RESEARCH

Long term Corneal multifocal stability following a PresbyLASIK technique analyzed by a light propagation algorithm

Asier Villanueva MSc *

Veronica Vargas MD †

David Mas PhD *

Magda Torky MD †

and Jorge L. Alió MD, PhD, FEBOphth †,§

From:

* Dpt. Optics and Optometry, University of Alicante, Spain

† Vissum Corporation, Alicante, Spain

§ Division of Ophthalmology, Universidad Miguel Hernández

Running Title: PresbyLASIK stability objective study

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Background: There is a lack of scientific evidence on long follow up studies of the outcomes of Presbylasik techniques. This study aimed to evaluate, using light propagation analysis, the stability of the results along 3 years follow up achieved with an excimer laser central PresbyLASIK technique.

Methods: Longitudinal retrospective, observational consecutive series of cases that comprises 24 eyes which had been treated by central either myopic or hyperopic Presbymax central PresbyLASIK. Eyes treated with the same version of Presbylasik software were included and followed by corneal topography at 3 months, 1 and 3 years after surgery. Based on the corneal topography data, a customized software based on a light propagation algorithm, developed with Matlab software, was used to analyze the simulated behavior of light through the ocular media, analyzing without the influence of changes in any other ocular structure other than the anterior corneal surface, the range of the corneal depth of focus in an objective form at each step of the follow up.

Results: The range of objective corneal depth of focus in Diopters was measured. Results were divided between the two groups (myops and hyperops) and each group was then studied at pupillary diameters of 3.0 and 6.0 mm. The results showed to be not statistically significant ($p > 0.05$) concerning the multifocality outcomes along all the follow up of the study.

Conclusion: The use of light propagation analysis of the multifocal anterior corneal surface following Presbymax presbylasik technique demonstrated stable outcomes over a 3 year follow up period.

The ageing of the human population is a reality that comes together with an age related conditions that have negative impact in population quality of life, presbyopia is one of this age related conditions.

Accommodation is the optical change in the dioptric power of the crystalline lens due to ciliary muscle contraction, which allows the change of the eye point of focus from distant to near objects. Presbyopia is a progressive age related condition in which the eye can not focus on near distance objects due to the loss of accommodation. Goerz et al.¹ reported that the quality of life in presbyopes is worse than those of younger subjects. The correction of presbyopia through refractive surgery can be a good alternative for these subjects. Its correction has always been a challenge for the refractive surgeon; it can be approached at a corneal level² (Monovision, PresbyLASIK, Conductive Keratoplasty, Intracor Femtosecond Laser, Corneal Inlay) at the lens (multifocal and accommodative intra ocular lens) or at the sclera (anterior ciliary sclerotomy).

The correction at a corneal level is very attractive because it is a less invasive procedure compared to intraocular procedures. PresbyLASIK is a technique that involves traditional LASIK creating a multifocal corneal profile, which increases the depth of focus (DOF) leading to pseudoaccommodation. Three corneal multifocal techniques have been described: transitional, peripheral, and central. The last one, described by Alio et al. as central presbylasik³, consists in creating a hyperpositive area which is created for the near vision at the corneal center (3 central mm), whereas the periphery is left for far vision (between 3 to 6 mm). It is unclear whether the subtle changes induced at the anterior cornea surface remain stable over time, maintaining the achieved refractive correction. The outcomes of presbylasik are affected by the progressive decay in accommodation that happens during the presbyopic age and criticisms have been raised about this type of lasik surgery as limited evidence has been reported at this regard^{3,4}. The subtle changes induced in the anterior corneal surface by the so called presbylasik techniques may be prone to regress due to epithelial compensation³. The analysis through objective methods like the propagation of wavefronts, allows to evaluate in a single parameter all changes in the optical behavior of the cornea in the

fulfillment of its function as the main refractive element of the eye, integrating comprehensively, in a single value, the effects on the quality and optical stability of both, low and high order aberrations, and, local changes in the curvature of the cornea surface. Light propagation study offers data about the focality of the corneal surface in a given diameter which is more complete than the study of the means of the main meridians in different diameters⁵. The use of objective methods like ray tracing has been reported as accurate and highly reproducible⁶, also, the software used on this study was used by Gharaibeh et al⁷ to set the stability of conventional Lasik treatments.

So far, light propagation analysis has not been used to assess the stability of the multifocal changes induced in the cornea by multifocal profiles of excimer laser surgery used with the purpose to compensate presbyopia. This paper reports herein the outcomes of a particular type of presbylasik treatment, PresbyMax Schwind, analyzed along 3 years follow up using an objective light propagation algorithm, to assess the stability of the corneal refractive outcome .

METHODS

This retrospective longitudinal ,consecutive study included 24 eyes of 12 operated patients who were the subject of central PresbyLASIK surgery and completed a full 3 year follow up corneal topography evaluation.

-PresbyLasik surgery technique :

All cases were the subject of LASIK excimer laser correction of presbyopia and the corresponding spherocylindrical refractive error using the same presbylasik software and version (PresbyMax Schwind v3.01; Schwind EyeTech solutions, Klionstatt Germany) and the same sixth Generation Excimer Laser technology (Amaris Schwind 500 , Klionstatt Germany) The cases were consecutive and all were operated using a femtosecond assisted flap of 110 microns (Intralase 60 KHz, AMO USA), by the same surgeon (JLA). The sample of eyes were equal in number of myopes and hyperopes, 12 eyes each group. The cases were selected consecutively with the only condition to have completed all the steps of the 3 years follow up with the same corneal topography device. Near vision add used at the PressbyMax software was in all cases 1.5 or 2 diopters.

-Patient's demography data :

The mean age (mean $\pm$ SD) in the hyperopic group was $53,50 \pm 4,89$ years and $43,50 \pm 2,88$ years in the myopic group. The mean pre surgery spherical equivalent in the hyperopic group was $1,56 \pm 0,57D$, and in the myopic group $-2,45 \pm 1,11D$. Near vision clinical addition ranged from +1 to +2.25D. No dry eye disease of any type or any level of ocular surface inflammation was present preoperatively in any patient.

-Postoperative follow up:

All corneal topographies were done along the whole follow up with the same placido rings based instrument (Eyetop™ Topographer CSO ,Costruzione Strumenti Oftalmici, Florencia, Italy). Clinical and corneal topography follow ups were performed at 3 months (3m), 1 year (Y1) and 3 years (Y3) after surgery. Corneal surface was preoperatively normal in all patients .

-Light propagation algorithm Ray Trace analysis study:

For the objective simulation of the depth of focus, a software tool developed and adapted using the computer program MATLAB R2016b (The Mathworks, Natick, USA) was used. This simulates the light propagation through the eye, in this case, the tool has been adapted to take into account only the changes at the anterior surface of the cornea, without any other eye parameter. For the purpose of the objective analysis of the depth of focus, two pupil diameters were studied, $d=3.0\text{mm}$ and $d=6.0\text{mm}$.

For each of the 24 eyes, 6 simulations were carried out (2 pupil sizes at 3 moments of interest).

The software represents the outcomes for each eye in a figure (**Figure 1**) with the simulated visual acuity (VA) along the visual axis in diopters (D).

Starting from the values of simulated visual acuity (VA), has been selected the cutoff value at 80% of the maximum simulated visual acuity for each eye, being the DOF simulated, the width in diopters (figure 1 "X" axis) of the segment that involves the area above that 80% of visual acuity.

In central PresbyLASIK, the corneal central zone (diameter=3.0) is optimized for near vision, and the mid periphery (diameter=6.0mm) for far vision. This increase in power assisted also by the induced spherical aberration, creates two focal zones (near and far), each of them with a proper amount of DOF.

As the pupil is a dynamic system in the human eye, and the DOF segments of both pupillary diameters do not be at the same special place of the visual axis, usually, the near DOF segment is expected to be first following the direction of light inside the eye, and, after this one, the peripheral one for long distance. The results of both have been combined in a way that the total interval will be offered by the superposition of the two intervals. In the area where the intervals of the DOF do not overlap at the optical axis, they are not combined for the purpose of the study.

With this method, all of the corneal multifocality that can be used by the eye is obtained, and, is more realistic than the sum of 2 separate intervals. This is feasible as the program gives the result of the zone at the optical axis that is

maintained above the theoretical VA values (80%), by this, is possible to work with definitive zones in the space, to see if they match at the same zone, or, if they are part of a wider interval with an overlapping zone.

A. Objective estimation of depth of focus

For the calculations of the optic path through the cornea, is considered that the cornea is a thin element and it does not produce a deflection of the ray light. This implies that the only delay on the wave is produced as an effect of the different thickness that crosses the wave as it goes through the surface. To evaluate this delay, two planes of reference were assumed, one at the entrance, perpendicular to the apex, and other at the exit, at a greater distance than the corneal sagittal maximal. Points at a plane beam sampled in a squared matrix represent the entrance beam. At the exit, each point of the matrix (that represents a fraction of the wavefront) will be affected by a proportional phase of the optical path traveled. The general approach describing the pass of a coherent wave through a transparent medium has been applied. Basically, this consists of calculating the optical path delay (or, equivalently, time delay) suffered by a ray entering the transparent surface at any point compared with that of the chief ray, which enters the surface through the optical axis.

For the present study, it was considered that the transparent surface is the cornea and the light ray passes through its center, at the corneal apex. For time calculation purposes, we took the plane perpendicular to the corneal axis tangent to the corneal apex as the zero reference. The time delay has been calculated at a plane arbitrarily situated after the cornea. It is important to underline here, that the time delay is relative to the chief ray, so the exact position of the plane only adds a constant time that does not affect the results. The time delay (t_{lo}) was then calculated by taking into account the path covered by the ray, both in the air and inside the eye, after passing through the cornea, using the formula:

$$t_{lo} = (n_{air} \times d_{IC} + n_k \times d_{CO})/c$$

with n_{air} and n_k being the air and keratometric indexes, respectively ($n_k=1.3375$). d_{ic} and d_{co} are the distances between the input plane and the corneal surface and from there to the output plane at a specific coordinate and finally, c is the speed of light in the vacuum. The calculation of the distances above written is done by considering the corneal shape at the considered coordinate, which is obtained through raw elevation points provided by the corneal topographer.

From the time delay, the wavefront at the output plane is reconstructed by the software, and thus, propagate the light distribution up to the plane of interest⁵. If the crystalline was not calculated, the light distribution calculated only took into account the optical quality of the cornea, ignoring the effect of other ocular structures.

The beam obtained at the exit plane spreads through a method of calculus of wave propagation until the plane of interest, ignoring the effect of the crystalline lens.

The method used is based on a Fresnel's propagation algorithm, used and described by Illueca et al.^{8,9}. In this case, it has been modified to avoid taking into account the axial length in order to study the simulated behavior of the light around the best plane provided for the treated cornea and isolate the generated DOF. The Optical and Vision Science Group, University of Alicante (UA) elaborated both programs, the ocular propagation⁵ and the path through the cornea¹⁰.

The used method to evaluate the simulated VA in an objective form can be summarized as:

1. Propagate through the chosen algorithm the light path through the cornea.
2. From the topography, the software calculates the theoretical focus and calculates the pattern of light intensity along the visual axis simulating the energy concentration in 512 planes along a 24mm length (1 every 0.046mm), half before and half after the theoretical position of the focus.
3. From the resultant light distribution at each 512 planes, a Fourier transform

is used to calculate the MTF.

4. A radial average is done (for minimizing the effects of astigmatism)
5. Considering that $AV=1$ corresponds to an MTF thickness of 30 cycles per degree, an objective VA is estimated.
6. By using the analysis of the maximum VA at each studied plane, the corneal segment of DOF is set up.

-Statistical Analysis

For the contrast of hypothesis, the Friedman non parametrical test was chosen¹¹. The level of significance $p=0.05$ was selected as it is considered values below 0.05 statistically significant. For the purpose of the statistical analysis, the IBM® SPSS® Statistics 23.0 (IBM®, USA) was used.

RESULTS

For the purpose of the analysis, the results are divided between the 2 groups (myops and hyperops), and each group is divided by 2 pupillary sizes and a combination of both. All the results are presented as Mean $\pm$ SD in Dioptres (D), and p value of Friedman's test. The results were divided into the three moments of interest, 3 months (3m), 1 year (y1) and 3 years (y3) after surgery.

In the hypers group (n=12 eyes), with a pupillary diameter of 3.0mm: DOF 3m=1,61 $\pm$ 0,41 (D); y1=1,75 $\pm$ 0,80 (D); y3=1,69 $\pm$ 0,41 (D). (p=1,00).

In hyperops with a pupillary diameter of 6,0mm:

DOF; 3m=1,36 $\pm$ 0,49 (D); y1=1,61 $\pm$ 0,69 (D); y3=1,40 $\pm$ 0,53 (D). (p=0,05)

In the myops group (n=12 eyes), with a pupillary diameter of 3.0mm, DOF values were: 3m=2,12 $\pm$ 0,82 (D); y1=2,07 $\pm$ 0,79 (D); y3=2,20 $\pm$ 0,76 (D). Friedman (p=0,191).

For a pupil d=6,0 mm: 3m=2,14 $\pm$ 0,80 (D); y1=2,07 $\pm$ 0,38 (D); y3=2,11 $\pm$ 0,64 (D). (p=0,434)

Finally, the results of combining 2 zones as previously described are:

Hyperops , 2 combined zones:

3m=2,24±0,70 (D); y1=2,45±0,90 (D); y3=2,37±0,68 (D). p=0,75

Myops, 2 combined zones:

3m=3,56±0,97 (D); Y1=3,59±0,72 (D); Y3=3,59±0,72 (D). p=0,50

The hyperops results are summarized in **(Table1)**, and presented in **(Figure2)**

The myopic group results are summarized in **(Table 2)**, and presented in **(Figure 3)**

DISCUSSION

Different authors such Mosquera, Alio and Pallikaris have previously reported^{2,4,12} the different PresbyLASIK techniques concluding that rigorous objective studies with adequately long follow up periods are necessary to better qualify the different Presbylasik techniques that have been proposed. Most of the studies remains at one year or have an even shorter follow up.^{4,12} The longest follow up reported by Epstein et al¹³ was 2.5 years in a study about a peripheral PresbyLASIK technique. Two main factors makes difficult to evaluate based only on clinical bases the stability of the results obtained by PresbyLASIK.

- As presbyopia is a condition that is aggravated over the years, therefore, in long follow-ups an increase in the near refraction addition and a decrease in the UCNVA is expected due to the decay in accommodation.
- The influence of a sensorial adaptation process^{14,15} has to be taken into account to avoid the introduction of a BIAS when we try to evaluate the stability of the results using only reports based in clinical bases.

The way to isolate the results obtained at the corneal level with our intervention, of, the previously mentioned confounding factors is by using only the topographic

profile of the treated cornea, and its analysis by purely objective methods, like the ones used in this study.

The development of purely objective techniques to evaluate the optical behavior of the light through the eye can help to better understand its optical behavior following the induction of corneal multifocality and its evolution along time. It may also allow the comparison of the different presbylasik ablation profiles under the same objective conditions due to one further problem is the frequent change in the ablation profiles of the prebylasik techniques that has happened even with the same technology, which makes it difficult to obtain patients ablated with the same software version as regression might be related to the steepness of the ablation profiles .

The main advantage of the method proposed here compared to other objective methods of measurement is that, by studying the propagation of wavefronts, we can combine several measures such as the analysis of the mean K values based on topographies and the influence of the optical aberrations (taking these last great importance in multifocal corneal treatments).

Small flattening during the period of follow-up in the cornea, specially by epithelial compensation would also modify the spherical aberration values of the same, causing instability of the refractive results of the Presbylasik surgery. For this reason, the method used in this paper is a complete objective method of measuring the results of corneal surgery.

As could be seen on this paper, in the case of the myops, better results of the DOF are obtained than in the case of hyperopes : the myopes showed between 3 and 4 diopters of corneal DOF, and hyperops between 2 and 3. A possible explanation to this, could be, because central Presbylasik provides a central hyper-positive area (for near distance), and in a myopic cornea, less or no ablation in central area ($d=3.0$ mm) is necessary to achieve the target refraction.

All cases behave similarly regardless of the stability of the results. In all the studied situations (pupil diameter of 3.0 and 6.0mm, as in the combination of both zones), the differences between the average results at 3 months and 3 years were not clinically relevant ($>0.25D$). The values of the differences over the different periods of the follow up were analyzed by the p value in the Friedman test and were above the chosen value of 0.05. As a consequence, it is possible to conclude, that the results achieved with the central PresbyLASIK technique PresbyMax , are stable for a 3 year follow up period post surgery. In this way, this study completes other previous reports^{9,16-19}, in which good clinical results with the technique were reported both in myops and hyperops .

The present study provides to the best of authors knowledge, and for the first time, objective evidence that demonstrates that the optical results achieved with the central Presbylask technique here used (PresbyMAX Schwind) are stable over time. Based on the results of this investigation , it is also adequate to propose that ray tracing analysis using a light propagation algorithm may be also used in the future for an objective assessment of other corneal surgical techniques for the correction of presbyopia with or without the use of excimer laser such as intracorneal inlays as well as other corneal refractive surgical techniques .

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Table 1 Hyperopic Group results simulated DOF Mean (SD) Dioptres

Hyperopic Group n=12	3m	y1	y3	p value
Mean (SD) Dioptres				
d=3.0 mm pupil	1,61 (0,41)	1,75 (0,80)	1,69 (0,41)	1,00
d=6.0 mm pupil	1,36 (0,49)	1,61 (0,69)	1,40 (0,53)	0,05
2 zones superposition	2,24 (0,70)	2,45 (0,90)	2,37 (0,68)	0,75

In this table it is possible to see the evolution of multifocality through time in the Hyperopic group.

Table 2 Myopic Group results simulated DOF Mean (SD) Dioptres

Myopic Group n=12	3m	y1	y3	p value
Mean (SD)				
d=3.0 mm pupil	2,12 (0,82)	2,07 (0,79)	2,20 (0,76)	0,191
d=6.0 mm pupil	2,14 (0,80)	2,07 (0,38)	2,11 (0,64)	0,434
2 zones superposition	3,56 (0,97)	3,59 (0,72)	3,59 (0,72)	0,50

In this table it is possible to see the evolution of multifocality through time in the Miopic group.

Corresponding Author:

Jorge L. Alio, MD PhD, FEBOphth

E-mail: jlalio@vissum.com

Figure Captions

Figure 1 Simulated Axial Visual Acuity VS Corneal Power (Hyperopic patient pupil diameter 3.0 mm)

Figure 2 Hyperopic Group Simulated DOF (D)

Figure 3 Myopic Group Simulated DOF (D)