Hanita Lenses

Clinical Evaluation Phase 2 Report Of SeeLens MF Intraocular Lens

11 June 2012

Version 1

CONTENTS

1. SCOPE

An increasingly important goal of modern cataract and implant surgery is to obtain the most desirable outcome for the patients, thus contributing to spectacle-free vision and highest quality of life.

The ideal state of the human phakic eye without any refractive error is known as emmetropia; Rays of light perfectly focused from an infinitely distant object onto the fovea without accommodation[1].

Refractive power of the eye is determined by three main parameters: power(s) of the cornea, power of the crystalline lens and axial length of the eye. Incompatibility between these parameters leads to various types of refractive errors among known as myopia and hyperopia.

The natural crystalline lens has the ability to accommodate in order to maintain a clear image (focus) of an object whatever the distance from the eye. At about the age of 40, the lens becomes less flexible and accommodation is lost gradually[2], making close-range activities increasingly difficult. This is called *presbyopia*. Once presbyopia has been diagnosed reading glasses or corrective contact lenses are necessary to maintain near vision.

With age, a normal crystalline lens opacifies (cataract) disabling the eye in generating a clear, well contrasted image. The only therapeutic solution to this problem is surgical replacement of the crystalline lens with an intraocular lens (cataract surgery).

New technologies in IOLs optic designs provide for better options for cataract patients to correct their visual deficits and to live their lives without visual aids.

The clinical demand for a solution to presbyopia is very high, as presbyopia afflicts the majority of the world's adult population.

Implantation of a bifocal IOL, like SeeLens MF, with a bifocal aspheric refractive/diffractive structure, pupil size dependence and asymmetrical light distribution provides for a satisfactory full range of vision, a high level of uncorrected and corrected distance, intermediate and near acuity and improved contrast sensitivity. Furthermore the SeeLens MF should allow for independence of spectacles, thus enhancing patients' satisfaction.

---

1 Diepes H. 2004, Refraktionsbestimmung

2 Lang G.K., Spraul C.W. (1998) Augenheilkunde

The optical performance of bifocal IOLs restores near, distance and intermediate vision for high patient satisfaction. With such optical performances, patients may benefit from independence from visual aids.

The SeeLens MF is designed for micro-incision cataract surgery (MICS), through sub-2mm incisions.

In order to confirm these statements, a post-marketing study was initiated: Clinical experience on the implantation of the SeeLens MF IOL. The main purpose of this study is to evaluate visual acuity and contrast sensitivity of patients receiving the new bifocal IOL.

2. OBJECTIVES

This intermediate report summarizes the 3 months follow-up results of a post marketing, prospective, non-comparative, non-randomized multicenter study of the SeeLens MF, a multifocal diffractive apodized intraocular lens.

The objectives of this study are to evaluate the visual quality, visual acuity, contrast sensitivity and patient satisfaction obtained after the implant of the intraocular lens.

The key safety and efficacy parameters are:

Best Corrected Visual Acuity (BCVA) for varied distance

Uncorrected Visual Acuity (UCVA) varied distance

3. EFFICACY AND SAFETY ASSESSMENTS

The efficacy and safety assessments were determined as defined by and according to the ISO 11979 directive. The following are the demands required by the directive:

1. Post Operative BCVA of at least 6/12 (20/40) within 88% of patients' population. For the "best cases" patients, BCVA 6/12 (20/40) or better, for at least 94% of the patients. (Requirements defined by ISO 11979-7 2006 for a sample size of 100 patients).
2. IOL related Post Operative complication and Adverse Events equal to or less then the allowed rate defined by ISO 11979-7 2006.

4. MEDICAL DEVICE SPECIFICATION AND ADMINISTRATION

The SeeLens MF intraocular lens is a multifocal apodized diffractive aspheric, foldable, one piece lens.

The intraocular lens is a CE-marked medical device sold worldwide.

Table 1 summarizes the lens specifications

SeeLens MF Specifications	
Optic Diameter	**6.0 mm**
Power range	**+10 to +35 (15-30D in 0.5D increments, 30-35D in 1D increments)**
Addition Power	**+3D**
Optic design	**Apodized diffractive aspheric Multifocal IOL**
Lens design	**360° Double square edge**
Haptic angulation	**5°**
Material	**Hydrophilic Acrylic 25% water content**
Light transmission	**UV blocker and violet light filter 2% transmission @400nm 90% transmission @460nm**
Refractive index	**1.462 (35°C)**
Nd-YAG laser	**Compatible**
Estimated A constant	**118.6**
Placement	**Capsular bag**

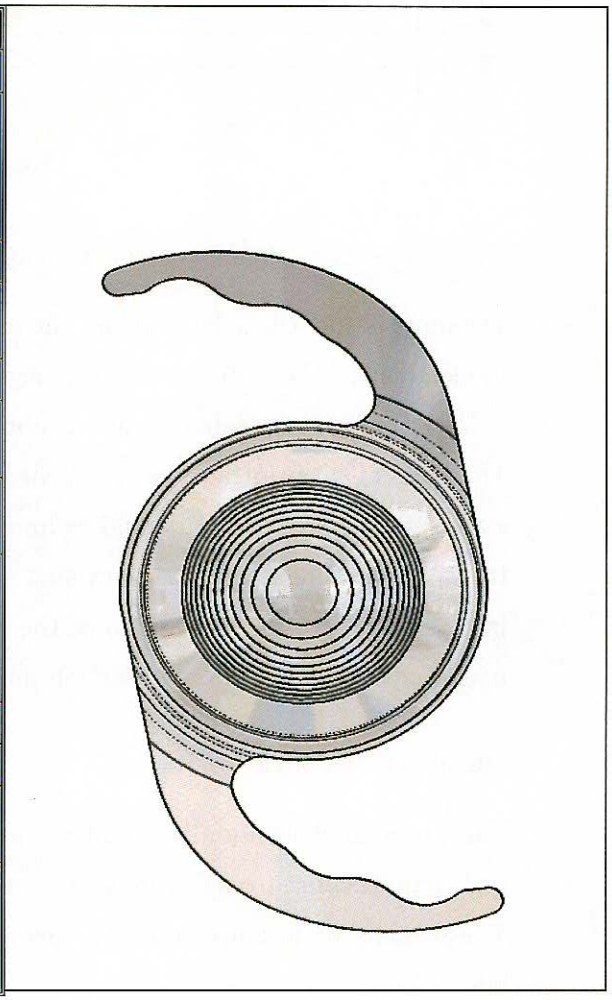


TABLE 1: SEELENS MF SPECIFICATIONS

SeeLens MF is an apodized diffractive bifocal lens; so that the IOL is dependent on pupil size, different proportions of the light energy are directed to each focus of the lens. Figure 1 below shows the relative energy distribution at different pupil diameters.

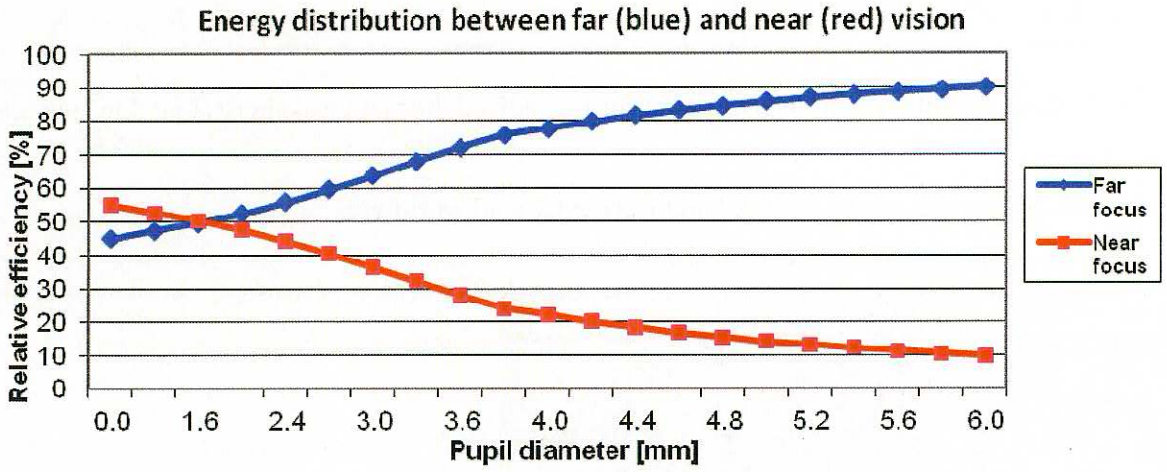


FIGURE 1 SEELENS MF HAS A FAR FOCUS, AND A NEAR FOCUS AT +3D ADDITION POWER.

The optic of the IOL is designed for the highest possible MTF in the well established Arizona eye model, which takes into account the negative spherical aberration required by the IOL in order to lower the positive spherical aberration of the human cornea.

The Hanita Lenses intraocular lens hydrophilic material has been in use at Hanita Lenses with an established efficacy and outstanding long-term behavior in the eyeI in terms of biocompatibility, transparency and stability of the visual function and centration. A foldable and highly adaptable implant for all bag conformations, the SeeLens MF displays outstanding tensile strength for maximum resistance during insertion, and offer controlled unfolding for rapid visual recovery.

Surgical Procedure

The phacoemulsification procedure and the lens implantation was performed following the instructions of use from the device's manufacturers, and surgeon's technique.

The SeeLens MF has directionality; such that the leading haptic must point left. The lens is dialed clockwise.

5. METHODS

For each of the above tests the following methods will be undertaken:

1. **Ocular and intraocular biometrical measurements**

   Patients were examined pre operatively for inclusion and exclusion criteria as well as for the post operative follow ups for the measurements specified in the flow chart (see Table

2). These include a validated IOL-Master, corneal topographer, specular microscope, ocular aberrometer, pupilometer, applanation tonometer, slit lamp microscope and ophthalmoscope.
IOL decentration and tilt estimation, and Scheimpflug imaging.

2. **Visual acuity** was measured using an ETDRS chart for distance at 85cd/m^2, and Colenbrander Mixed Contrast Cards (Precision Vision) with ETDRS at 100% contrast for near (40cm), intermediate distances (63cm and 100cm) and far vision all at 85cd/m^2 (calibrated with a light meter). All results expressed in logMAR values.

3. **Contrast sensitivity** will be evaluated using a sine wave gratings chart (FACT) on the Optec 6500 Functional Vision Analyzer (Ginsburg Box, Stereo Optics), at 1.5cpd, 3cpd, 6cpd, 12cpd and 18cpd for mesopic and photopic conditions. Luminance for photopic conditions will be 85cd/m^2 and 5cd/m^2 for mesopic conditions. all results expressed as $\log_{10} CS$ values.

4. **Patient satisfaction** Subjective evaluation was performed using the VF-14 questionnaire.

5. **Depth of focus** was evaluated using an ETDRS chart, patient's pupilometry was evaluated. In the statistical stage patients will be categorized according to smaller than 2.5mm, between 2.5 and 4.5mm and above 4.5mm for mesopic and photopic conditions. The test will be performed using a phoropter to create defocus in 0.5D increments, starting from -3D corrective lenses to +6D relative to emmetropia so that the patient will be corrected for far vision.

6. **Intraocular aberrometry** was measured at each centre. The data was reported according to ISO 24157:2008; Total ocular aberration, corneal aberration and IOL induced aberration as the difference between the two.

7. **Reading speed** was measured using Radner reading charts[3] on the Salzburg reading desk at 85cd/m^2 and at 5cd/m^2. The patient was corrected to best distance vision. Patients were asked to read a sentence as quickly as possible while other sentences are covered with a piece of paper. The results were calculated as words per minute for sentences in each LogRAD optotype; the reading distance was noted.

Assessment of observational measures according to the below flowchart of Table 2:

Parameter	Test*	Inclusion/ preop	OP	7-10 days	M1 30-40 d.	M3 90-110 d.	M6 170-190 d.
Grade of cataract	Slit lamp	x					
Control of cornea / anterior chamber	Slit lamp	x		x	x	x	x
Control of iris / pupil	Slit lamp	x		x	x	x	x
IOP	Tonometer	x		x	x	x	x
Pupil diameter (mesopic / photopic)	Pupilometer					x	
Monocular distant UCVA/BCVA	ETDRS	x		x	x	x	x
Binocular distant BCVA	ETDRS	x			x	x	x
Monocular near UCVA/BDCVA (40 cm)	ETDRS	x		x	x	x	x
Binocular near BDCVA (40 cm)	ETDRS	x			x	x	x
Monocular intermediate (63cm) UCVA/BDCVA	ETDRS			x	x	x	x
Binocular intermediate (63cm) BDCVA	ETDRS				x	x	x
Monocular intermediate (100cm) UCVA/BDCVA	ETDRS			x	x	x	x

3
-Design of short spanish sentences for measuring reading performance: Radner-Vissum test J Cataract Refract Surg 2008; 34:638–642 Q 2008 ASCRS and ESCRS was performed in Vissum.
-Design of Radner test in the German language was performed in BERI.
-No Radner test was performed in Hospital at the University of Verona.

Binocular intermediate (100cm) BDCVA	ETDRS				x	x	x
Subj. refraction		x			x	x	x
Obj. refraction		x			x	x	x
Corneal topography	Placido	x			x	x	x
Biometry	IOL Master	x					
Ocular aberrometry					x		x
Corneal aberrometry							x
Monocular contrast sensitivity (mesopic / photopic)	Optec 6500 (Stereo Optics) , FACT chart					x	x
Binocular contrast sensitivity (mesopic / photopic)	Optec 6500 (Stereo Optics) , FACT chart					x	x
Binocular Defocus curve	ETDRS					x	x
Reading speed	Radner						x
Quality of life questionnaire	VF-14						x
PXF	Slit lamp	x		x	x	x	x
Control of PCO	Slit lamp						x
Control of lens / capsule	Slit lamp	x		x	x	x	x
Control of IOL position / rotation	Slit lamp			x	x	x	x
Lens positioning	AC Scheimpflug			x			x
Control of ocular fundus	Ophthalmoscope			x	x	x	x
Other tests for inclusion		x					
Control for AEs			x	x	x	x	x

*recommended test method. In case of deviations please document details thoroughly.

UCVA = uncorrected visual acuity; BCVA = best corrected visual acuity; BDCVA: best distance corrected visual acuity

TABLE 2: FLOW CHART OF THE PROCEDURES REQUIRED IN EACH FOLLOW UP

3 centers were included in this evaluation, each of the patient was bilaterally implanted with the SeeLens MF IOL.

Surgeon	number of eyes 3 months followup
Prof. Roberto Belluci, Italy.	20
Prof. Jorge Alio, Spain.	20
Prof. Manfred Tetz, Germany.	14

The study begun in September 2011.

6. STATISTICAL METHODS

The following analyses were used to describe the data in this report:

Descriptive statistics: continuous variables are described with mean.

Nominal scale variables are described with absolute and relative (percents) frequencies.

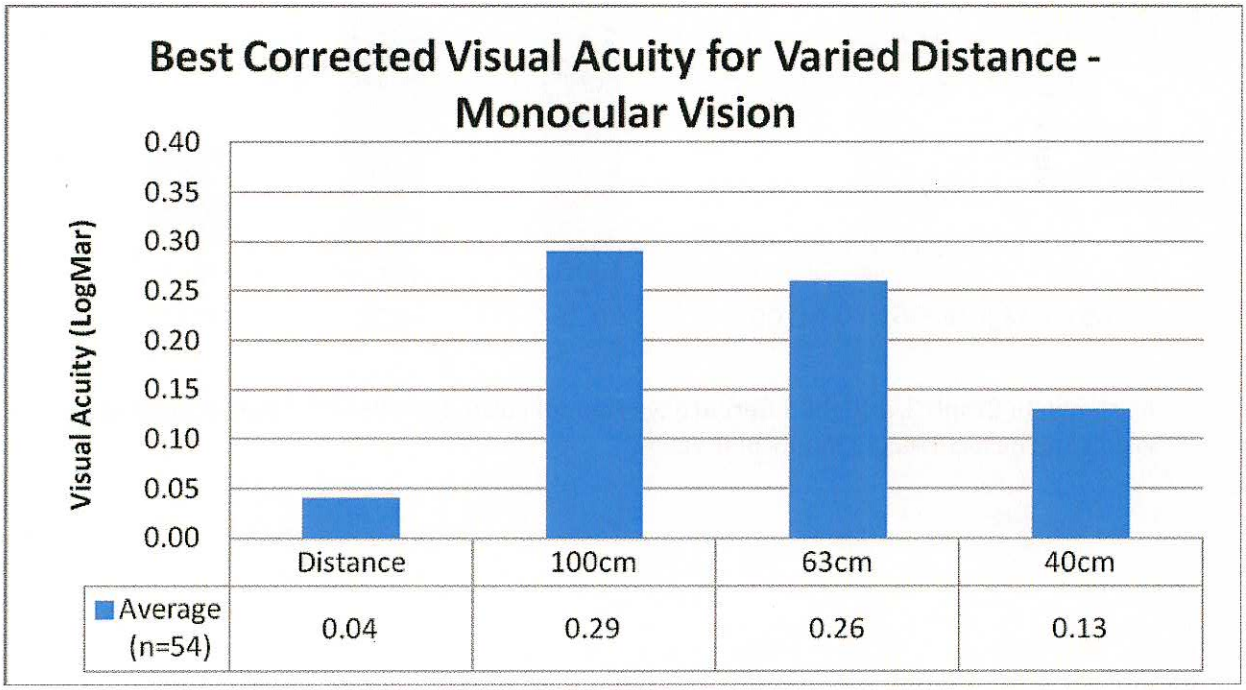
All analyses were done using Excel 2007 statistics tool package.

7. RESULTS

7.1. POSTOPERATIVE BEST CORRECTED VISUAL ACUITY (BCVA)

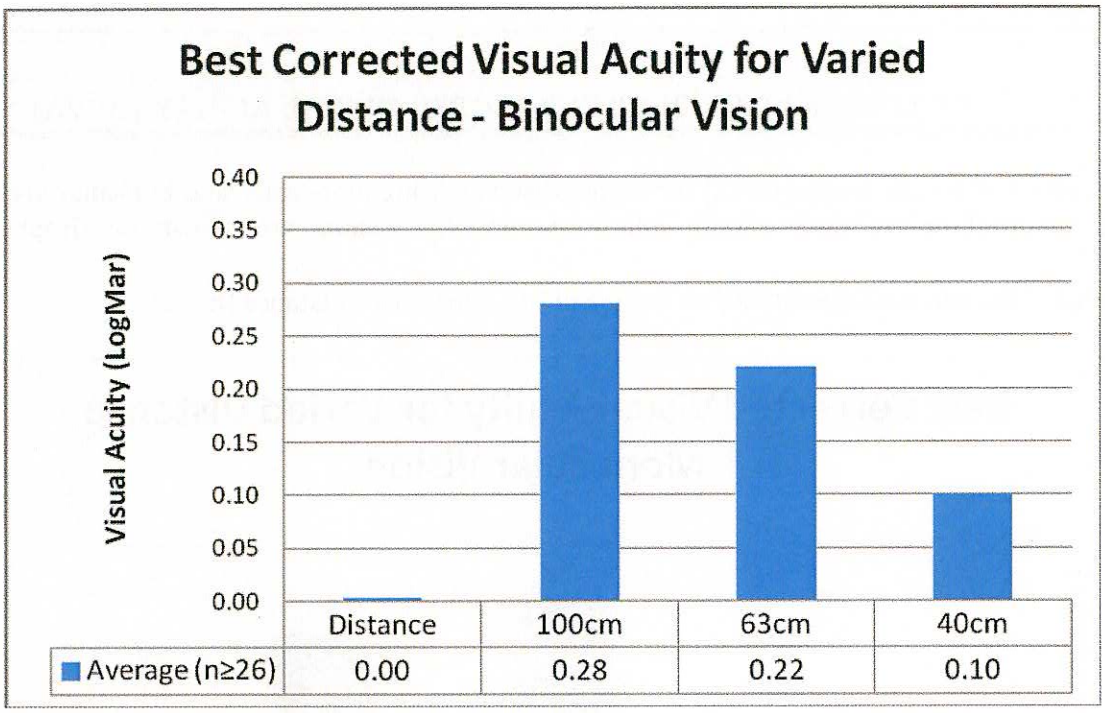
Best corrected Visual Acuity (BCVA) for varied distance using monocular and binocular vision were reported in the three month follow-up visit, the results are shown on Graph 1.

Graph 1: 3 months post-operative distribution of BCVA for varied distance (n=54).



As shown in Graph 1, visual acuity results were demonstrated in the three months follow up with an average of more than 6/12 for intermediate vision and excellent vision in the near and far distances, all distances using monocular vision.

Graph 2: 3 months post-operative distribution of BCVA for varied distance (n≥26).

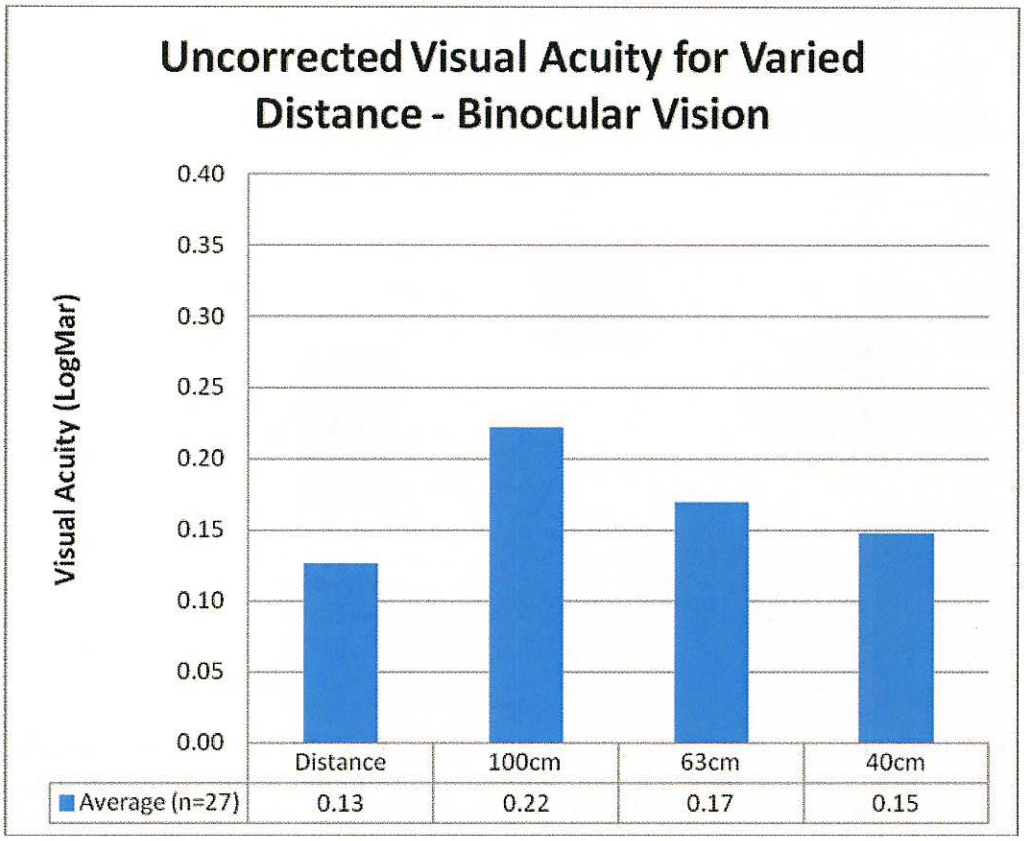


As shown in Graph 2, a slight difference was demonstrated between the best corrected binocular vision and best corrected monocular vision.

7.2. POSTOPERATIVE UNCORRECTED VISUAL ACUITY (UCVA)

Uncorrected Visual Acuity (UCVA) for varied distance was reported in the three month follow-up visit, the results are shown on Graph 3.

Graph 3: 3 months post-operative distribution of UCVA for varied distance (n=27).

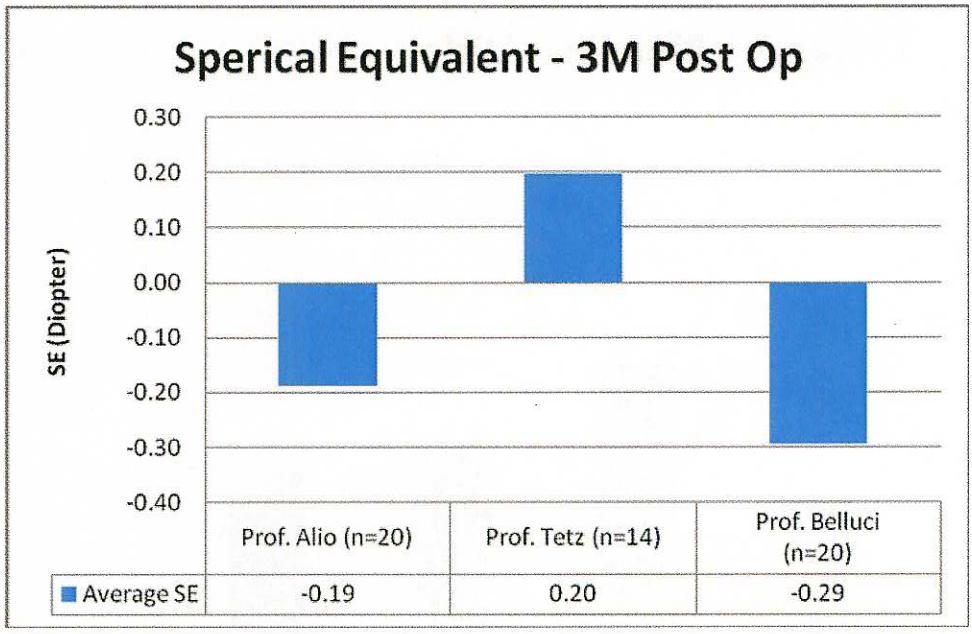


As shown in Graph 3, uncorrected binocular visual acuity results were excellent, providing great functional vision for near, far and intermediate distance.

7.3. PREDICTABILITY OF REFRACTIVE CORRECTION

Postoperative refractive deviation, calculated by Spherical Equivalent (SE), was reported in the follow- up visits.

Graph 4: 3 months post-operative spherical equivalent (n=54).

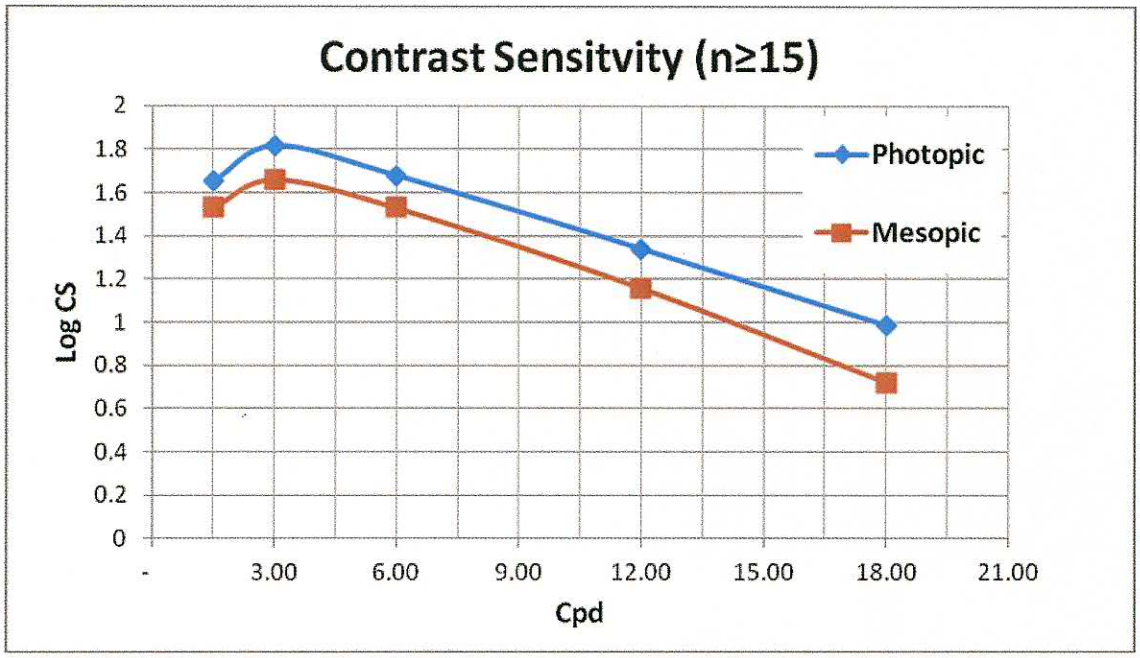


As can be seen the spherical equivalent was in the range of -0.29D to 0.2D with excellent refractive stability. The minor deviations between the surgeons is associated to the fact that this is a multi-center study, and many subjective parameters such as surgical techniques, instruments and surgeon profession could affect the refractive outcomes. In general, it's recommended that a surgeon will optimize the A-constant value for the IOL according to his technique.

7.4. CONTRAST SENSITIVITY RESULTS

Postoperative contrast sensitivity was evaluated using a sine wave gratings chart (FACT) on the Optec 6500 Functional Vision Analyzer (Ginsburg Box, Stereo Optics), at 1.5cpd, 3cpd, 6cpd, 12cpd and 18cpd for mesopic and photopic conditions. Luminance for photopic conditions was determined as 85cd/m^2 and 5cd/m^2 for mesopic conditions. Results were expressed as $\log_{10} CS$ values.

Graph 5: 3 months post-operative Contrast Sensitivity (n≥15).

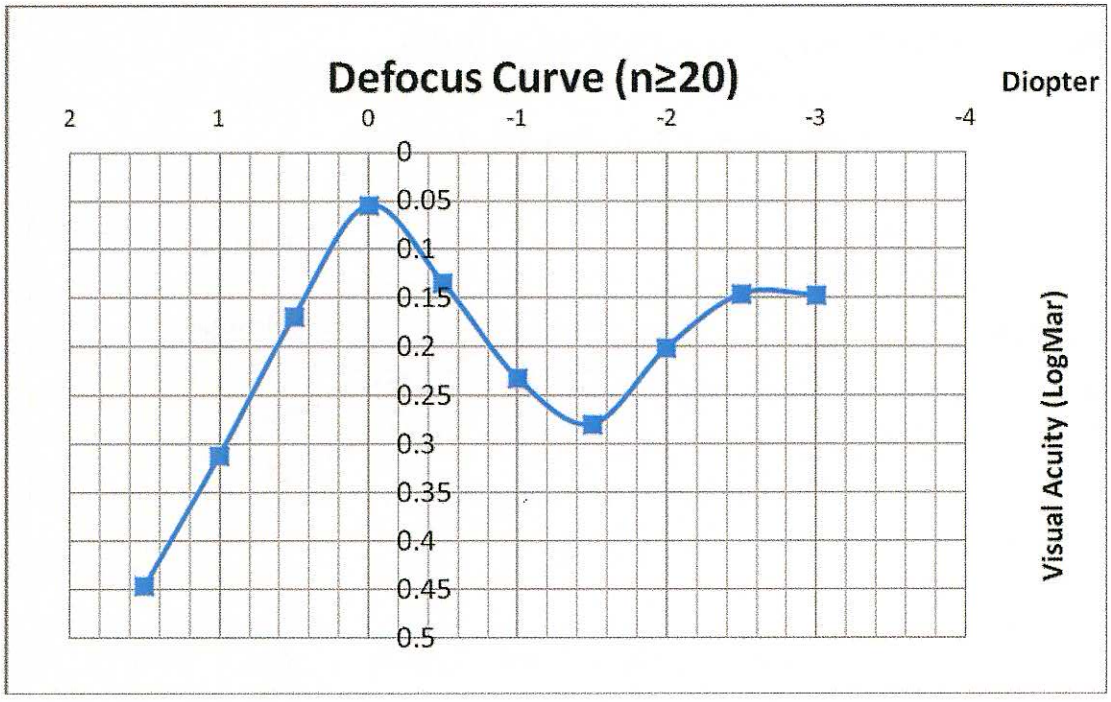


As can be seen in Graph 5, the contrast sensitivity results were excellent and can be compared to other marketed diffractive IOLs.

7.5. DEFOCUS CURVE

Depth pf Focus was tested using 0.5 D increments and testing visual acuity using the ETDRS chart.

Graph 6: 3 months post-operative Depth of Focus (n≥20).



As can be seen in Graph 6, The depth of focus of 2.4-3 Diopters was well established with an excellent quality of functional vision in the full range of defocus once again demonstrating the depth of field achieved with the SeeLens MF unique optical design.

7.6. INTERNAL ABBERATIONS

Low internal aberrations were observed as can be seen in Figure 2 and 3:

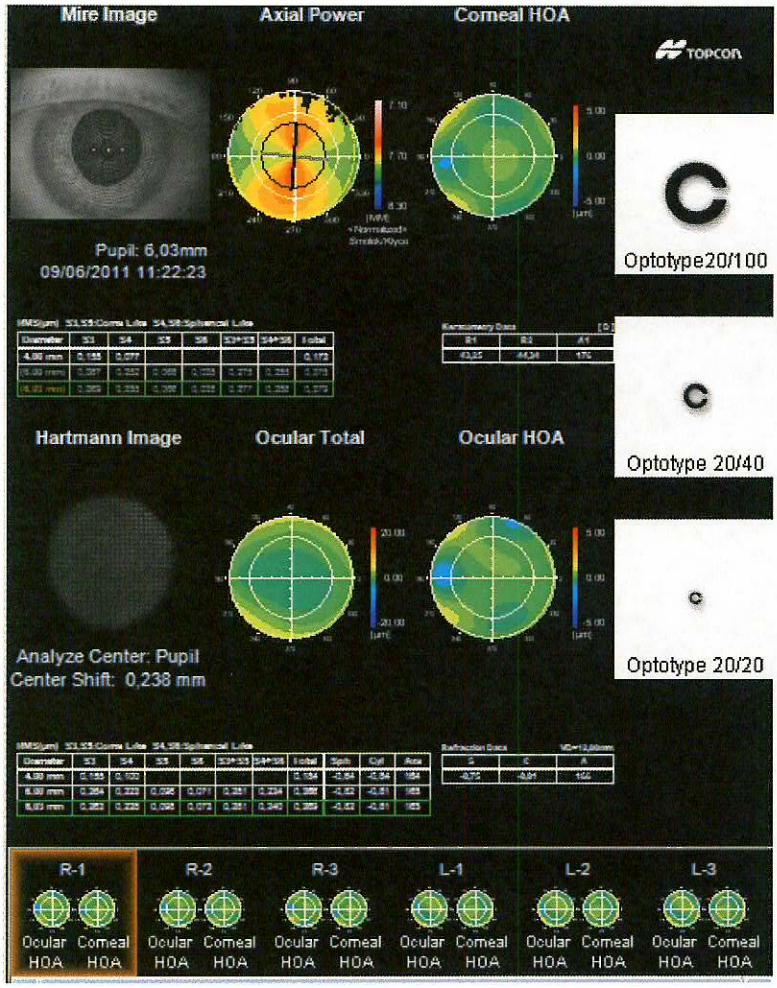


FIGURE 2

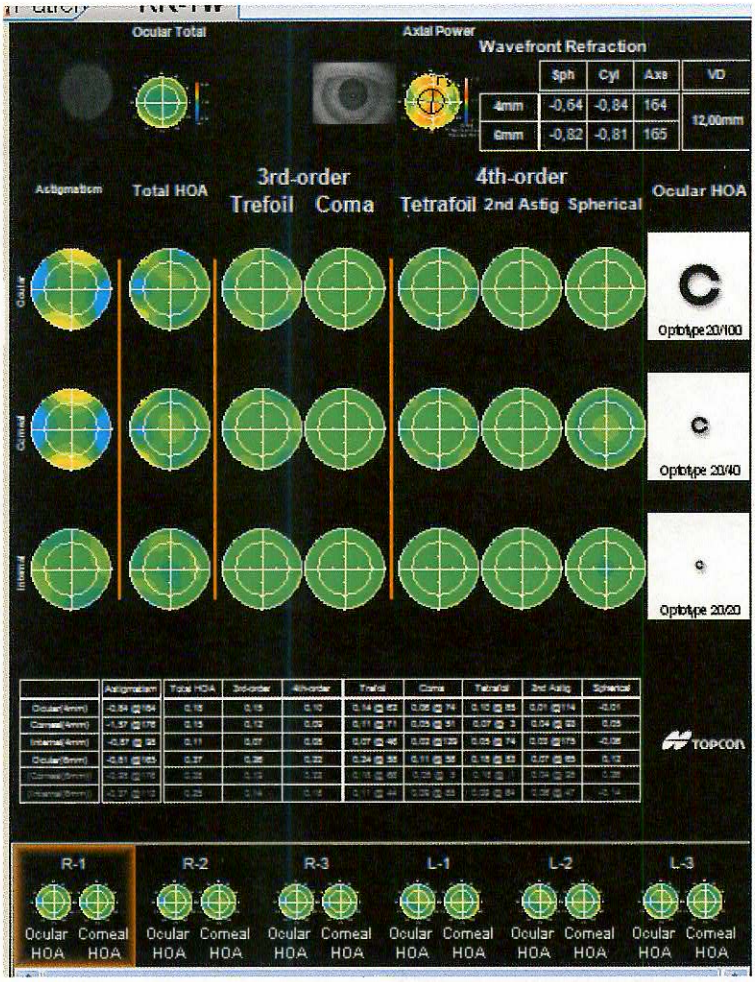


FIGURE 3

The internal aberrations in all patients were low and therefore contributes to the lens performance and visual quality in all distances.

7.7. INTRA-OPERATIVE COMPLICATIONS

No intra-operative complications were reported.

7.8. POSTOPERATIVE COMPLICATIONS

No post-operative complications were reported.

7.9. ADVERSE EVENTS

During the three months follow up period only one adverse event was reported as cystoids macular edema has developed in both eyes of one patient.

According to the investigator this adverse event is not IOL related. Therefore, it can be concluded that safety of SeeLens MF was demonstrated.

8. CONCLUSIONS:

The detailed data from the current study on 54 eyes shows the following benefits of the SeeLens MF IOL:

- Excellent visual acuity for distance and for near.
- Intermediate vision surprisingly high.
- Contrast sensitivity results equivalent to marketed IOLs.
- Independency of glasses achieved despite small refractive errors
- The study is ongoing up to 6 Months follow-up . update of results will be presented as finalized .
- Very good safety profile as reflected by a very low rate of post-operative complications at 3 months.

9. APPROVALS

Title	*Name*	*Signature*	*Date*
R&D Engineer	*Yuval Bonen*		17/06/12
Regulatory Affairs	*Zoya Zilberfarb*		18/06/12
Yakir Kushlin	*R&D Manager*		18/06/12

10. SLIT LAMPS PHOTOS OF IMPLANTED SEELENS MF IOLS