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In vitro and in vivo analysis of the optical quality of an extended depth-of-focus intraocular lens with isofocal design.

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Abstract:	Purpose: The aim of this study is to compare optical quality results obtained in laboratory analysis (in vitro) versus clinical data (in vivo). Methods: The optical quality of ISOPure intraocular lens was assessed both in vitro and in vivo using the modulation transfer function (MTF) for 3.0 and 4.5 mm pupil diameters. In vitro measurements were obtained using deflectometer NIMO TRF1504, while in vivo measurements were taken with OPD-Scan III in a set of patients implanted with this lens. Ray tracing techniques were used to determine the MTF and area under MTF curve (MTFa) from the measured wavefront for the isolated lens and for the whole eye. Results: The MTF of the isolated lens obtained under both in vitro and in vivo conditions showed comparable results for both pupil sizes. However, differences were found when comparing the MTF of the whole eye with the lens implanted versus the MTF measured in vitro for 4.5 mm pupil size. Also, the MTFa defocus curve was compared with the defocus curve measured in vivo. Conclusion: The defocus curve from the in vivo study aligns closely with the MTFa of the in vitro model, with a useful defocus range of 0.40D. Thus, it is possible to anticipate the visual results of the implanted isofocal lens by using measurements on an optical bench and conducting optical simulations.

TITLE PAGE

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Key messages:

What is known

-Extended depth of focus (EDoF) lenses are prominent for expanding vision range in pseudophakic eyes, exceeding traditional limits.

-The ISOPure lens is characterized as a bi-aspheric refractive design that produces an extended depth of focus design

What is new:

-The MTF of the isolated lens obtained under both in vitro and in vivo conditions showed comparable results

-The defocus curve from the in vivo study aligns closely with the MTFa of the in vitro model, with a useful defocus range of 0.40D.

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Declarattions

Ethical approval: Approval for the study was obtained from the clinical research ethics committee of Hospital Clínico San Carlos de Madrid (Madrid, Spain) under the code number 20/030-R_P. The study adhered to the principles outlined in the Declaration of Helsinki.

Conflict of Interest: The authors declare no competing interests

Data availability: Data underlying the results presented in this paper are not publicly available at this time but may be obtained from the authors upon reasonable request.

ABSTRACT

Purpose: The aim of this study is to compare optical quality results obtained in laboratory analysis (*in vitro*) versus clinical data (*in vivo*).

Methods: The optical quality of ISOPure intraocular lens was assessed both in vitro and in vivo using the modulation transfer function (MTF) for 3.0 and 4.5 mm pupil diameters. In vitro measurements were obtained using deflectometer NIMO TRF1504, while in vivo measurements were taken with OPD-Scan III in a set of patients implanted with this lens. Ray tracing techniques were used to determine the MTF and area under MTF curve (MTFa) from the measured wavefront for the isolated lens and for the whole eye.

Results: The MTF of the isolated lens obtained under both in vitro and in vivo conditions showed comparable results for both pupil sizes. However, differences were found when comparing the MTF of the whole eye with the lens implanted versus the MTF measured in vitro for 4.5 mm pupil size. Also, the MTFa defocus curve was compared with the defocus curve measured in vivo.

Conclusion: The defocus curve from the in vivo study aligns closely with the MTFa of the in vitro model, with a useful defocus range of 0.40D. Thus, it is possible to anticipate the visual results of the implanted isofocal lens by using measurements on an optical bench and conducting optical simulations.

Keywords: IOL, EDoF, optical quality, optical bench,

INTRODUCTION

The design of intraocular lenses for compensating both cataract and presbyopia is constantly evolving, achieving significant progress in recent years. The goal is not only to attain independence from glasses for patients at various distances but also to achieve excellent optical quality, ensuring that patients are satisfied with the final visual outcome [1].

Therefore, when new designs emerge, it becomes necessary to conduct both objective and subjective evaluations. This includes analyses in both optical bench and clinical studies. The aim is not just to understand the obtained results but also to establish correlations between these results, particularly between the clinical results obtained and the optical quality of the lens. This approach provides a better understanding of the behavior of the lenses under analysis.

Among the various solutions aimed at extending the range of vision for the pseudophakic eye, extended depth of focus (EDoF) lenses stand out. These lenses utilize aspheric refractive surfaces to achieve good visual quality at multiple distances. One of the latest commercially available EDoF designs is the ISOPure lens, developed by BVI Medical (Liége, Belgium). What sets this lens apart is its unique distinction as the sole isofocal design lens currently available, according to the inventors [2]. Initially, it may seem challenging to draw parallels with results obtained from lenses of entirely different designs.

As per the manufacturer's information, the ISOPure lens aims to achieve superior intermediate vision compared to standard monofocal IOLs, demonstrating, on the optical bench, an extended depth of focus of around 1.00 D, surpassing standard aspheric monofocal IOLs by 50% [3]. Additionally, when compared to multifocal IOLs, the ISOPure design reduces the incidence of photic phenomena that are inherent to multifocal designs presenting a discrete number of separate foci [4].

The ISOPure lens is characterized as a bi-aspheric refractive design that produces an extended depth of focus design. The lens exhibits a continuously varying power distribution from the center to the periphery, characterized by rotationally symmetric concentric zones of constant power with seamless transitions between them. According to the patent [2], the central region of the lens has a higher power, while the periphery has a lower one. The aspheric surfaces are a combination of a conicoid and a polynomial with even powers of the radial coordinate (“even asphere”) commonly used in optics [5]. The inclusion of even aspherical coefficients from the 4th to the 10th order in the ISOPure aspheric surfaces significantly enhances its multifocal optical performance, as noted by the designers [2].

Various authors have demonstrated discrepancies between results obtained on an optical bench [6, 7] with large pupils and clinical outcomes [8], indicating worse laboratory results compared to those achieved in the clinical setting with ISOPure lens. Therefore, the aim of this study is to compare optical quality results obtained in laboratory analysis (*in vitro*) versus clinical data (*in vivo*), considering pupils of 3.0 and 4.5 mm. The comparison will encompass the modulation transfer function (MTF) and the through focus area under the modulation transfer function (MTFa). Also, we will compare the MTFa defocus curve with the average of visual acuity (VA) defocus curve under *in vivo* conditions in eyes implanted with ISOPure lens. The results will be evaluated under conditions simulating an artificial cornea on the optical bench scenario, and the complete ocular system in the clinical measurements.

METHODS

Intraocular lenses

The ISOPure lens incorporates a patented polynomial design featuring bi-aspherical surfaces. This design shows specific surface modifications affecting Zernike coefficients up to the 10th order, resulting in an anterior and posterior surface profile characterized by heightened negative spherical aberration from the center to the periphery of the optic [2]. The primary objective of this design is to enhance the depth of focus in comparison to a monofocal lens. It is manufactured with a hydrophobic acrylic glistening-free material, and it has an ultraviolet and light-blue filter. The refractive index is 1.53 and the Abbe number is 42.

Optical Bench

The lens ISOPure of +20.00 D was analyzed using a deflectometer, the NIMO TR1504 device (Lambda-X, Nivelles, Belgium), which operates under the Schlieren principle, combined with the interferometry method of phase shifting [9]. Zernike coefficients from the first to the eighth order were obtained through this system, acquiring wavefront data of the lens under *in vitro* conditions. The measurement light source exhibits a radiance peak at 546 nm, which closely aligns with the spectral relative luminance efficacy peak of the human visual system, positioned at 555 nm in photopic conditions. The measurement protocol adhered to the same procedure outlined by Gómez-Pedrero *et al*. [10] for intraocular lenses. This involved conducting 10 measurements for each evaluation without the application of filters, treating the lens as a thin lens.

Clinical Study

A prospective study was carried out at Miranza IOA in Madrid, Spain, involving patients undergoing cataract surgery with bilateral implantation of the isofocal ISOPure. Prior to participation, all patients provided written informed consent after being thoroughly briefed on the study's nature, protocols, and the implications of their involvement. Approval for the study was obtained from the clinical research ethics committee of Hospital Clínico San Carlos de Madrid (Madrid, Spain) under the code number 20/030-R_P. The study adhered to the principles outlined in the Declaration of Helsinki. This clinical study was aimed to have *in vivo* results (defocus curve and aberrometric information) to be compared with the *in vitro* results obtained with the optical bench.

The inclusion criteria for all patients comprised being aged 50 years old or older, with healthy eyes, exhibiting regular corneal astigmatism of less than 1.0 D, and having clear intraocular media, excluding cataracts. The calculated lens power for emmetropia was required to be 20.00 ± 2.00 D. Exclusion criteria encompassed prior ocular pathologies like uveitis, age-related macular degeneration, or previous intraocular or corneal surgery, as well as irregular astigmatism and the presence of pupillary abnormalities.

After computing the sample size, eighteen participants were recruited. The sample size calculation involved using the primary spherical aberration variable reported for the ISOPure lens by Mencucci *et al*. [11]. The mean value obtained was 0.060 ± 0.035 microns for a 4.0 mm pupil [11]. Considering this standard deviation, and with an alpha risk of 0.05 and a beta risk of 0.2 in a two-sided test, 18 subjects were required to identify a statistically significant difference equal to or greater than 0.025 microns. A dropout rate of 10% was anticipated.

Aberrometric measurements were conducted using the OPD- III Scan III system (Nidek Technologies, Gamagori, Japan), and the monocular VA defocus curve was assessed with 100% contrast ETDRS test at 4 meters under photopic conditions within a range of +1.50 to -1.50 D in steps of 0.50D. The clinical data analyzed in this study pertain to measurements taken three months post-surgery. Although all participants in the study underwent bilateral symmetric IOL implantation, only the right eyes were included in this study.

Optical Quality Functions Calculation

Optical quality functions, such as MTF and MTFa were computed from the wavefront data obtained under both *in vitro* (using NIMO) and *in vivo* (using OPD-Scan III) conditions. Computations based on wavefront data obtained under *in vitro* conditions were conducted for both the isolated lens measured with NIMO and for the optical system formed by IOL measurements coupled with an ISO2 cornea model. The ISO2 cornea model presents a +0.28 μm spherical aberration for a pupil diameter of 5.15mm, as described by the ISO 11979-2:2014 standard [12]. Notice that, to maintain consistency, we have performed our calculations by keeping the same diameter of the beam incident at the lens plane regardless of the pupil diameter. For example, when the pupil diameter is 3mm, the diameter of the incident beam at the lens plane should be 2.55mm, considering the pupil magnification of the human eye as 0.86x.

Additionally, computations based on *in vivo* data were performed considering both total ocular aberrations (*in vivo* ocular) and internal aberrations (*in vivo* internal). The *in vivo* MTF was calculated from the wavefront described by the average values of the Zernike polynomials coefficients for the whole set of participants. Notice that OPD-Scan III can measure the total aberrations of the eye, including corneal aberrations. So, the wavefront data obtained corresponds to *in vivo* conditions of the whole eye. Additionally, by subtracting corneal aberrations at the exit pupil of the eye, it is possible to estimate the inner aberrations of the eye. In this case, these inner aberrations would correspond to those of the IOL implanted in the eye.

To compute MTF from the measured wavefront, the commercial ray-tracing software (Zemax Optics Studio (ZOS) version 18.9, Ansys Inc., USA) was employed [5]. The lens measured by NIMO was described in ZOS by a Zernike phase surface both isolated and in the system with the ISO2 cornea lens. On the other hand, the *in vivo* eye was always described as a Zernike phase surface in ZOS. In this simulation, all Zernike's coefficients up to the order 5th as well as SA of the order 6th and 8th were included. All calculations were performed considering two pupil sizes, 3.0 and 4.5 mm, respectively.

To quantify the EDoF performance of the isofocal lens, the area under the MTF curve, MTFa, was computed for different values of defocus following the procedure of Vega *et al*. and Alarcon *et al*. [13, 14]. Furthermore, an estimation of VA from the MTFa was performed using the models described by Armengol *et al*. [15].

RESULTS

Eighteen eyes from eighteen patients were included in this study, of whom 55.5% were male. The mean age was 72.22 ± 7.16 years. The mean power value of the implanted lens was 20.08 ± 1.05 D. The mean pupil size was 3.10 ± 0.58 mm for photopic conditions and 4.31 ± 0.67 mm for mesopic ones.

The MTF computed from the *in vitro* and *in vivo* measurements was analyzed. First, we compared the MTF of the lens alone, for pupil sizes of 3.0 and 4.5 mm. Thereafter, we studied the MTF of the *in vivo* eye with an eye model *in vitro*, considering the same pupil diameters. Fig. 1 depicts the MTF for an entrance pupil diameter of 3.0 mm (left side) and 4.5 mm (right side) for the four analyzed situations: two of them obtained under *in vitro* conditions, labeled in the Fig. 1A and 1E as "NIMO" and in the Fig. 1C and 1G as "NIMO + Cornea ISO2", and the other two obtained under *in vivo* conditions, labeled in the Fig. 1B and 1F as "*in vivo* internal" and in the Fig. 1D and 1H as "*in vivo* ocular". Notice that in the first four panels (1A, 1E, 1B and 1F) the MTF is computed for the lens isolated with a total power around 20 D and the last four panels (1C, 1G, 1D and 1H) corresponds to an eye model (*in vitro*) or the proper eye (*in vivo*) with a total power around 60D, hence the change of the cut-off frequency.

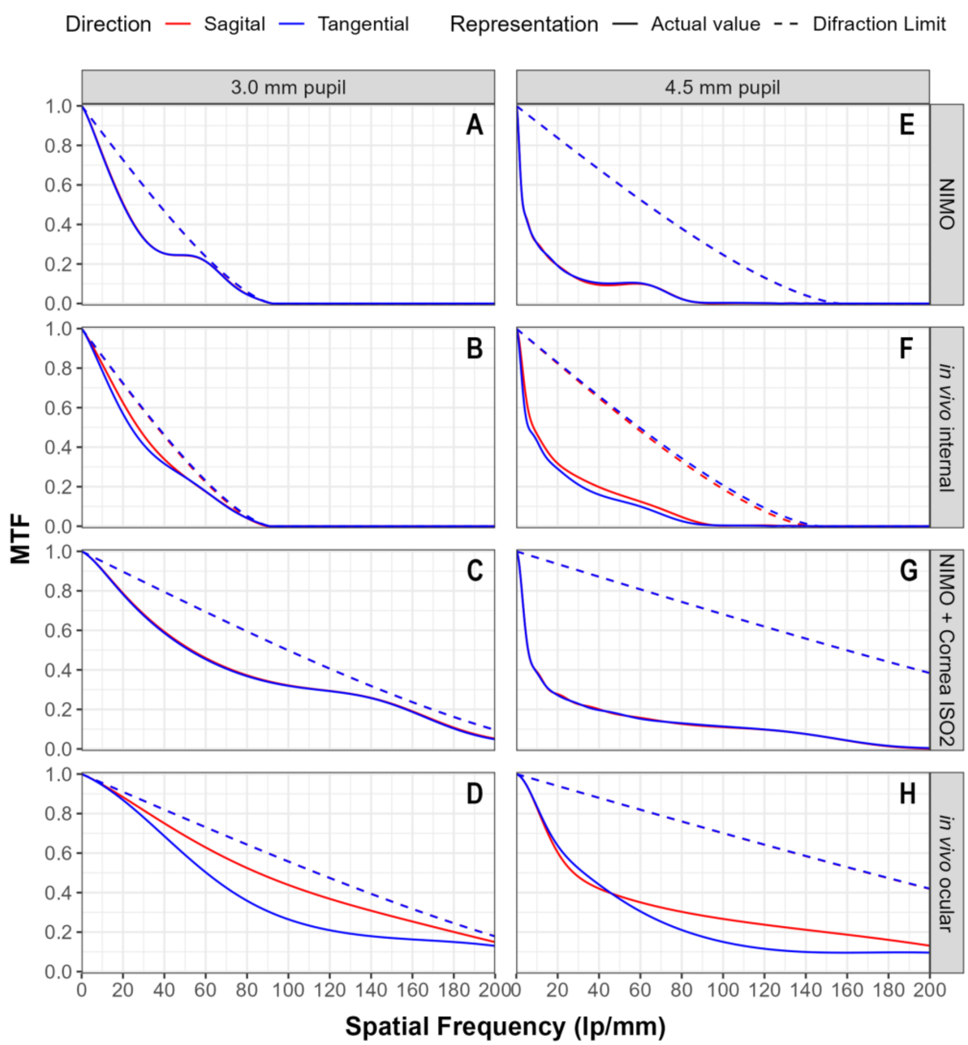

Fig. 1. Representation of the MTF for a 3.0 mm entrance pupil diameter (left side) and a 4.5 mm entrance pupil diameter (right side) for the four analyzed situations: under *in vitro* conditions, labeled in the Fig. 1A and 1E as "NIMO" and in the Fig. 1C and 1G as "NIMO + Cornea ISO2", and the other two obtained under *in vivo* conditions, labeled in the Fig. 1B and 1F as "*in vivo* internal" and in the Fig. 1D and 1H as "*in vivo* ocular". lp/mm: line pairs per millimeter.

The MTF obtained for the isolated IOL measured *in vitro* with the NIMO for both pupil sizes (Figs. 1A for 3 mm and 1E for 4.5 mm pupil size) shows a very similar pattern to MTF measured *in vivo* with the OPD III (Figs. 1B for 3 mm and 1F for 4.5 mm pupil size). Both the *in vitro* (NIMO) and *in vivo* (OPD III) MTF show a comparable area under the curve and cut-off frequency. Considering the whole eye for a 3 mm pupil, *in vitro* MTF obtained by coupling the NIMO-measured wavefront with the ISO2 cornea (Fig. 1C) is also close to *in vivo* MTF measured with the OPD III (Fig. 1D). But some differences arise when the comparison is done for a 4.5 mm pupil, with the *in vitro* results (Fig. 1G) being slightly worse than the actual *in vivo* measured results, especially for spatial frequencies below 80 lp/mm. Both the *in vitro* and *in vivo* results show a much better optical quality once the IOL is inserted in a model eye (or implanted in a real eye) than that of the isolated lens, both in terms of area under the MTF curve and in terms of the cut-off frequency.

To show the EDoF of the ISOPure lens, we have also computed the area under the MTF curve, MTFa, for different defocus. Fig. 2 plotted the MTFa computed from the average *in vivo* MTF ocular measurements and the MTFa computed from the *in vitro* MTF from the eye model with ISOPure IOL measurements coupled with an ISO2 cornea model for different values of defocus considering an entrance pupil of 3 mm.

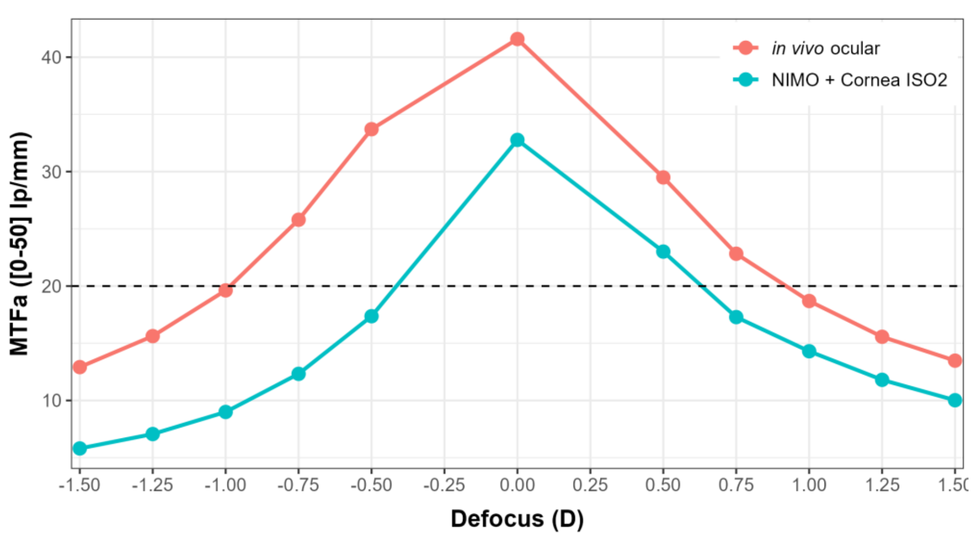

Fig. 2. MTFa-derived defocus curves for the *in vivo* eye (red line labelled as "*in vivo* ocular") and for the model eye with ISOPure IOL measurements coupled with a ISO2 cornea model measurements (green line labelled as "NIMO + Cornea ISO2").

The extended range of vision of an optical system aim to extend a continuous axial range of the image space, known as depth of focus (DOF). For defocus values where the MTFa value is ≥ 20, the expected visual acuity would be around 0.0 logMAR [7]. So, according to the results depicted in Fig. 2, it may predict around 1.00 D of useful range of vision with a visual acuity around 0.0 logMAR for *in vivo* conditions and 0.40 D for *in vitro* conditions.

To further demonstrate the EDoF nature of the studied lens, Fig. 3 shows the simulated VA defocus curve computed from the MTFa derived from the *in vitro* MTF of the lens plus ISO2 cornea eye model, using both Armengol`s models [15] as compared to the monocular VA defocus curve obtained in the clinical study.

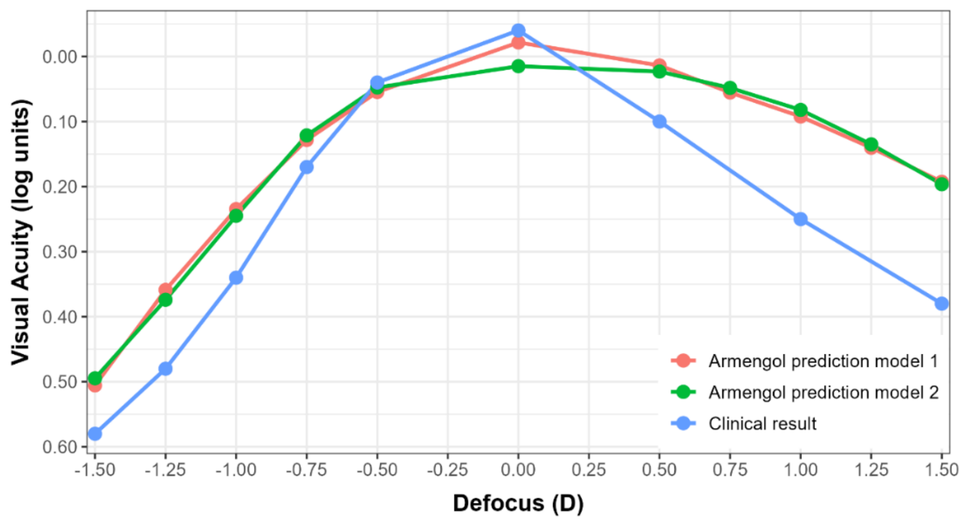

Fig. 3. Comparison between monocular VA defocus curve obtained in the clinical study (blue line) vs estimated with Armengol model 1 (red line) and model 2 (green line) data obtained under *in vitro* conditions.

DISCUSSION

The MTF of an optical system, such as an intraocular lens, whether isolated or implanted in a pseudophakic eye, provides information about how accurately the optical system transfers contrast from the object to the image for various spatial frequencies. An important question is whether it is possible to predict the MTF of a pseudo-phakic eye from the assessment of the MTF of an isolated lens of the same design. In this study we have carried out this analysis for a refractive EDoF lens with an isofocal design.

The ISOPure lens exhibits superior optical quality for a 3.0 mm pupil compared to a 4.5 mm pupil, as measured by the MTF metric. The difference is evident in contrast reduction for all spatial frequencies, particularly pronounced in lower frequencies. Specifically, at a spatial frequency of 50 lp/mm, the MTF decreases from 0.23 for a 3.0 mm pupil (Fig 1A) to 0.10 for a 4.5 mm pupil (Fig 1E). This suggests that the ISOPure lens delivers superior optical performance with a 3.0 mm pupil compared to 4.5 mm, especially noticeable at lower spatial frequencies. This is consistent with the highly aspherical design of both lens surfaces. It's important to note that there are no previously published results for the MTF of ISOPure isolated.

Under *in vitro* conditions ("NIMO + Cornea ISO2"), a significant improvement in MTF is observed, particularly for 3.0 mm pupil size. At a 50 lp/mm cut-off frequency, the MTF increases from 0.23 (Fig 1A) to 0.50 (Fig 1C) for 3.00 mm pupil, and from 0.10 (Fig 1E) to 0.18 (Fig 1G) for 4.5 mm pupil size. The *in vitro* eye model ("NIMO + Cornea ISO2") exhibits a MTF close to diffraction limits for 3.0 mm pupils, especially at higher spatial frequencies (Fig 1C), but experiences a 50% degradation in MTF for low spatial frequencies (around 10 lp/mm) for a 4.5 mm pupil size (Fig 1G). We must stress that the effective diameter of the beam at the lens plane is the same for the lens alone and for the *in vitro* eye model. The *in vitro* results are consistent with those reported by Alarcon *et al*. [6] who assessed the impact of pupil diameter on the through-focus optical performance of enhanced monofocal IOLs, including the ISOPure lens. Their findings revealed a significant dependence on the pupil size for the ISOPure lens, particularly for far and intermediate vision. In addition, Azor *et al*. [7] showed similar results on the MTF for defocus 0.00 D.

The substantial degradation of ISOPure MTF for large pupils when the lens is isolated contrasts with its performance when implanted within the eye. This highlights how the optical characteristics of the anterior segment of the eye are considered in the IOL lens design to achieve optimal performance in pseudophakic eyes for each pupil studied. Additionally, the spherical aberration (SA) of the ISOPure differs for a 3.0 mm or 4.5 mm pupil. According to Pérez-Sanz *et al*. [8] the ISOPure lens exhibits an increasing negative spherical aberration across its aperture. This negative spherical aberration may be compensated by the positive spherical aberration introduced by the eye's cornea. Such compensation could explain why the MTF of the pseudophakic eye surpasses that of the isolated lens.

It is important to emphasize that results obtained under *in vitro* conditions represent the overall optical quality of the entire system using an artificial model. Therefore, real patient analysis is necessary to understand how the ISOPure lens behaves in a context closer to clinical reality.

When calculating the MTF from aberrometric data of patients implanted with ISOPure under *in vivo* conditions ("*in vivo* ocular"), a pattern very similar to that obtained under *in vitro* conditions ("NIMO + Cornea ISO2") is observed, although with slight differences associated to pupil size. A substantial agreement is noted between *in vivo* and *in vitro* conditions for a 3.0 mm pupil (Fig 1C vs 1D). However, with a pupil diameter of 4.5 mm, the MTF *in vivo* surpasses the computed one significantly, especially for spatial frequencies below 60 lp/mm (Fig 1G vs 1H). There is a significant improvement at the 50 lp/mm spatial frequency, increasing from 0.18 (Fig 1G) to 0.40 units (Fig 1H). Furthermore, for low spatial frequencies, the curve does not decrease as abruptly as observed in the MTF of the *in vitro* model, observing a significant improvement at the 50 lp/mm spatial frequency, from 0.18 to 0.40 (Fig 1G vs 1H).

Additionally, in comparison with the MTF of the *in vitro* model, it is noticeable that, for low spatial frequencies, the *in vivo* curve does not decrease as abruptly, indicating possibly a more gradual and adaptive response of the system in real patients compared to the artificial laboratory model.

Our hypothesis suggests that the lack of correlation between MTF obtained under *in vivo* and *in vitro* conditions may be attributed to the Stiles–Crawford effect [16, 17] with is tantamount to a pupil apodization with an exponential function transmittance [18] for both incident and reflected light on the retina [19]. Another potential source of the observed discrepancies could be the inadequate representation of the eye's anatomy by the ISO2 cornea model plus lens. These differences between the Cornea ISO2 plus lens and the anatomical eye may also produce discrepancies in the computed values of the MTF.

Finally, we have to consider the feasibility of the hypothesis that the MTF which corresponds to the inner aberrations of the eye, measured *in vivo*, corresponds to that of the isolated lens. In comparing the MTF computed from the internal aberrations of the average pseudophakic eye, measured *in vivo* (Fig 1B and 1F), with the MTF of the lens alone measured *in vitro* (Fig 1A and 1E), a robust agreement was observed for both pupil diameters considered (3.0 and 4.5 mm). This suggests a close correspondence between the internal aberrations of the pseudophakic eye and the aberrations of the isolated lens.

Moreover, regarding the ISOPure lens, it seems that, on average, any potential tilts or misplacements resulting from the surgical procedure are of minor magnitude. The analysis of *in vivo* results considered the possibility of slight decentrations, and tilts of the lens implanted in the capsular bag. Nevertheless, the closeness between the MTF of the isolated lens, and the MTF estimated from the *in vivo* internal model suggests that the IOL maintains commendable stability within the capsular bag. Previous studies [20, 21] have highlighted the rotational stability and centration of the four-loop IOL (Micro F FineVision model), demonstrating comparability with that of the ISOPure (closed-loop quadrifocal) with a posterior angulated haptic. Given these considerations, the *in vivo* internal MTF analysis proves to be a valuable tool for identifying potential decentrations of the intraocular lens.

The objective evaluation of optical quality through the MTFa, , as depicted in Fig. 2, revealed superior visual performance for the *in vivo* model compared to the *in vitro* model for a 3 mm pupil. Both curves exhibit a similar shape, but with a discrepancy on the y-axis for each defocus point of approximately 10 MTFa units.

The *in vivo* MTFa (depicted by the red line in Fig. 2) indicates an MTFa value beyond 40 units for corrected distance optical quality at defocus 0.00 D. For defocus -1.00 D, the MTFa value is 20 units. Indeed, this suggests a potential useful range of vision around 1.00 D with a corresponding visual acuity of approximately 0.0 logMar (MTFa value 20) [7]. These findings align with those reported by other authors [22, 23].

In contrast, the *in vitro* MTFa (represented by the green line in Fig. 2) exhibits poorer performance and a narrower range of defocus compared to the *in vivo* MTFa. At defocus values of 0.00 D and -1.00 D, the MTFa values are 32 and 9 units, respectively. Consequently, the potential useful range of vision is approximately 0.40D. Other authors [7] showed a similar peak at 0.00 D of defocus but with a better focus range, reaching 0.86 D.

The extended depth of focus design of the ISOPure lens is evident in the defocus curves presented in Fig. 2 for both *in vivo* (actual pseudophakic eye) and *in vitro* (cornea ISO2 plus lens model). However, the useful range of vision provided by the *in vitro* model is only 0.40 D, compared to the 1.00 D offered by the *in vivo* model.

In addition to objective metrics, such as the MTFa, formulas to predict patients' visual acuity had been developed [15], establishing a connection between optical quality and vision quality under the premise of pre-clinical measurements [7]. Simulated visual acuity for the *in vivo* model has been calculated based on the MTFa to compare with the defocus curve of real patients.

Upon analyzing the defocus curve corresponding to real patients, it is observed that distance visual acuity remains between 0.00 and 0.05 logMAR from distance (defocus 0.00 D) to -0.50 D defocus, and beyond that value, visual acuity declines to 0.35 logMAR for -1.00 D defocus. This defocus curve of real patients aligns more closely with the MTFa of the *in vitro* model, encompassing useful defocus ranges of 0.40 D. Notice that the EDoF behavior of the isofocal lens is manifested in the different rate of the decrement of the VA when defocus rises depending on whether defocus is positive or negative.

Other authors have reported values of the defocus curve measured under *in vivo* conditions in real patients, but in binocular conditions, so their results showing better behavior is not directly comparable with ours [11, 24-25]. Specifically, the values of the study with the largest sample studied [25], 65 eyes implanted with ISOPure, showed VA values of -0.01, 0.15 and 0.24 logMAR for defocuses of 0.00, -1.00 and -1.5 D, respectively. Regarding results in monocular and photopic conditions, such as those of the present study, Salgado *et al*. [22] obtained better results than ours for the 1.00 and 1.50 D defocus. The differences may be due to various factors that affect the VA of the patients, such as neural pathway and processing of the retinal image [26].

The simulated VA reflected in the calculated VA defocus curves plotted in Fig. 3 has a similar behavior for the two formulas, presenting the peak at 0.00 D, a slight decrease until around -0.50 D and a continuous decrease until 0.20 logMAR and 0.50 logMAR for defocus of -1.00 D and -1.50 D respectively. The results of Azor *et al*. [7] provided better performance, maintaining distance VA up to -1.00D defocus.

Knowing the strong influence of the pupil in the objective metrics of optical quality and visual performance, the MTFa and VA simulations were only computed for a 3.0 mm pupil size, considering the average age of cataract patients and age-related changes in pupil size under photopic conditions. While pupil size was not specifically controlled during the clinical study, it was carried out under photopic conditions, and the average pupil size was approximately 3.0 mm (3.10 ± 0.58 mm).

Notice that the computed VA from the model eye with ISOPure IOL measurements coupled with an ISO2 cornea model ("NIMO + Cornea ISO2") is remarkably similar to the actual defocus VA. Consequently, we can conclude that predicting visual outcomes of the implanted isofocal lens is feasible through optical bench measurements and optical simulations.

CONCLUSIONS

In this paper we compare the MTF and MTFa of a refractive EDOF intraocular lens, with isofocal design, from *in vitro* and *in vivo* measurements. Using a commercial deflectometric system we have measured the wavefront aberrations (expressed as Zernike polynomials) of an ISOPure lens. In parallel, we have determined the average aberrations among a population of patients implanted with the same model of intraocular lens. Using a ray tracing program, we have computed the MTF and MTFa of the lens measured with the deflectometer *in vitro*, the optical system formed by an ISO2 cornea and the lens *in vitro*, the pseudophakic eye *in vivo* and the internal aberrations of the pseudophakic eye. In addition, the average VA vs defocus curved of the population studied has been compared with the defocus curve estimated from the MTFa following Armengol's model [15].

Regarding the performance of the lens, we have found that the MTF curve of the lens isolated is lower than the MTF curve of system formed by an ISO2 cornea plus lens. This may indicate that the lens design considers the fact that the lens is implemented within a human eye with a given spherical aberration pattern. Therefore, the aspherical geometry of the lens is optimized to compensate the aberrations of the cornea to obtain the best overall optical quality.

When comparing the MTF curve obtained for the ISO2 cornea plus lens model with corresponding curve for the average pseudophakic eye implanted with the same model of IOL, we observed a very good agreement for the lower pupil diameter and a somewhat lesser agreement for the large pupil diameter. Therefore, we consider that it is feasible, at least for small pupils, to predict the MTF of the pseudophakic eye implanted with an isofocal lens by measuring the lens wavefront aberrations and using this data in an ISO2 cornea plus lens model. This fact is highlighted when comparing the MTF of the measured lens isolated with the inner aberration of the pseudophakic eye, as these curves show a fair agreement even for large pupil diameters.

The EDoF nature of the isofocal lens is demonstrated by the variation of the MTFa against the defocus which present a small decreasing rate for positive defocus for both *in vitro* and *in vivo* conditions. These findings are corroborated also by the curve of VA versus defocus measured for the pseudophakic patients. We have also found a good fit between this curve and the VA computed from the MTFa using either of the phenomenological models proposed by Armengol *et al.* [15].

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FIGURE LEGENDS

FIGURE 1. Representation of the MTF for a 3.0 mm entrance pupil diameter (left side) and a 4.5 mm entrance pupil diameter (right side) for the four analyzed situations: under in vitro conditions, labeled in the Fig. 1A and 1E as “NIMO” and in the Fig. 1C and 1G as “NIMO + Cornea ISO2”, and the other two obtained under in vivo conditions, labeled in the Fig. 1B and 1F as “in vivo internal” and in the Fig. 1D and 1H as “in vivo ocular”. lp/mm: line pairs per millimeter.

FIGURE 2. MTFa-derived defocus curves for the in vivo eye (red line labelled as “in vivo ocular”) and for the model eye with ISOPure IOL measurements coupled with a ISO2 cornea model measurements (green line labelled as “NIMO + Cornea ISO2”).

FIGURE 3. Comparison between monocular VA defocus curve obtained in the clinical study (blue line) vs estimated with Armengol model 1 (red line) and model 2 (green line) data obtained under in vitro conditions.

Figure 1

Click here to access/download;Figure;Figure 1.tif

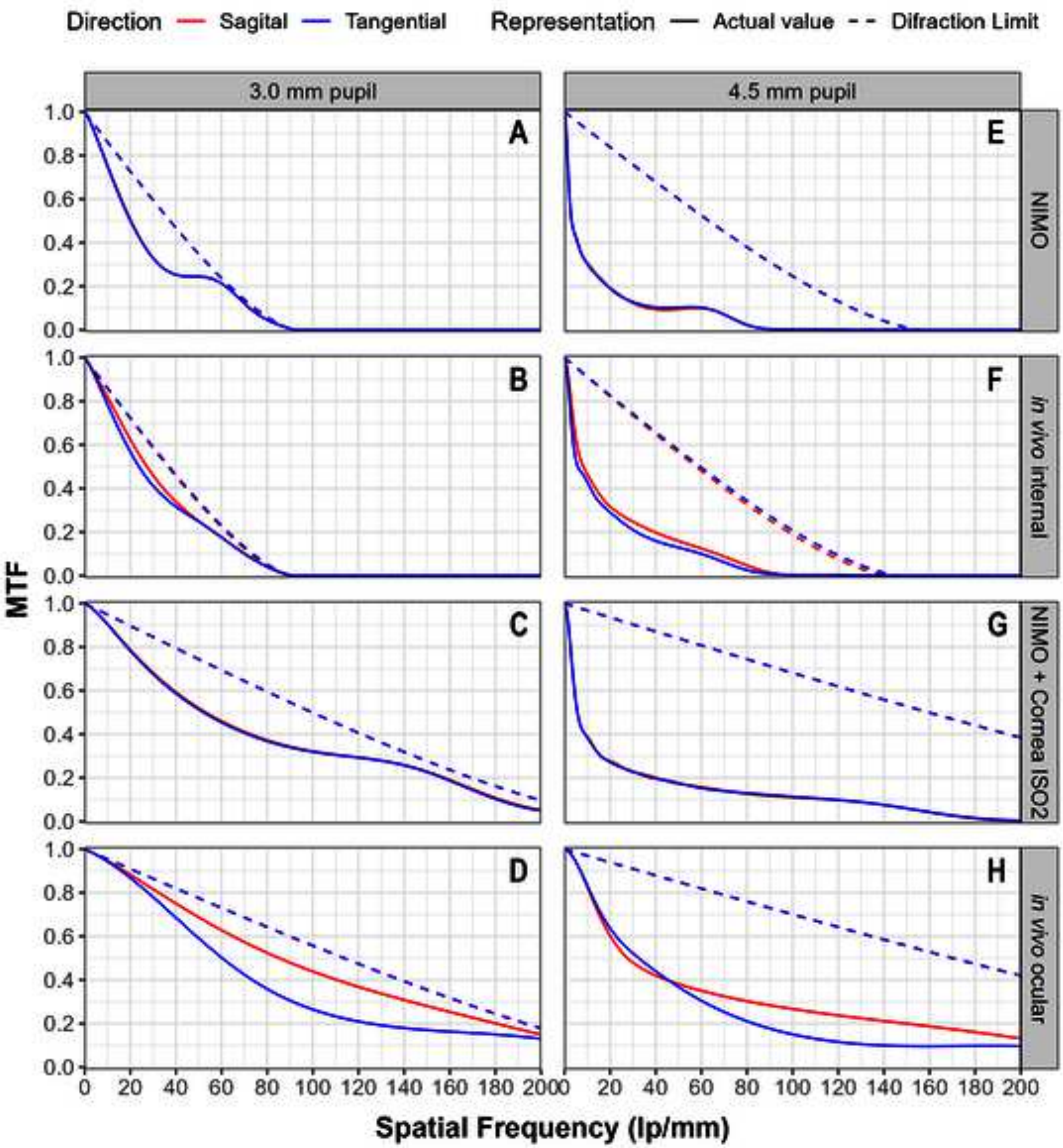


Figure 2

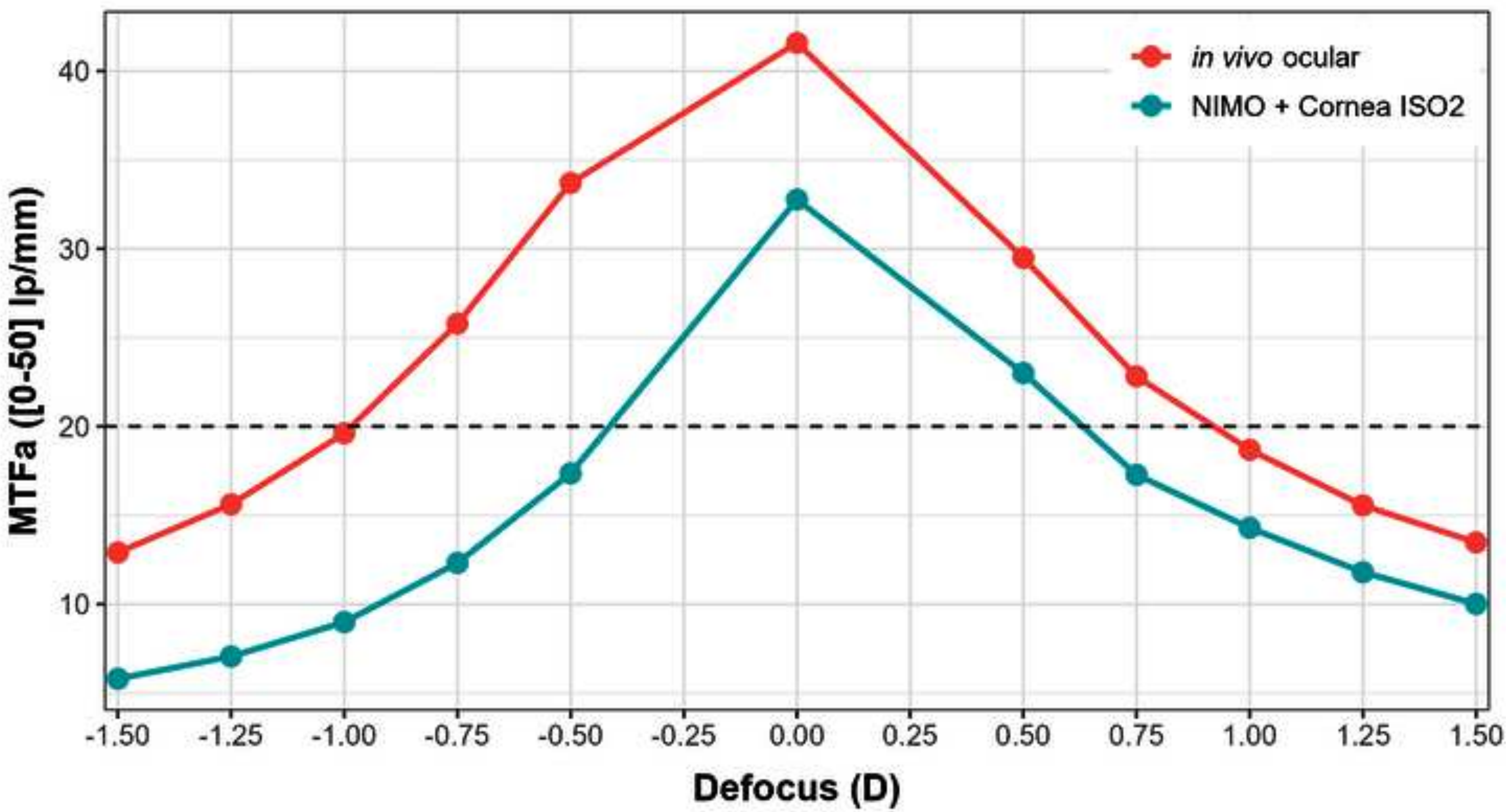
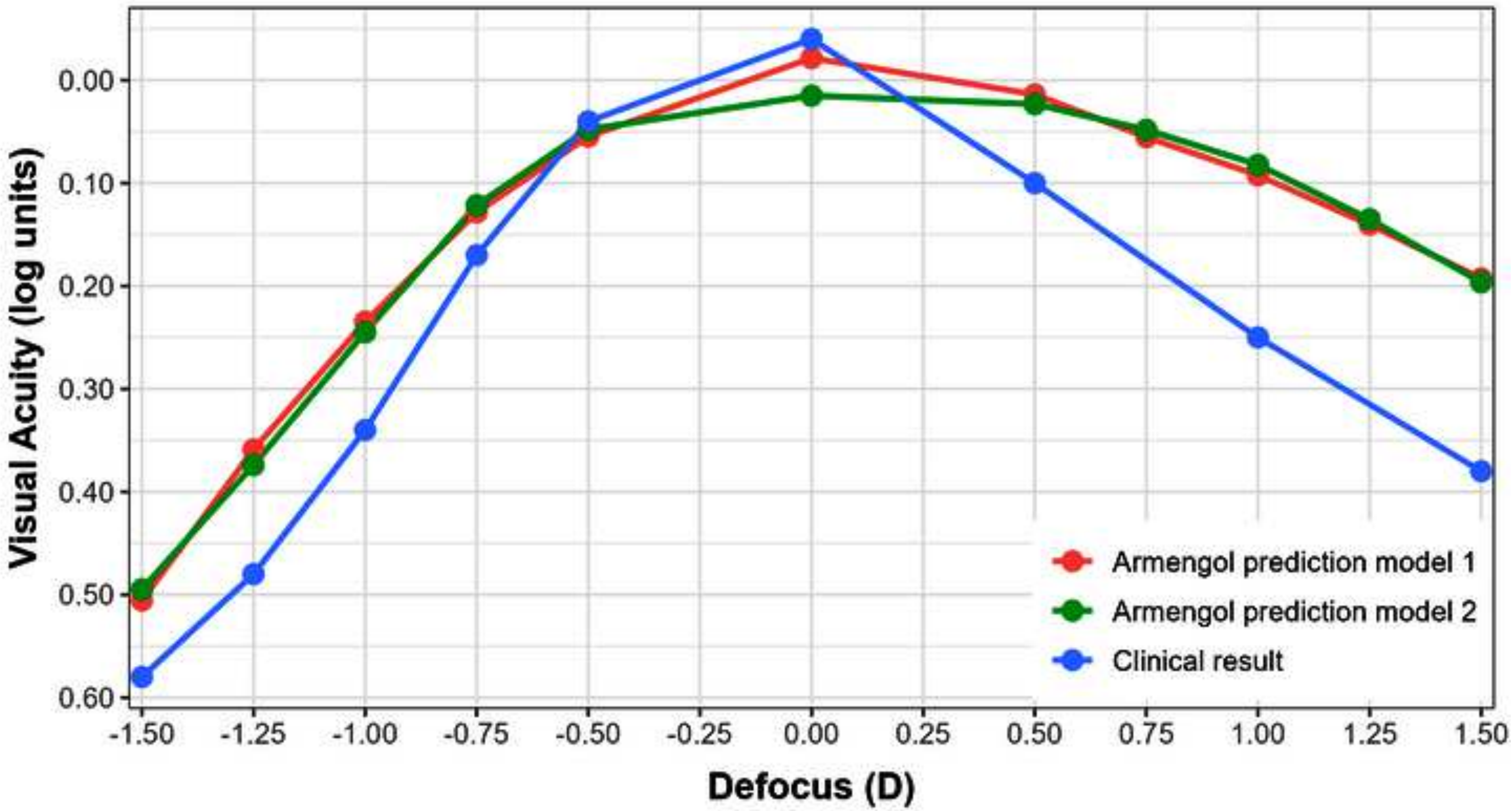

in vivo ocular
NIMO + Cornea ISO2
MTFa ([0-50] lp/mm)
40
30
20
10
-1.50
-1.25
-1.00
-0.75
-0.50
-0.25
0.00
0.25
0.50
0.75
1.00
1.25
1.50
Defocus (D)

Figure 3



Visual Acuity (log units)
0.00
0.10
0.20
0.30
0.40
0.50
0.60
-1.50
-1.25
-1.00
-0.75
-0.50
-0.25
0.00
0.25
0.50
0.75
1.00
1.25
1.50
Defocus (D)
Armengol prediction model 1
Armengol prediction model 2
Clinical result