Evaluation of ophthalmic lenses for myopia management

Project code: IOT-MIO-2018-01

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C/ Suero de Quiñones 34-36 3º
28002 Madrid, Spain
(+34)91 833 37 86

1. State of the art

Myopia currently affects approximately 30% of the global population, although it is estimated that the prevalence will increase to 50% by 2050. According to these predictions, about 5 billion people will be nearsighted by 2050.

Although it is not clear what different factors may contribute to the onset and development of myopia, some studies have suggested that myopia is a multifactorial consequence involving numerous genetic, ethical, and environmental factors.

Experimental studies using animal models have suggested different strategies to control the growth of the eye and consequently the evolution of myopia progression. The results of these studies have shown that the visual signal related to retinal defocus controls the refractive development of the eye. Thus, visual signals in the periphery of the retina cause changes in growth that affect axial length and central refraction. On the other hand, animal studies have shown that imposing myopic defocus in the periphery inhibits eye growth.

Although the results of studies provide sufficient evidence of the efficacy of different clinical interventions for myopia control, there are still unresolved questions related to the underlying mechanisms. This includes, but is not limited to, the contribution of central and peripheral retinal regions to the regulation of eye growth, as well as the influence of aberration changes such as positive spherical aberration.

1.1. Human studies with glasses for myopia control

There are different options being worked on to prevent or delay the onset of myopia, from an optical, pharmacological, environmental, and surgical perspective. However, the option of using glasses to delay myopia progression has quite a few advantages compared to other myopia control strategies: they are easy to fit, they are well accepted and tolerated, they are affordable for most, and they are minimally invasive.

The different myopia management spectacles options that have been worked on are as follows:

- **Under-correction** for distance vision around +0.50D to +0.75D has been a strategy used in clinical practice for many years to reduce myopia progression. However, recent studies have shown that it provides no proven benefit compared to full correction.

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- **Bifocal lenses** to reduce accommodative demand and/or reduce accommodative lag during near tasks. Most published studies suggest that there is no difference in myopia progression between single-vision and bifocal wearers.

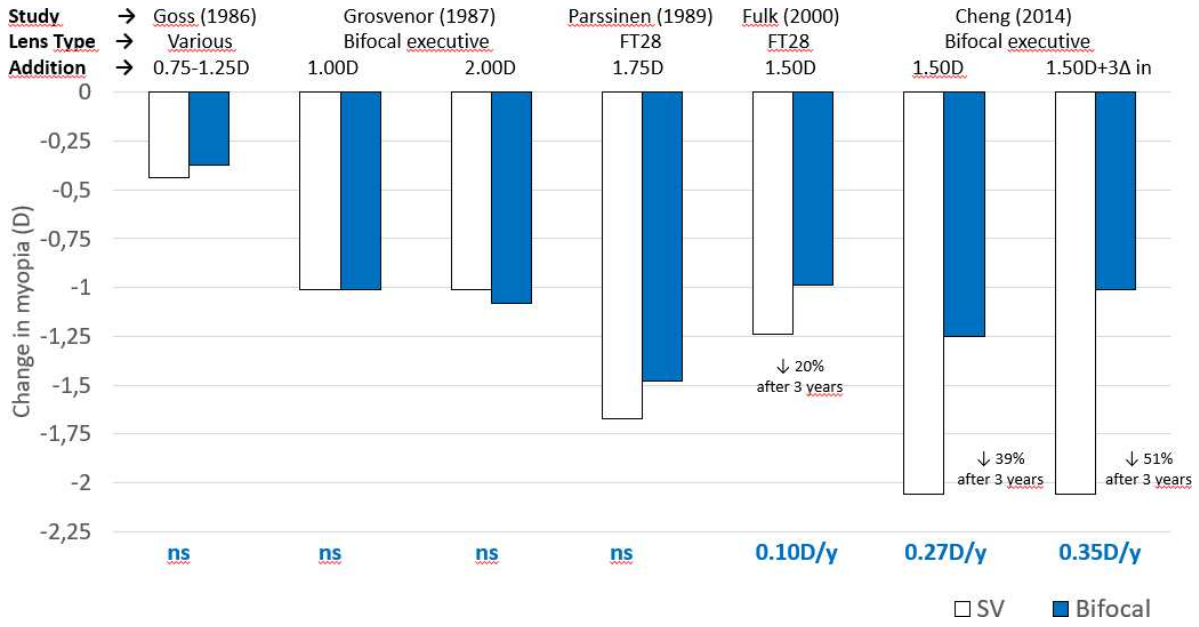

Figure 1. Results of clinical studies that have evaluated the efficacy of bifocal lenses as a treatment for myopia management.

- **Progressive lenses** have been the most studied spectacle treatment. The results have shown positive effects of their use as a treatment for myopia, but these effects are questionable from a clinical point of view.

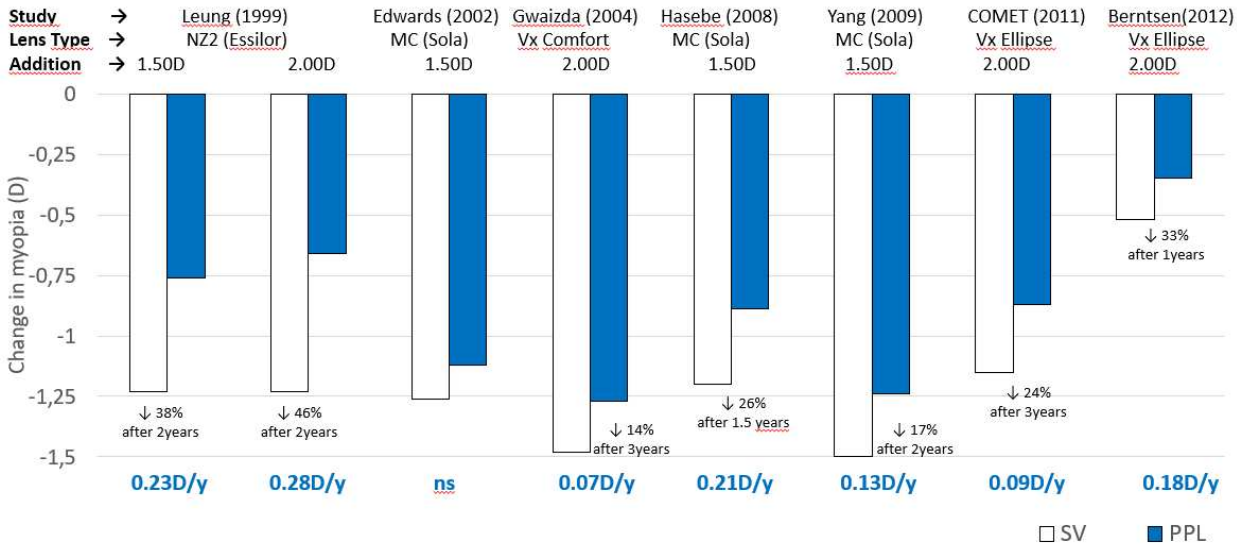

Figure 2. Results of clinical studies that have evaluated the efficacy of progressive lenses as a treatment for myopia management.

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- **Single vision lenses that induce positive defocus in the periphery:** These lenses are characterized by having an optical zone free of defocus and a peripheral zone that has a positive defocus induced from +1.00 to +3.50D. The results of these lenses show moderate benefits, being the lenses with smaller optical zone and higher peripheral defocus power the ones that have shown a greater delay in myopia progression.

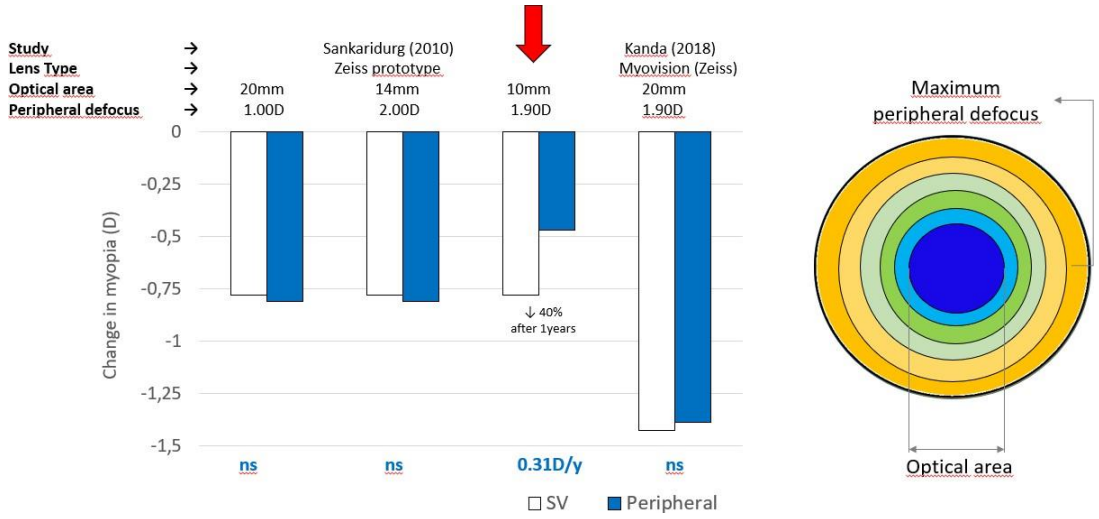
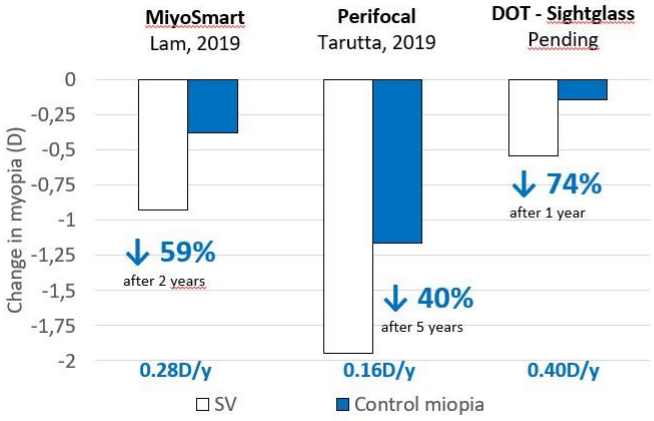


Figure 3. Results of clinical studies that have evaluated the efficacy of single vision lenses that induce positive defocus in the periphery as a treatment for myopia management.

- **Other options:** Finally, in recent years different lenses specifically designed for myopia management have been presented that induce a reduction of visual quality in the periphery of the lens by different techniques such as the use of microlenses (Miyosmart lens, Hoya and Stellest, Essilor), asymmetric positive defocus (Perifocal Lens) or scattering by laser (DOT Lens, SightGlass), whose results appear to be promising.

Figure 4. Results of clinical studies that have evaluated the efficacy of new lenses as a treatment for myopia management.



12 months follow up

	SV	MC
MiyoSmart - Hoya	-0.55D	-0.17D
DOT - SightGlass	-0.54D	-0.14D
Perifocal	-0.63D	-0.38D

24 months follow up

	SV	MC
MiyoSmart - Hoya	-0.93D	-0.38D
Perifocal	-1.18D	-0.78D

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2. Justification

During the last few years, myopia has been recognized as a public health problem that causes significant vision loss and is also a risk factor for the development of other important ocular conditions. The prevalence of this condition is increasing globally for reasons that are still unknown. Therefore, this increase in myopia has important implications for an adequate vision care service, including refraction services such as spectacle prescription and myopia prevention and management systems, especially in those with high degrees of myopia.

Previous studies in animal models have shown that retinal defocus plays an important role in the emmetropization process of the eye and therefore in the development and progression of myopia. According to published studies, optical compensation that includes an alteration of image quality in the periphery of the retina produces a decrease in myopia progression, with lenses with smaller optical zone and greater peripheral defocus showing greater efficacy. Based on previous literature, different ophthalmic lens prototypes have been developed consisting of a central optical zone surrounded by a peripheral zone that induces a reduction in optical quality.

In this study we propose to conduct a controlled study to evaluate the safety and effectiveness of the proposed ophthalmic lens prototypes as a myopia control system.

3. Hypothesis

The proposed ophthalmic lenses provide an adequate level of visual function while helping to slow the progression of myopia in myopic children.

4. Goal

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The main purpose of this study is to evaluate the short-term efficacy in decreasing myopia progression of 2 different prototypes of proposed ophthalmic lenses, compared to a control group, in a group of myopic children.

5. Methodology

5.1. Type of study

Double-blind experimental study to analyze the effect of 2 ophthalmic lens prototypes on myopia progression. The follow-up period to evaluate the efficacy of the lens will be 6 months including a total of 4 visits.

5.2. Subjects of the study

The sample will consist of a group of 92 myopic children who must meet the inclusion/exclusion criteria indicated in Table 1 and who will be randomly assigned to one of the treatment groups:

- Control group who will receive a standard single vision lens.
- Group 1 who will wear a prototype lens based on peripheral positive defocus.

Inclusion criteria	Exclusion criteria
- Age: 5 to 12 years - Myopia (spherical equivalent with cycloplegic) ≤ -0.50D - Astigmatism < 1.50D - Anisometropia < 1.50D - Best-corrected visual acuity ≥ 20/20	- Patients who have received any previous treatment for myopia control, including the use of RPG contact lenses. - Participants with ocular pathology such as retinal detachment. - Participants using drugs that may affect pupillary size and accommodation or produce effects on the ocular surface. - Participants with systemic diseases that may affect their vision.

Table 1. Inclusion/Exclusion criteria

5.3. Material

5.3.1. Facilities and infrastructure

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The study will be coordinated at the offices of Indizen Optical Technologies (Madrid, Spain) and the ophthalmological measurements will be performed in collaboration with Clinica Novovisión/Universidad Europea de Madrid, with a collaboration agreement to be defined. The children will be recruited by the Amires association.

5.3.2. Tests, questionnaires, and instruments for optometric and ophthalmologic evaluation:

- **Sociodemographic questionnaire**: participants' parents will complete a questionnaire that includes information regarding age, sex, ocular and general history, ocular surgeries, history of parents with myopia, age of onset of myopia, history of myopia progression and previous ocular treatments.
- **Objective refraction:** will be performed using an autorefractometer after cycloplegic using preferably 3 drops of cyclopentolate.
- **Ocular health assessment:** It will be performed according to Novovisión's standard procedures.
- **Biometry:** the axial length of the eye will be measured with the optical biometer preferably IOL Master (Carl Zeiss Meditec, Jena, Germany).
- **Binocular vision:** Distance and near phoria will be measured by Von Graefe's technique, the accommodative amplitude will be measured by Sheard method, and accommodative lag by MEM retinoscopy.
- **Usability questionnaires:** Questionnaires to assess children's satisfaction while wearing the spectacles, to record the wearing period and spectacle-associated problems and adverse effects.

5.3.3. Prototypes of ophthalmic lenses:

All lenses and frames required for the study will be provided by Indizen Optical Technologies. For the duration of the study, glasses will be provided free of charge (lenses + frames) ensuring that children always have a spare pair of glasses. In addition, we will change the lenses and glasses free of charge in case the prescription changes or the glasses break. Likewise, the ophthalmological examinations will be completely free of charge, so that the participation in the study does not entail any cost or commitment for the participants.

Children can be assigned to one of the three types of lenses to be tested:

- Control lenses: Standard spherocylindrical lenses.

- Prototype 1 lens: Lenses with a central zone that provides the patient's optimal prescription surrounded by a zone of positive defocus that increases progressively from the center to the periphery of the lens, in an asymmetrical manner between the different zones of the lens.

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5.4. Procedure

- Visit 1 (Recruitment and Baseline measurements): The optometrist will provide information about the study to the parents of the children, who then signed a written consent form after any doubts will be cleared up. The optometrist also will check that the children met the inclusion criteria. In this same visit, baseline measurements will be taken. All children shall be submitted an ophthalmology exam to evaluate their ocular health, and their cycloplegic autorefraction, binocular vision, and axial length will be recorded in the case report form. Additionally, parents will complete a sociodemographic questionnaire, and the children will select the frames for their spectacles.

Once the visit is completed, the IOT team will order 2 pairs of glasses with the same prescription and customization parameters, which will be the final glasses that the participants will wear during the study period. Before delivering the glasses to the participants, a full quality control will be performed on the quality and fit of the lenses.

- Visit 2 (Delivery of glasses): Previous glasses are removed, and 2 new glasses will be delivered to be used during the study period. Verification of fit and delivery of glasses usability questionnaire.

- Visit 3 (6 months follow-up): Collection of spectacle usability questionnaire and data collection after treatment period. Ophthalmological data will be recorded after treatment including cycloplegic refraction, biometry, and usability questionnaires.

- Visit 4 (12 months follow-up): Collection of spectacle usability questionnaire and data collection after treatment period. Ophthalmological data will be recorded after treatment including cycloplegic refraction, biometry, and usability questionnaires.

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Task	Responsible Partner
Recruitment	Amires
Visit 1: Patient information, verification of criteria, ophthalmological evaluation, and selection of frames.	Clinica Novovisión/Universidad Europea de Madrid/IOT
Visit 2: Delivery of glasses	IOT
Visit 3: 6 months follow-up	Clinica Novovisión/Universidad Europea de Madrid
Visit 4: 12 months follow-up	Clinica Novovisión/Universidad Europea de Madrid
Statistical analysis and final report	IOT/ Clinica Novovisión/Universidad Europea de Madrid

5.5. Data collection and statistical analysis plan

All variables for each individual and in each phase will be collected in the data collection notebook designed for this purpose. All data will be included in a database developed for this purpose for subsequent statistical analysis. The main variables of the study will be the values of axial length and refraction with cycloplegia.

A comparative statistical analysis of absolute (mm) and relative (%) axial length growth between the lens for the management of myopia and the standard single vision lens groups will be done done using the software STATA®. Absolute axial length growth will be calculated as median relative difference after 6 and 12 months of treatment as (AL at 6m – baseline AL)/ baseline AL *100 and (AL at 12m – baseline AL)/ baseline AL *100, respectively. Significance level will be set as p-value < 0.05. Efficacy of myopia management lenses will be evaluated by comparing the means of relative axial length growth in children treated with myopia management lenses to that of children treated with the standard single vision group.

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