from our sample. The corneal astigmatism and refractive astigmatism data were converted into a vector key (see Figure 1) and the analysis was carried out to derive a possible relationship between the two (Liu et al., 2011; Remón et al., 2009).

After converting all data from clinical notation to vector notation and estimating the average value of internal astigmatism ( $-0.60 \pm 0.01$  D axis  $90.47^\circ$ ), four linear regressions were performed to study a relationship between:

- 1) refractive astigmatism RJ0 and corneal astigmatism CJ0
- 2) refractive astigmatism RJ45 and corneal astigmatism CJ45
- 3) internal astigmatism LJ0 and internal astigmatism LJ45
- 4) and refractive astigmatism and corneal astigmatism.

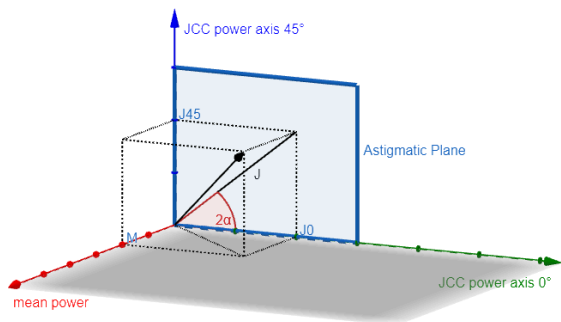


Figure 1: Cartesian representation of power vectors.

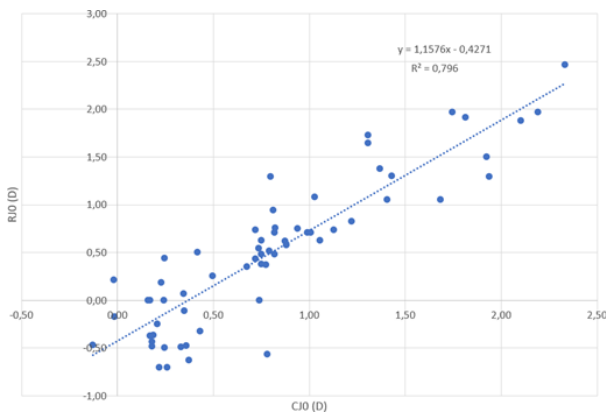


Figure 2: Linear regression of refractive astigmatism RJ0 vs corneal astigmatism CJ0.

Since refractive and corneal astigmatism are linearly correlated, it is possible to estimate refractive astigmatism using corneal astigmatism:

Refractive astigmatism = corneal astigmatism  $\times (0.94 \pm 0.06) - (0.60 \pm 0.01 \text{ D})$  axis  $90^\circ$

This formula is very similar to the approach of the Javal's rule, with the added possibility of making oblique astigmatism predictions by making them more exact and plenary.

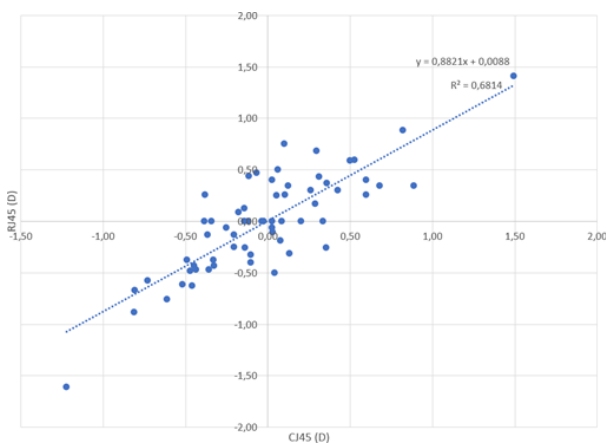


Figure 3: Linear regression of refractive astigmatism RJ45 vs corneal astigmatism CJ45.

Power vectors have been found to facilitate the description of refraction more accurately and comprehensively. In this case it allows us to conduct the analysis and calculations related to the various elements in a mathematical way (Harris, 2007), something that could not happen with clinical notation alone.

Comparisons with previous studies showed that some of the detected parameters of the linear relationship between refractive and corneal values were compatible with those determined in this study.

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## Evaluation of automatic morphometric analysis of the corneal endothelium with Perseus

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## Abstract

The aim of this study was to compare results obtained from the automatic analysis of endothelial cells operated by the Perseus Specular Microscope's software (CSO, Florence, Italy) with results obtained from a manual analysis of the same images.

A sample of 73 subjects was selected from the Perseus database (CSO, Florence, Italy). For each subject were exported endothelial images from seven different positions of each eye (central C, superior S, superior temporal TS, superior nasal NS, inferior I, inferior temporal TI and inferior nasal NI) were exported. For each image acquired, the software automatically identified the cells and returned the main morphological parameters of the endothelial mosaic. For the same images, the operator manually identified and corrected any errors made by the automatic recognition software in the number of cells and / or in the number of sides of their shape. Once the editing phase was ended, the modified images modified were processed using the same algorithm as the automatic analysis. Of the analysed images, 890 were selected, those with reliability greater than 50% and number of cells recognised greater than 75, for which the number of cells, cell density, coefficient of variation (CoV) and hexagonality were reported, for automatic and manual analysis.

Comparison between the automatic and manual method of analysis was performed for the four indices, separately for the two eyes and for the 7 positions. Between the two procedures, in all positions examined, for both right and left eye, no significant differences were found for CoV and cell density (with the exception of the left eye TS position [paired *t*-test,  $p < 0.05$ ]); while the differences were always significant for cell number (paired *t*-test,  $p < 0.001$ ; Wilcoxon  $p < 0.001$  NS left eye) and for hexagonality (paired *t*-test,  $p < 0.001$ ). The correlation between the considered parameters with the two methods was significant, more specifically from moderately to strongly positive in all positions.

The integration with the manual analysis of the acquisitions made with the Perseus requires more time than the automatic analysis alone. With manual analysis it is possible to recognize and analyse a significantly higher number of cells, determining a significant difference on the morphological parameter of the hexagonality only. Furthermore, a robust positive correlation was found for all variables.

## Ophthalmic applications of Metalenses

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### Abstract

Metalenses, also defined as planar lenses, allow you to focus the entire visible spectrum in a single point, thus eliminating the chromatic aberrations from which all optical systems are affected. The nanostructures of which they are composed are designed to manipulate the phase, amplitude and polarisation of light. The nanometric thickness and the way they interact with light make these lenses particularly suitable for applications in the ophthalmic field, such as corrective lenses or contact lenses.

The purpose of this study is to present the development and production phases of a Metalens, highlighting its peculiarities, in particular in relation to the interaction of light with nanostructures, and to investigate the possibility of its use in the ophthalmic field.

The following study was conducted at the QR (Nanofacility) laboratory of the National Institute of Metrological Research (INRiM), under the coordination of Dr. Luca Boarino. The sample of Metalens, under study, was made as follows: Plasma Enhanced Chemical Vapor Deposition (PECVD) of amorphous silicon (a-Si) on a glass substrate; Spin deposition of negative resist; Electron beam lithography (EBL); Development and finally Chemical Etching.

A Metalens with a diameter of 100  $\mu\text{m}$  was designed to focus light with a wavelength  $\lambda = 633 \text{ nm}$  (red) at a focal length of 200  $\mu\text{m}$ . For the measurement of the focal length, we used an optical bench consisting of a monochromatic laser source ( $\lambda = 633 \text{ nm}$ ), a series of biconvex lenses for the manipulation of the beam, a 10x objective for the imaging of the lens and, finally, a camera with a photographic sensor for the acquisition and processing of the light signal.

Metalenses open up to different possibilities of use. These lenses have been proposed for use in various electronic optical devices such as cameras and smartphone displays, but also in wearable optics, in particular virtual- and augmented-reality.

To answer the question that this research concerns, there is, in accordance with scientific evidence, the concrete possibility of a future use of these metastructures in the ophthalmic field. Glasses and contact lenses will be able to make use of these particular lenses with wave guides arranged in patterns, correcting the various refractive errors. Studying the applications of Metalenses on patients suffering from ametropias and comparing the results with the traditional corrective lenses currently on the market will be the subject of research in the coming years.

## Decrease of myopic progression rate by Orthokeratology. Three-year results of a retrospective study

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### Abstract

The aim of this work was to study the effectiveness of overnight orthokeratology treatment in a group of young myopic subjects, throughout a period of three years. In this retrospective study the data from clinical records of 41 myopic children who

received the overnight orthokeratology (OK group) and of 41 myopic subjects treated with single vision glasses (control, C group) are compared.

The clinical records were acquired in two different private optometric clinics, one for the OK group and the second for C group. The inclusion criteria for treated subjects were those indicated by IMI (International Myopia Institute). Refraction was carried out without cycloplegia by two different optometrists, one for OK group and the other for the C group. The C groups have been matched for ethnicity, age, and refractive error with the OK group.

The mean spherical baseline equivalent was  $-2.85 \pm 1.55 \text{ D}$  and  $-2.51 \pm 1.61 \text{ D}$ , for OK and C group respectively. The follow-up data was available for two years for all 41 subjects of each group, and for three years for 30 subjects in the experimental group vs 25 in the C group. The data from the three years follow-up were analysed.

The increase in myopia at 3 years was  $-0.48 \pm 0.43 \text{ D}$  for the OK group and  $-1.52 \pm 0.90 \text{ D}$  ( $p < 0.001$ ) for the C group. The comparison between the two groups is summarised in Table 1 and in Figure 1. The differences found in the myopia progression rates between the two groups (OK vs C) for each year were:  $-0.15 \text{ vs } -0.47$  ( $p < 0.01$ ) in the first year,  $-0.13 \text{ vs } -0.47$  ( $p < 0.001$ ) in the second year,  $-0.19 \text{ vs } -0.39$  ( $p < 0.01$ ) in third year).

	OK group	DS	Control group	DS	<i>p</i>
Spherical equivalent					
BL	-2.85	$\pm 1.55$	-2.51	$\pm 1.61$	0.183
1	-3.00	$\pm 1.58$	-2.99	$\pm 1.72$	0.831
2	-3.13	$\pm 1.59$	-3.46	$\pm 1.83$	0.329
3	-3.16	$\pm 1.54$	-4.24	$\pm 2.11$	0.018
Myopisation					
BL	0	$\pm 0.000$	$\pm 0.00$	0.0001	
1	-0.15	$\pm 0.25$	-0.47	$\pm 0.46$	<0.0001
2	-0.28	$\pm 0.34$	-0.94	$\pm 0.70$	<0.0001
3	-0.48	$\pm 0.43$	-1.52	$\pm 0.90$	<0.0001
Annual myopia rates					
BL	0	$\pm 0.00$	0	$\pm 0.00$	0
1	-0.15	$\pm 0.25$	-0.47	$\pm 0.46$	0.004
2	-0.13	$\pm 0.24$	-0.47	$\pm 0.44$	<0.0001
3	-0.19	$\pm 0.28$	-0.39	$\pm 0.41$	0.004

Children treated with OK lenses were found, after three years, to have 68% lower myopic progression compared to children corrected with monofocal ophthalmic lenses. There have been no serious complications or adverse events in the three years of the study.

The results of this retrospective study confirm that overnight OK treatment slows down myopic progression in a reliable way compared to monofocal lenses. The percentage reduction of the myopic progression of the OK group is in line with other published literature. No adverse events have disturbed the wearing of the lenses or caused a drop-out. Overnight orthokeratology can therefore be used as a myopia correction technique, and its increased use among practitioners could help contain the increasing prevalence of this refractive error.

## Should we expect corneal warpage with the use of scleral contact lenses in keratoconus?

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### Abstract

Wearing scleral contact lenses, especially when applied inadequately, may induce a change in corneal curvature and corneal thickness (Consejo et al., 2019). Variations may be induced by abnormal lacrimal fluid pressure or mechanical contact between the lens and the corneal surface (Consejo et al., 2020). Iatrogenic effects may be changes in corneal thickness more or less associated with corneal signs of disorder, and possibly associated with more or less transient transparency reductions (Consejo et al., 2017). The purpose of this study was to measure the change in corneal shape after the use of properly applied scleral contact lenses in eyes with keratoconus.

Sixty-nine eyes, 38 males and 31 females, aged between 35 and 66 years, average age 46 years, with medical diagnosis of keratoconus, indicated for the use of contact lenses, were measured with an ocular tomograph (Sirius, CSO, Italy) before and after the use of scleral contact lenses. The measurement after use was carried out according to the clinical application protocol, that is a specific timetable of follow-up and minimal activities that has to be executed for verification of efficacy and safety. The first control of the application protocol involves observations and measurements after 15 days of use and with contact lenses worn from 5–6 hours per day continuously. Measurements and observations should be made first with the contact lenses worn and immediately after their removal. The measurements were carried out at Mauro Frisani's optometric and optical centre for the application of specialised contact lenses in Turin.

The clinical data collection procedure for this study, unchanged for all measurements, included corneal curvature detection at 3, 5 and 7 mm from the corneal apex, respectively. All the contact lenses applied followed an appropriate procedure of adaptation to each individual eye. Each contact lens was applied based on tomographic data and direct observations in the slit lamp. Central and peripheral clearance were checked before the trial period and after 15 days of use. Scleral contact lenses have been used with materials with very high transmissibility to gases and built with optimised thicknesses. Each application procedure was performed by the same operator.

The data show no statistically and clinically significant difference.

The difference in keratometric values, in the central area around 3 mm from the corneal vertex, before and after 15 days of contact lens use, was -0.0214 mm ( $p > 0.05$ ; Student's  $t$ -test); in the area around 5mm from the corneal vertex, before and after 15 days of contact lens use, was -0.0174 mm ( $p > 0.05$ ; Student's  $t$ -test); and in the area around 7 mm from the corneal vertex, before and after 15 days of contact lens use, it was -0.0203 mm ( $p > 0.05$ ; Student's  $t$ -test).

It is expected that there will be no changes in corneal curvature in keratoconus, when contact lenses are applied appropriately. Any corneal warpage requires a revision of the fitting of the lenses in respect to the surface of the eye.

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## Can we use two different corneal topographers with keratoconus?

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### Abstract

The aim of this study was to investigate the degree of agreement between corneal shape measurement in eyes with keratoconus performed by a Placido-disk optical reflection corneal topographer (Keratron, Optikon 2000 spa, Italy) and an acquisition system that combines Placido-disk optical reflection topography with anterior segment Scheimpflug tomography (Sirius, CSO, Italy).

After the verification of the videokeratoscopic reliability, a total of 76 eyes of 76 subjects affected by keratoconus were evaluated by the following parameters: the simulated keratometries related to the two main corneal meridians (Sim-K flat, Sim-K steep), mean corneal keratometry (mean Sim-K) and the geometric coefficient ( $p$ ). The results obtained with the Keratron corneal topographer were compared with the Sirius acquisition system.

The differences between the two devices in all parameters examined in this study were not statistically significant. The correlation coefficients (95% CI) between the two instruments are 0.865 (upper 0.798, lower 0.912) for the Sim-Ks and 0.757 (upper 0.646, lower 0.837) for the form factor  $p$ . The mean differences detected between the two instruments were 0.03 mm for the Sim-K flat parameter, 0.04 mm for the Sim-K steep parameter, 0.03 mm for the mean Sim-K parameter and 0.01 for the  $p$  parameter.

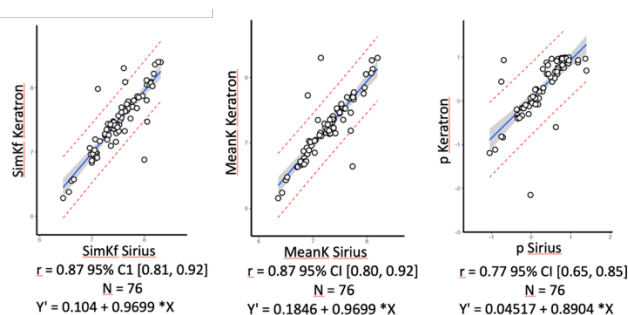


Figure 1: Graphs of the correlation estimate between Keratron and Sirius in the measurement of keratometries, mean corneal power and corneal shape in eyes with keratoconus. The blue line indicates the regression line, the area around the 95% confidence interval, the dashed red lines indicate the prediction interval of the distribution of values for the upper and lower extremes of 95%.

The degree of agreement between the two instruments is good. For the procedure of contact lenses fitting the devices are interchangeable.

## Can we use two different corneal topographers before and during orthokeratology?

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### Abstract

The aim of this study was to compare the measurement of corneal parameters with two different topographers during a year of orthokeratological treatment for myopia control.

An experienced operator used two different corneal topographers on the same sample. The simulated keratometry data on the flat meridian (K1) and curved meridian (K2), the mean value in a central area of 3mm (Kmax) and the corneal shape index (factor form  $p$ ) were extrapolated. They were compared before the use of orthokeratology lenses at seven follow-up dates, according to the normal application protocol of effectiveness and safety verification, carried out in the following twelve months.

Two different corneal topographers (Sirius, CSO, Italy; Keratron Onda, Optikon, Italy) were used during each follow-up visit during one year of orthokeratology treatment. 132 eyes (58% female) were measured in subjects between the ages of 8 and 15 years. Prior to treatment myopia was on average  $-2.91 \pm 1.08$  D, ranging from  $-0.75$  to  $-5.25$  D.

Statistically and clinically significant differences were found between the two instruments for each measured parameter. At  $t_0$ , the difference in the 95% match limits between the two devices for K1 was 0.28 mm with less curved measurements found by Sirius than by Keratron. During orthokeratological treatment, the differences were greater than at the baseline and with an opposite estimate, less curved measurements by Keratron than by Sirius. After orthokeratological treatment, the differences for K1 measurement were 4 times higher than the baseline data, for all other parameters the differences were greater than those found for K1. A statistical relevance was found between the two devices for both Kmax and the form factor. For each parameter, no statistical differences between measurements were found in a subsequent follow-up visit, for both devices.

Before and after orthokeratological treatment, the two devices showed a significant clinical and statistical difference. Their use is not interchangeable without considering the distortion estimate observed as the opposite between the two devices before and during treatment. The corneal eccentricity on an 8 mm string and the mean corneal power of 3 mm around the corneal vertex measurements showed poor agreement between the two devices. Stability of the orthokeratological effect on corneal parameters over time has been detected.

### Analysis of accommodative microfluctuations

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### Abstract

The accommodation carried out by the eye does not remain constant, but it presents some microfluctuations even if the accommodative stimulus is steady (Metlapally et al., 2016). The accommodative microfluctuations cause the observed object to change between the state of perfect sharpness, when the exercised accommodation is very similar to the requested accommo-

modation, and the state of slight blur, when the actual accommodation moves away from the theoretically required accommodation (Charman & Heron, 2015). This study analyses the trend of these accommodative microfluctuations and the relative interval for constant stimuli, in a sample with homogeneous age and occupation.

The dynamic accommodation of 67 students, 48% female, with an average age of 23 years, was measured by means of the aberrometer Osiris (CSO, Italia). This group was made up of 21 emmetropic, 10 hyperopic and 36 myopic subjects. Each measurement had a duration of 30 seconds, with a progressive and constant scale of stimuli. Every stimulus was presented for about 2.5 seconds. Four measurements were taken on each eye, in a complete darkness and after some minutes of dark adaptation.

Table 1: Accommodative response to the three different stimuli.

	Stimulus 4	Stimulus 5	Stimulus 6
Media	3.10	4.04	4.79
Standard deviation	0.618	0.490	0.566
95% CI mean bound	2.92	3.91	4.63
95% CI mean upper bound	3.27	4.18	4.95
Minimum	1.31	2.58	3.03
Maximum	4.05	5.04	6.22

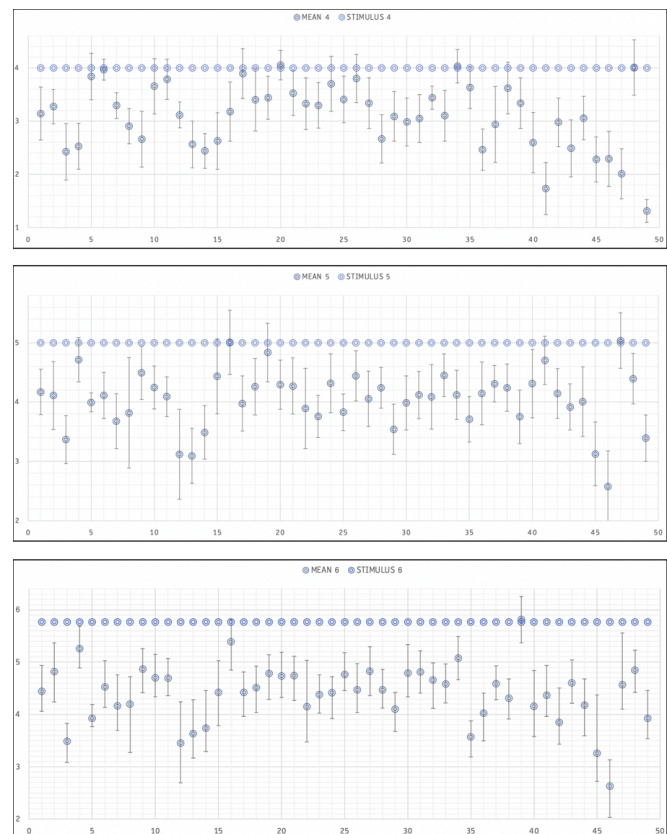


Figure 1: Summary graphs of the behaviour of each individual subject with respect to the accommodation exercised for three different stimuli (4, 5 and 6 D from above, respectively) and expressed microfluctuations in the error bars around the mean value. The values are in diopters.

Three intermediate intervals one dioptre apart were chosen for the analysis, from 4 to 6 D. By analysing the trend of the average accommodation values of both eyes, it can be shown that only the average values of the first stimulus interval (4 D) follow a normal distribution ( $p = 0.18$ ). The average values of the subsequent intervals (5D; 6D) do not follow a normal distribu-

tion ( $p = 0.03$ ;  $p = 0.003$ ). Observing the trend of the box plots of each subject along the three stimuli, 17 subjects presenting a non-progressive trend for an increasing stimulus can be identified. By repeating the analysis, neglecting the subjects with anomalous accommodation, a normal distribution of the average values in all the intervals is obtained. See Table 1 for average values and standard deviations of accommodative response to the different stimuli and Figure 1 for individual subjects' responses.

With the examined data, neglecting the subjects with anomalous accommodation, it was possible to calculate an average value of accommodation for each interval. As confirmed by other studies, the data present an increasing accommodative lag for an increasing stimulus demand (Gambra et al., 2009). The average standard deviation for the single stimuli is around 0.50D, which again is confirmed to be true by scientific literature. It increases slightly as the stimulus demand grows. For subsequent studies a more detailed analysis of the microfluctuations is required. In order to get more significant results, the low frequency microfluctuations should be subtracted from the entire data. In this way only the high frequency band is analysed.

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## Evaluation of the applications of corneoscleral contact lenses on regular corneas

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## Abstract

The purpose of this study is to illustrate the evaluation of corneoscleral contact lens (CScL) fitting from trial sets on regular corneas and to describe the observations necessary to allow the design of these contact lenses through case reports.

Each CScL is made up of two geometric zones: base curve (CB) and peripheral curve (PC). During the first phase, 40 eyes were selected on which the CScLs were applied according to the application protocol proposed by the manufacturer, which considers, as a parameter, the horizontal diameter of the visible iris, in respect to which, the first applied lens was a flatter, equal or steeper CB than corneal Sim-K. The study consisted of preliminary tests (tear film analysis and ocular morphological evaluation made with slit lamp) and instrumental tests (topography and OCT). The applications were evaluated by observing the fluorescein pattern formed. Applications deemed unsuitable were appropriately replaced before proceeding with a 2-hour adaptation.

The analysis of the results was carried out considering the incidence of the various cases. Particularly an incidence of alignment of 35% was shown post-adaptation (see Figure 1), while an important correlation was been noticed in the presence of insufficient post-lens tear turnover, especially in applications with

CB aligned-PC steep and CB steep-PC steep (see Figure 2), causing alteration of the corneal physiology.

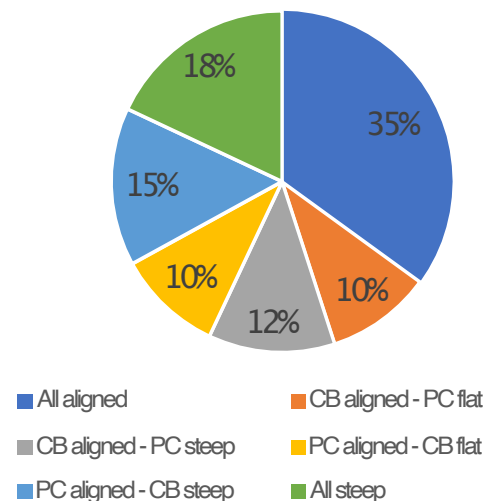


Figure 1: Incidence of post-fitting cases.

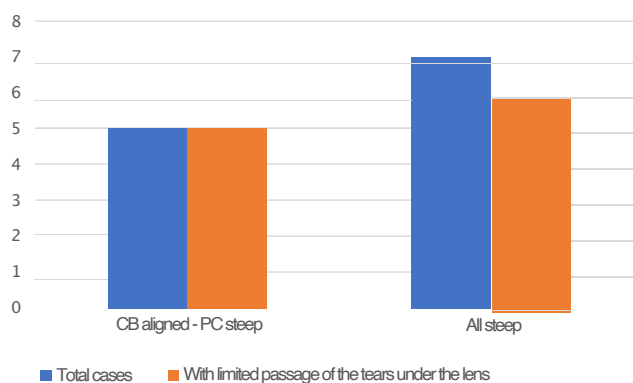


Figure 2: Incidence of the limited post-adaptation tear turnover.

During the second phase of the study, the design of CScL was described for each eye in two case reports. The two subjects (aged 32 and 25) initially had CScL from trial sets applied. Based on observations obtained, each lens was suitably made with the necessary modifications through the manufacturer. Once the CScL obtained was considered overall suitable, a one-month follow-up period was carried out. For the first case report, a suitable application was obtained. The application limitations that emerged, in particular for the second case (which presents an important scleral asymmetry and dry eye due to aqueous deficit), correlate to the limited exchange of the tears behind the lens and the impossibility of making a CScL with asymmetrical periphery in order to manage this condition.

It was possible to observe, through this study, how CScL can be a valid contactological alternative in cases of dry eye, managing to be well tolerated and to maintain a high optical quality thanks to the RGP material of which they are composed, unlike soft contact lenses which tend to dehydrate more rapidly. However, it remains essential to pay attention to the physiological complications that an incorrect application can cause. The possible customisation of additional parameters (e.g., asymmetrical scleral area) would allow for a more versatile and adaptable application to a wider range of cases.