

***Clinical Evaluation
3-month Follow-up
Report***

***Of
BunnyLens AF
Intraocular Lens***

28 March 2011

version 1

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Objectives:

The objective of this study is to evaluate the safety and efficacy of the BunnyLens AF IOL, implanted following cataract removal by phacoemulsification.

1. The key efficacy parameters are:

Primary:

- Best Corrected Visual Acuity (BCVA)
- Predictability of refractive correction

Secondary:

- Un Corrected Visual Acuity (UCVA) – for data gathering only

2. The key safety parameters include:

- IOL behavior during implantation and follow-up
- IOL related infection and/or inflammatory reactions

Efficacy and Safety Assessments

The efficacy and safety assessments were determined as defined by and according to ISO 11979 directive. The following are the requirements of 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.

High order aberrations / Spherical aberrations were evaluated in one medical center (BEAR Institute, Berlin). Total aberrations should be statistically significant lower then reported literature data for spheric lenses.

Medical Device Specification and Administration:

Specification:

1. Device description

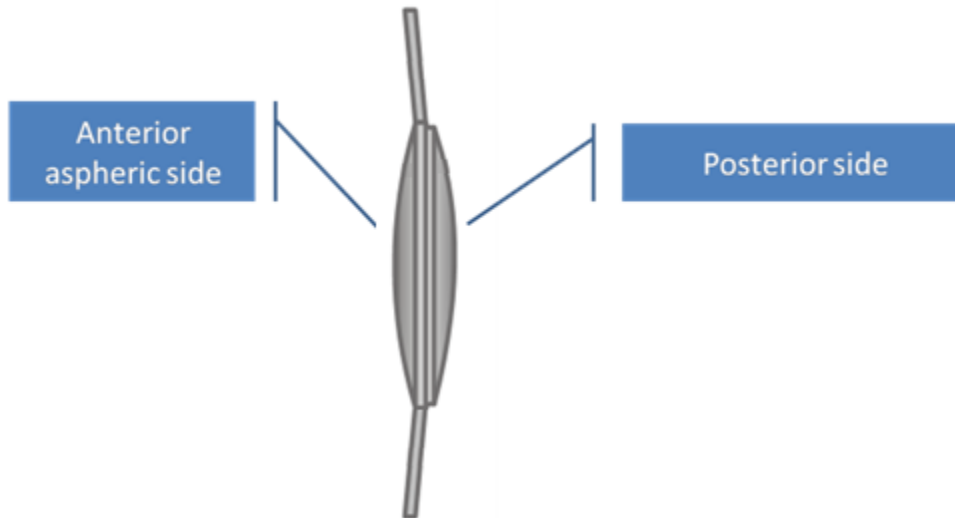
The BunnyLens AF is an aspheric asymmetric biconvex intraocular lens, which has a CE mark since 2010.

BunnyLens AF Specifications

Total diameter	11 mm
Optic Diameter	6.0 mm
Power range	+10.5 to +30 (0.5 increments) +31 to +35 (1.0 increments)
Optic design	Asymmetric Bi convex aspheric lens
Lens design	4 loop haptic design, double square edge with stepped barrier
Haptic angulation	5°
Material	Hydrophilic Acrylic with UV and violet blocker
Refractive index	1.462 (35° c)
YAG laser	Compatible
A constant	118.5
Placement	Capsular bag
incision size	1.8 mm incision



Figure 1: BunnyLens AF Intraocular lens



2. BunnyLens AF design

a. Motivation – visual acuity

Hanita Lenses search for vision quality improvements has a shared objective for both refractive and cataract surgery. The main goal for the refractive and cataract surgery is to provide the patient with the best *visual acuity* and good *post operative refraction* that current technology allows.

The quest for an improved visual acuity for the cataract patient led Hanita Lenses to develop an aspheric-shaped lens, designed to allow the patient a sharper image in the regular photopic vision (daylight vision), and reduce the aberrations of mesopic and scotopic vision (twilight and night vision), which are noticed by some of the conventional spherical Intra Ocular Lens implanted patients.

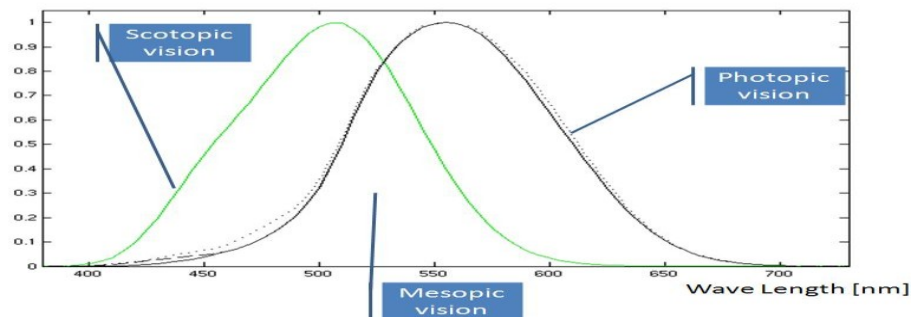
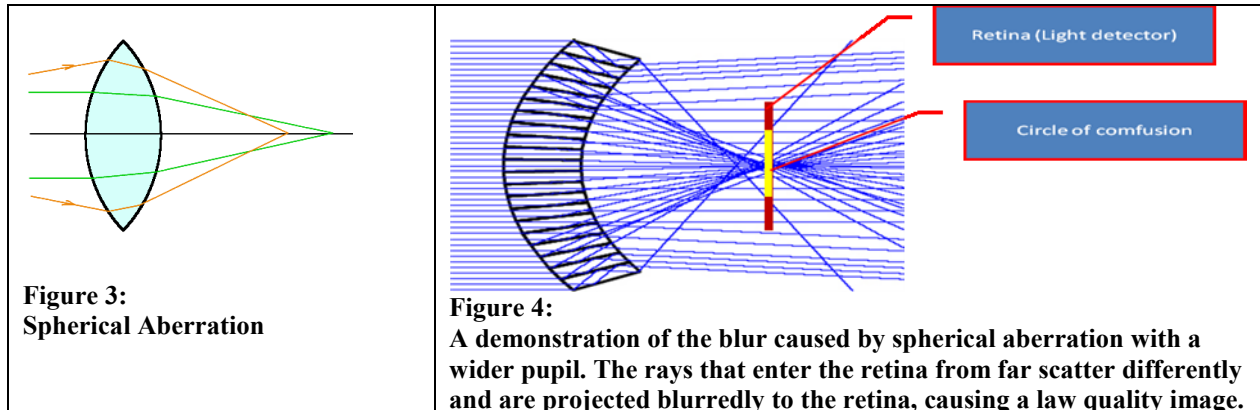


Figure 2:

**The Black line defines the photopic vision and the green line defines the scotopic vision.
The area between the graphs defines the scotopic vision.**

b. Spherical aberration:

The spherical aberration is a well known phenomenon in the optic field. The spherical aberration occurs when rays of light that pass through different parts of the lens intersect at different points on the optical axis of the lens (Figure 3). Due to this aberration, a dot projected on the retina produces a larger circle, thus inducing low quality optics, an unclear vision and low contrast (Figure 4).



Contributors to spherical aberration (SA) in the eye are the cornea (average $+0.27 \mu\text{m}$) and the crystalline lens (negative in the young eye). Cataract surgery removes the lens component and leaves positive SA on average. Traditional intraocular lenses (IOLs) are spherical with positive SA, further increasing the SA of the pseudophakic eye.

c. Clinical demand:

As it gets darker and the pupil dilates, the spherical aberration becomes more apparent, and starts to be noticeable by the patient. Thus patients with conventional spherical lenses complain of unclear vision and poor contrast in the mesopic and scotopic conditions.

d. Lens Design:

There are three options to optimize lens surface:

- 1) Aberration free lens- all aberrations of the eye remain.
- 2) Reduce spherical aberration to zero (theoretically for 6mm pupils).
- 3) Optimize the lens surface to achieve best functional visual acuity.

The BunnyLens AF was designed using the third option: obtaining maximum Contrast Sensitivity by optimizing the Modulated Transfer Function using Arizona eye model designed to match clinical levels of aberration, both on and off axis (the model is based on Navarro eye model and the Koojiman model and uses eye modeled for a 60 year old patient).

The BunnyLens AF optical design was performed using the symmetric aspheric surface equation described below.

$$z = \frac{cr^2}{1 + \sqrt{1 - (1+k)c^2r^2}} + \alpha_1r^2 + \alpha_2r^4 + \alpha_3r^6 + \alpha_4r^8 + \alpha_5r^{10} + \alpha_6r^{12} + \alpha_7r^{14}$$

C = 1/R: R – Radius of curvature.
 K- Conic Constant
 R – Radial distance from optical axis.

The theoretical asphericity value of BunnyLens AF for 6mm pupil opening was calculated using ZEMAX simulation:

- IOL asphericity: -0.14µm
- Total Spherical Aberration of an eye: +0.13µm

This pupil opening was used to compare BunnyLens AF with other aspheric IOLs available in the market.

Table 1 – Spherical aberrations for different aspheric IOLs, 6mm pupil opening:

Lens	IOL asphericity[µm]	Total spheric aberration[µm]
Spheric IOL	+0.18	+0.45
AMO Tecnis	-0.27	0
Alcon IQ	-0.2	+0.07
ReStore aspheric	-0.1	+0.17
Staar Afinity	-0.02	+0.25
B&L sofport AO	0	+0.27
BunnyLens AF	-0.14	+0.13

The key concept of the design was the definition of the way the eye perceives shapes under the various conditions of contrast and luminance. The underlying principles of the concept are the analysis of contrast vision and the MTF – The Modulated Transform Function. Optimizations of these parameters lead to the BunnyLens AF Visual Acuity improvement.

In order to confirm accurate perception of image quality by the new designed optics, the BunnyLens AF optic design relies on the MTF (Modulation Transfer Function), the best tool for objective quantitative measurement of visual performance and contrast sensitivity. The MTF is also an extremely sensitive measure of image quality degeneration, enabling an accurate evaluation of the aberration degree.

The BunnyLens AF exceed the standard spherical intraocular lenses, ensuring improved quality of image and high contrast sight sensitivity for a higher range of spatial frequencies. This advantage is kept even at difficult visual situations, such as low light conditions with enlarged pupils, or decentration of the lens. The reduction and control of spherical aberrations results in superior vision quality for pseudophakic patients, by providing the best image quality the retina can interpret.

In order to provide a quantitative demonstration of the improvement in sensitivity of the contrast of the BunnyLens AF in comparison with the standard equal convex spherical BunnyLens a wide range of optical simulations was performed using the ZEEMAX software.

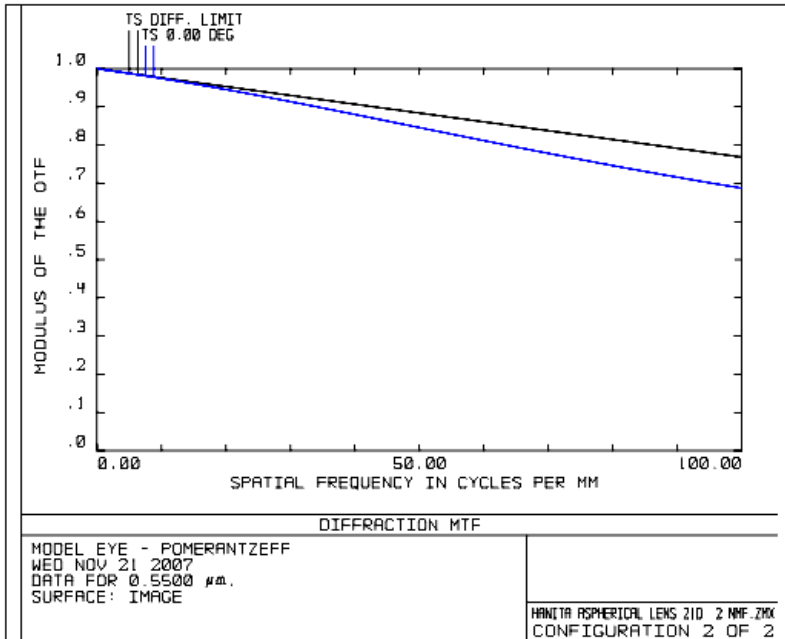


Figure 5:
BunnyLens AF 5mm pupil MTF Hanita Lenses advanced optics. ZEEMAX simulation vs. spatial frequency 0-100 [Cyc/mm] . The black line defines the ideal diffraction limit of the MTF. The blue line defines the lens actual simulated performance.

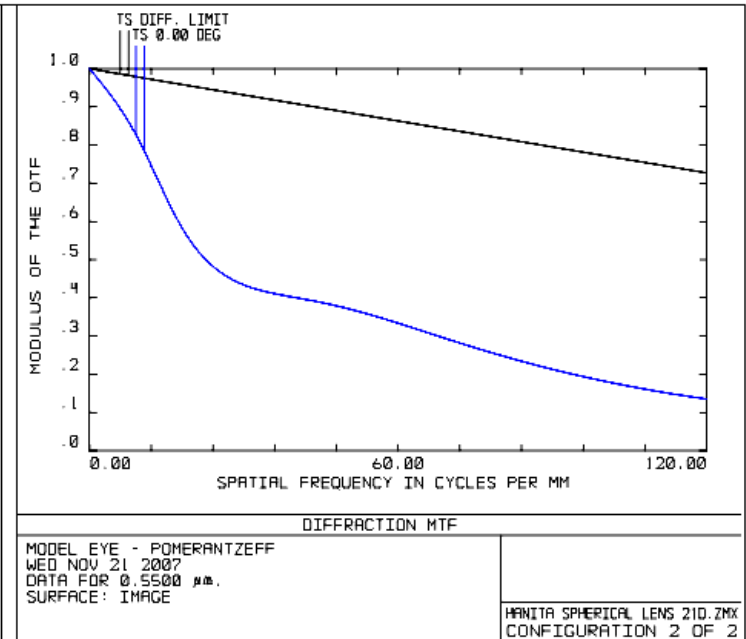


Figure 6:
Equi-convex conventional 5mm pupil MTF spherical optics. ZEEMAX simulation MTF vs. spatial frequency 0-120 [Cyc/mm]. The black line defines the ideal diffraction limit of the MTF. The blue line defines the lens actual simulated performance.

Figures 5 and 6 demonstrate the simulated MTF result of the lens in a dilated pupil of 5 mm which corresponds to the normal mydrated pupil. The BunnyLens superiority is straightforwardly noticed as the MTF decreases much faster as the spatial frequency rises in the standard lens with respect to the BunnyLens AF which remains very close to the MTF refraction physical limit.

e. Influence of tilt and decentration

The BunnyLens AF is based upon the mechanical design of BunnyLens equi-convex spherical lens. The BunnyLens design was proven to have good stability and good resistance to tilt and centration as well. Moreover, the BunnyLens AF Optical design was demonstrated by the ZEEMAX to have good resilience in terms of tilt and decentration as presented in the attached graph.

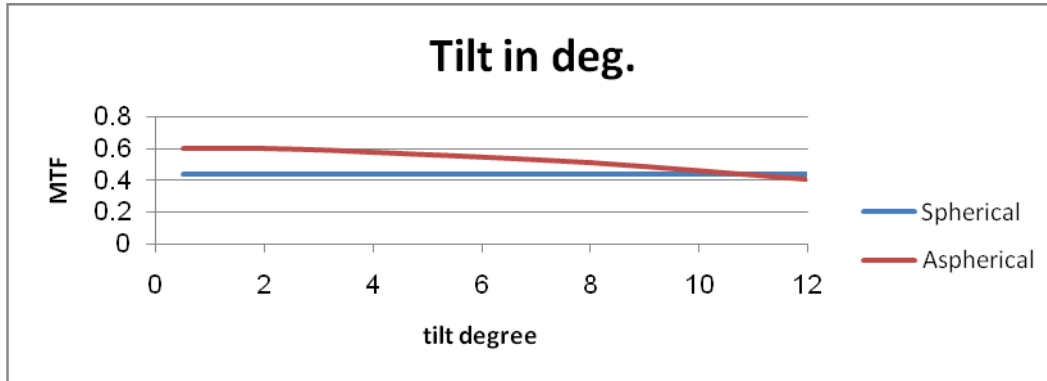


Figure 7: The influence of the degree of Tilt on the resultant MTF

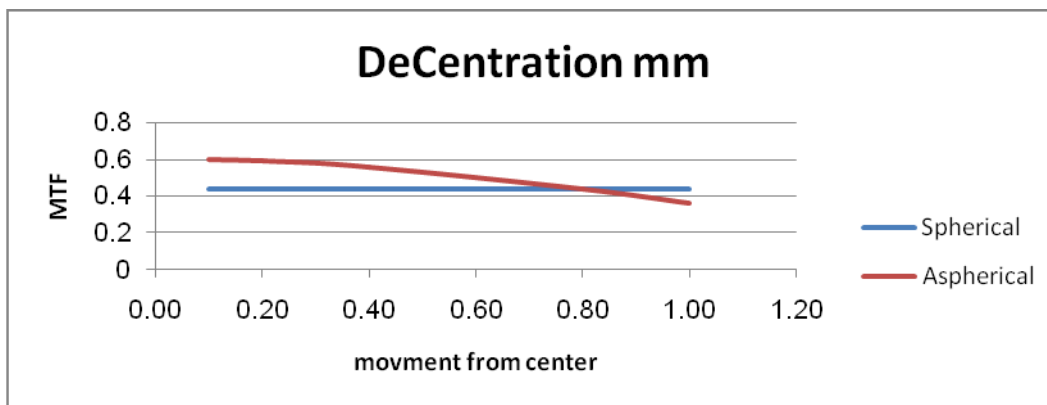


Figure 8: The influence of the degree of Tilt on the resultant MTF

The Hanita Lenses intraocular lens hydrophilic material has been in use at Hanita Lenses for more than 7 years and effectively verified its outstanding long-term behaviour in the market in terms of biocompatibility, transparency and stability of the visual function and centration. A foldable and highly adaptable implant for all bag conformations, the BunnyLens AF displays outstanding tensile strength for maximum resistance during insertion, and offer controlled unfolding for rapid visual recovery.

f. **Micro incision cataract surgery**

Another advantage, which is derived from the BunnyLens AF design, is its Micro Incision Cataract Surgical (MICS) property. The BunnyLens AF can be injected through a 1.8 mm incision. This property makes the BunnyLens AF surgical procedure almost free of induced surgical cylinder to the eye.

3. Surgical Procedure

The study Surgery Procedure: cataract extraction by ECCE Phacoemulsification. Operation was performed according to the routine surgery technique of the investigative sites. The surgical procedure was conducted according to protocol.

Methods:

The study was a prospective, open, non-randomized, multi-center study. The study was initiated on June 2010.

Sample size: a dual-center study of 40 patients, who met the inclusion / exclusion criteria of the study protocol. Protocol of the study is attached in Annex A.

The Investigative sites were:

Site #	Surgeon & Site	Number of implanted eyes	Number of eyes 3 months follow up
1	Dr. R. Benhamou <i>Private Clinic, France</i>	20	20*
2	Dr. J. Novak <i>Regional Hospital Pradubice, Czech republic</i>	20	20
	Total	40	40

* Follow up on 6 patients was performed 1 month post-operative instead of 3 months.

Additional study was performed to evaluate IOL rotational stability.

Sample size: single-center study of 20 patients.

The Investigative site was:

Site #	Surgeon & Site	Number of implanted eyes	Number of eyes 3 months follow up
3	Dr. J. Novak <i>Regional Hospital Pradubice, Czech republic</i>	20	17

Statistical Methods

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

1. Descriptive statistics: continuous variables are described with mean \pm standard deviation (SD), median, minimum and maximum. Nominal scale variables are described with absolute and relative (percents) frequencies. Ordinal variables are described with means \pm SD and frequencies of the ordinal grades.
2. Comparisons between pre and post operative variables were done with paired-samples t-test. The critical level of significance is $\alpha=0.05$.
3. All analyses were done using Excel 2007 statistics tool package.

Results:

a. IOL performance during implantation

Implantation parameters were measured to indicate the performance of the BunnyLens AF IOL implantation during the standard cataract surgery.

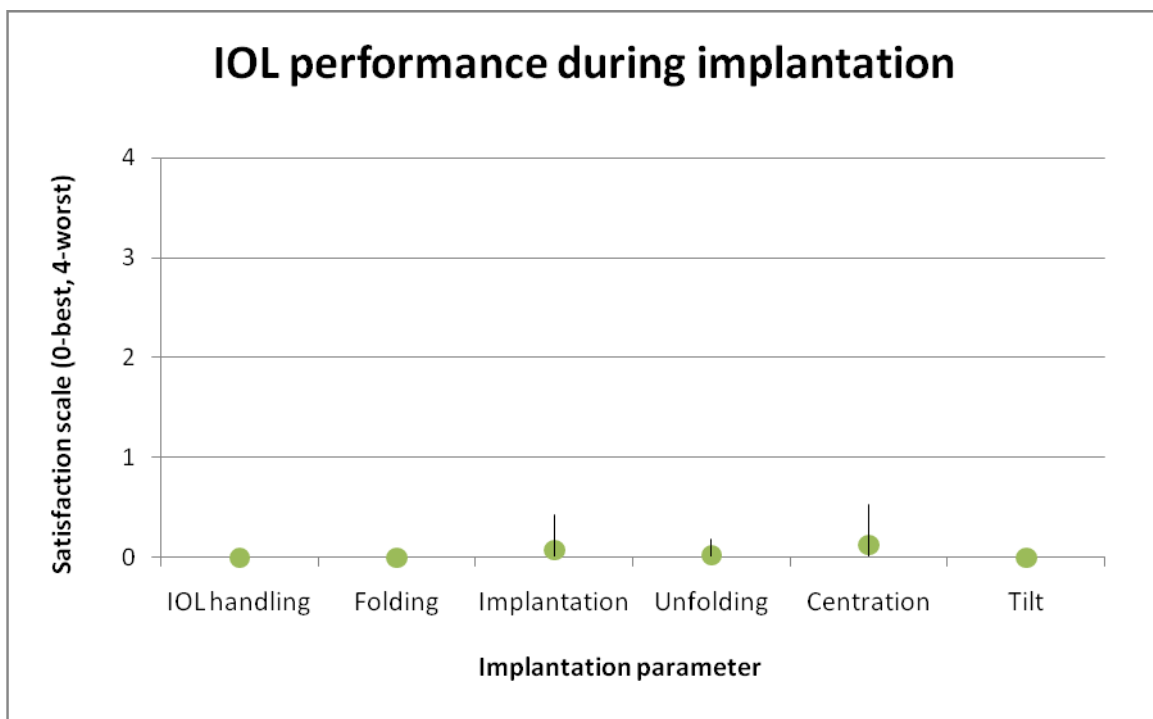
The implantation parameters measured: BunnyLens AF handling, folding, implantation, unfolding, need to manipulate the lens and the final centration and tilt of the lens position at the end of the procedure.

All parameters were graded on a 0 (best) to 4 (worst) scale.

See Appendix B of the Study Protocol in Annex A of this report for additional details.

The results are presented in Graph 1.

Graph 1: IOL performance during implantation (implantation parameters):



As can be seen in graph 1, all surgeons reported that the BunnyLens AF handling, folding and injection are easy and smooth. IOL unfolded gently and no difficulties in IOL positioning and centration were reported.

b. IOL location and centration

Lens location and centration were noted and reported in all follow-up visits. Centration and tilt were graded on a 0 (best) to 4 (worst) scale.

All lenses during all follow up visits were reported as zero (best) centration and tilt. In addition, on a scale of 0-4 for clarity, all lenses were reported as zero (best).

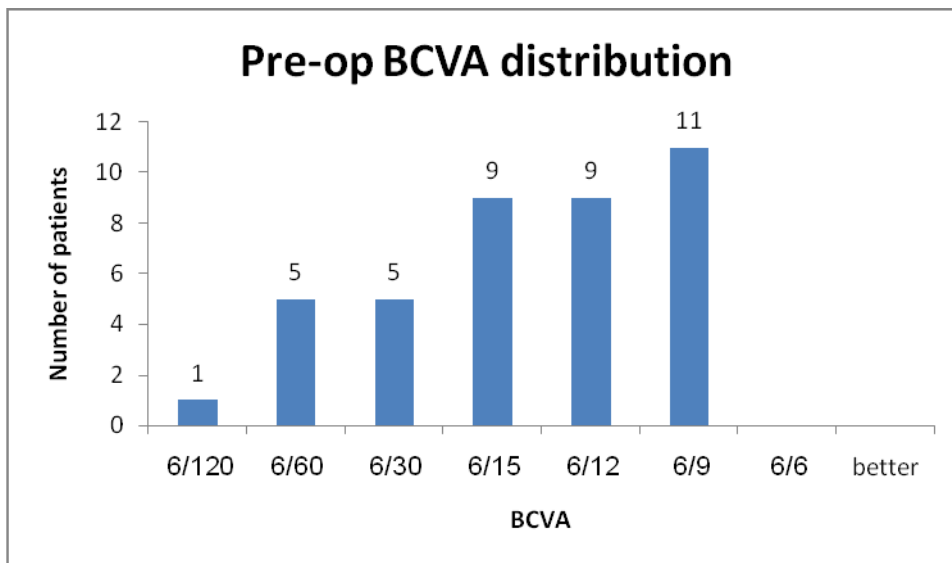
Therefore, the BunnyLens AF demonstrated good stability and centration during implantation and throughout the 3 month follow-up period.

c. Postoperative Best Corrected Visual Acuity (BCVA)

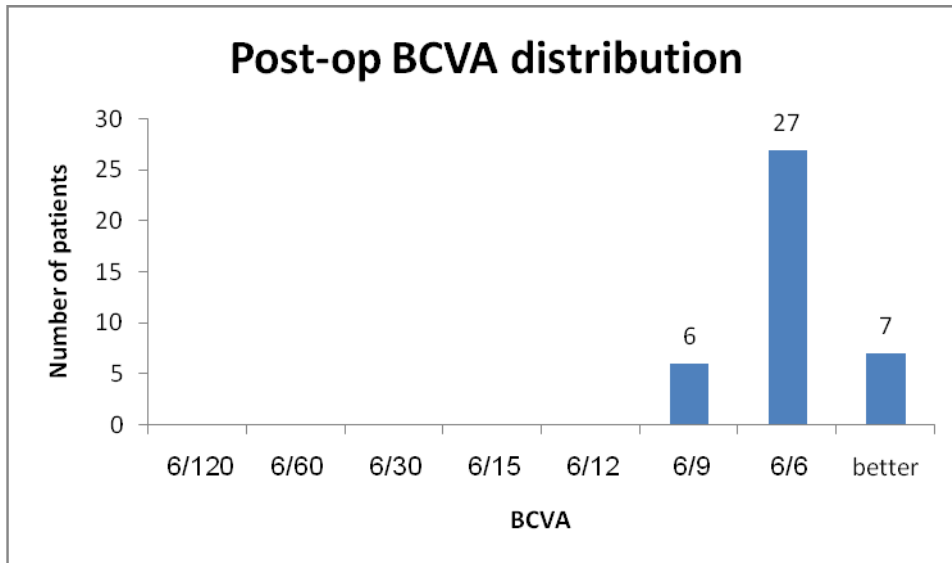
Best Corrected Visual Acuity (BCVA) was reported in the pre-operative and the three month follow-up visit.

Pre-operative BCVA results are shown in Graph 2, and Post-operative BCVA results are shown in Graph 3.

Graph 2: Pre-operative BCVA distribution



Graph 3: 3-month Post-operative BCVA distribution



As shown in graph 3, postoperative (3 months) BCVA value of 6/9 or higher was reported in 100% of the eyes.

Pre and post-operative BCVA are compared in Table 2:

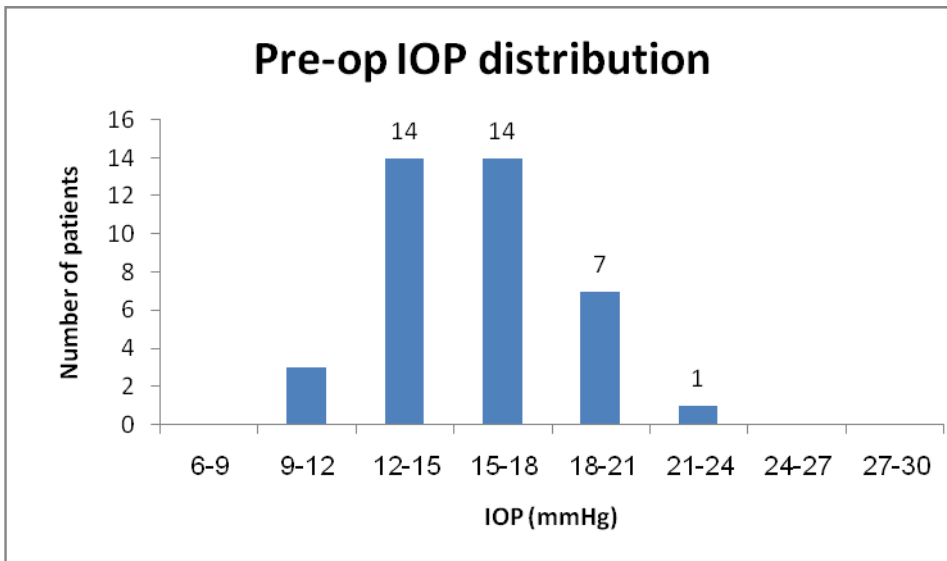
Table 2: Pre-operative BCVA vs. Post-operative BCVA

Measured parameter	Average	Standard Deviation
Pre Op BCVA	0.44 (6/13.6)	0.21
Post Op BCVA	0.99 (6/6.1)	0.15

d. Intraocular Pressure Changes:

Changes in intraocular pressure (IOP) from the pre-operative to 3-month postoperative visit are shown in graphs 4-5 below.

Graph 4: Pre-operative IOP



* Pre-operative IOP data of 1 patient from center 1 was not received.

Graph 5: Post operative IOP pressure

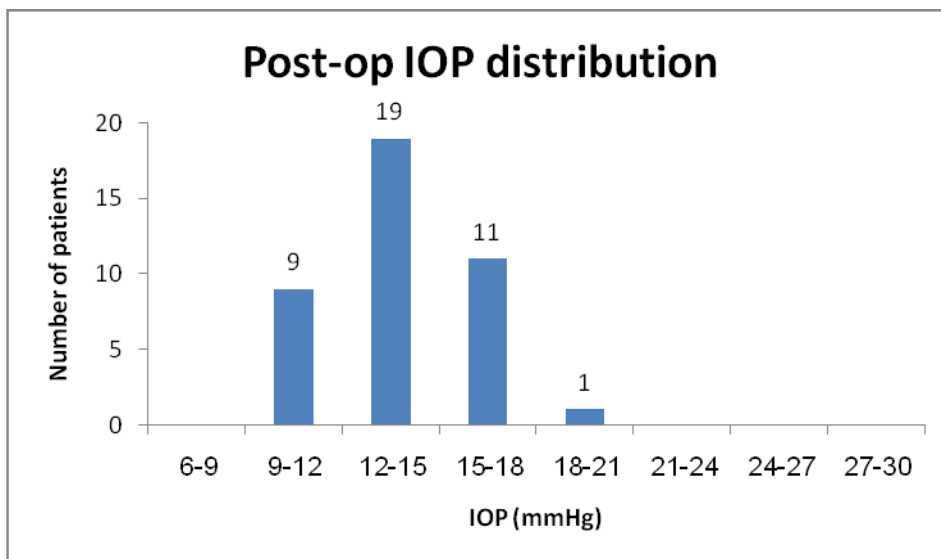


Table 3: Pre operative IOP vs. Post operative IOP

Measured parameter	Average	Standard Deviation
Pre Op IOP [mmHg]	16.2	2.8
Post Op IOP [mmHg]	14.2	2.1

The comparison detailed in table 3, between pre and post operative IOP, demonstrates that there was a decrease of the intra ocular pressure (mean±SD: 1.57±4.2 mmHg), which was found to be statistically significant (Paired samples t-test, p<0.005).

Nonetheless, for 100% of the examined eyes, IOP remained within the normal range (7mmHg - 21mmHg).

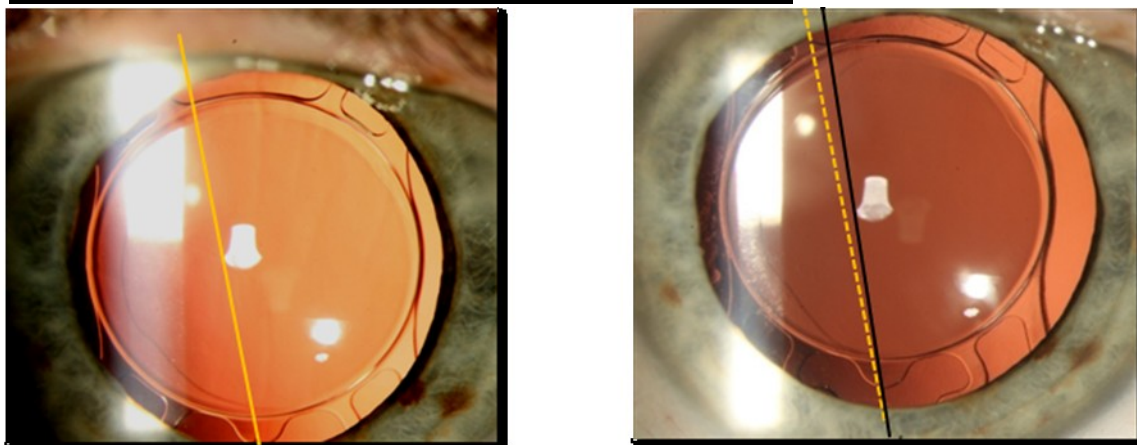
e. Rotational stability:

Changes in angular IOL position from the 1 day visit to 3-month post-operative visit were recorded in center 3 (17 eyes)

Rotation of IOL was evaluated using the following method:

The IOL was photographed at 1 day post-op and 3 months post-op visits. Images were compared, axis of the IOL was chosen to be a line between fillet of the left haptic and a top marker of the IOL, as shown by yellow line in the left image below.

Image 1: IOL position at 1 day (left) and 3 months (right)



The results of the rotational stability evaluation are shown in graph 6 below.

Graph 6: IOL rotation

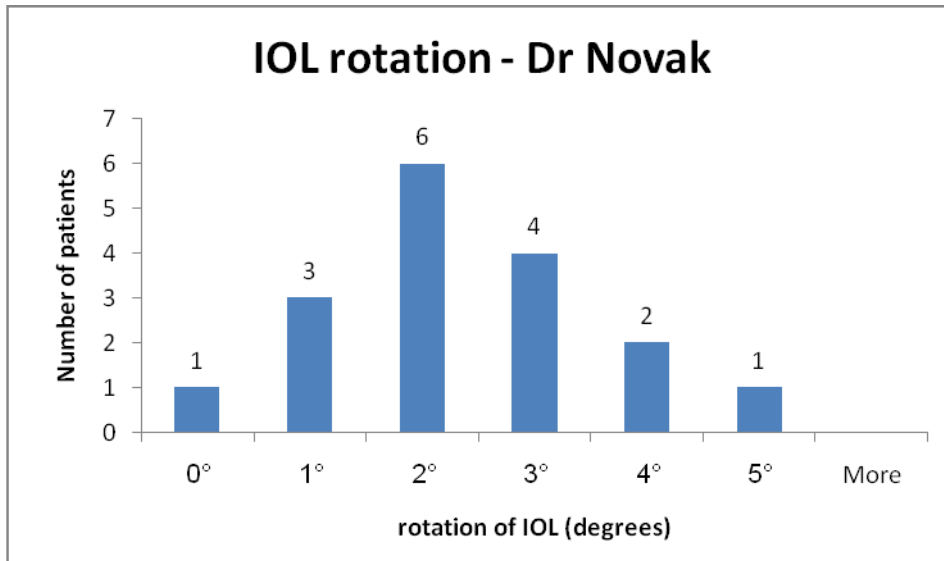


Table 4: Rotation of IOL between 1 day and 3 months

Measured parameter	Average	Standard Deviation
Rotation of IOL	2.41	±1.24

The data from the rotational stability study on 17 eyes shows that the BunnyLens AF IOL is rotationally stable and therefore, can be used as a platform for toric IOL.

f. Intra-operative complications

One intra-operative complication was reported (patient ID - BH15). The posterior capsule was ruptured during the surgery, and the surgeon experienced difficulty centering the IOL. Regardless, the BCVA of the patient at 7 days, 1 month and 3 months follow-ups was 6/6.

g. Postoperative Complications

No evidence of post-operative infection or exceptional inflammation was reported for any of the patients.

The BunnyLens AF IOL position as seen through a slit lamp is presented in Image 2.

Image 2: The BunnyLens AF IOL as seen through a slit lamp, 3 months post operatively

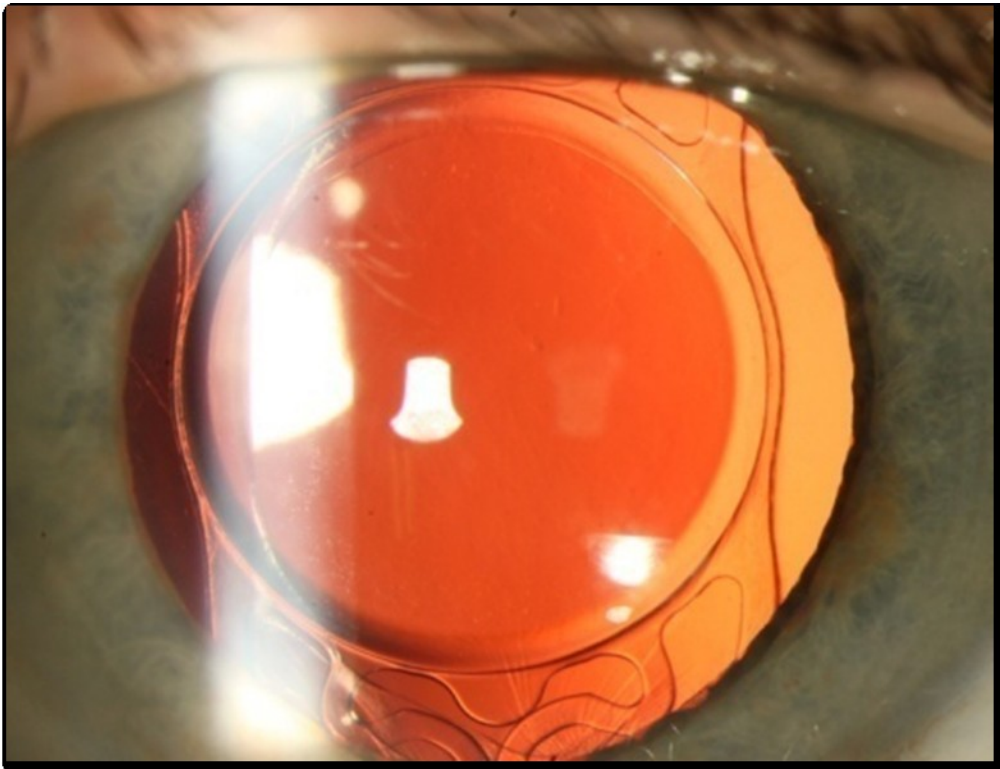


Image 2 shows that the BunnyLens AF is well centered, and a typical clear cornea can be indicated, as was seen in all BunnyLens AF implants 3 months & 1 month post operatively. Implantation was performed by Dr. J. Novak, Regional Hospital, Pradubice, Czech republic.

h. Adverse Events

Table 5: Adverse Events as Defined by ISO 11979-7 2006:

Adverse Event	SPE rate ¹ (%)	Number of subjects = 100		Rate of adverse effect occurred at this study	Number of adverse events cases	Pass / Fail
		Maximal allowable rate (%)	Max. number of cases allowed			

Cumulative (total number of occurrences at any time postoperative):

Cystoid macular oedema	3.0%	8.9%	6	5 % ²	2	Pass
Hypopyon	0.3%	3.0%	1	0%	0	Pass
Endophthalmitis ³	0.1%	3.0%	1	0%	0	Pass
Lens dislocation from posterior chamber	0.1%	3.0%	1	0%	0	Pass
Pupillary block	0.1%	3.0%	1	0%	0	Pass
Retinal detachment	0.1%	3.0%	1	0%	0	Pass
Secondary surgical intervention ⁴	0.1%	4.2%	2	0%	0	Pass

Persistent (total number of occurrences at 3 months postoperative):

Corneal stroma oedema	0.1%	3.0%	1	0%	0	Pass
Cystoid macular oedema	0.1%	4.2%	2	2.5%	1	Pass
Iritis	0.1%	3.0%	1	0%	0	Pass
Raised IOP req. treatment	0.1%	4.2%	2	0%	0	Pass

As shown in table 6, 95% of 44 implanted eyes did not reported any adverse events. 5% of patients presented CME, which is acceptable rate in cataract surgery.

Thus, it can be concluded that safety of BunnyLens AF is in accordance to the ISO 11979-7 2006.

¹ SPE (safety and performance endpoint) rate is the target rate for each event.

² N09, N13

³ Endophthalmitis is defined as inflammatory reaction (sterile or infectious) involving the vitreous body.

⁴ Excludes posterior capsulotomies.

i. Clinical Evaluation of Aspheric Optics

A clinical evaluation of aspheric optics feature was performed using SeeLens AF, IOL which has the same optical design as BunnyLens AF.

The evaluation was performed by Prof. M. Tetz, ATK Spreebogen, Berlin, Germany, from January till August 2009. 15 patients were included in 3 months post operative evaluation and 11 patients in 6 months post operative evaluation. For the detailed data of the study, see DHF 65C.

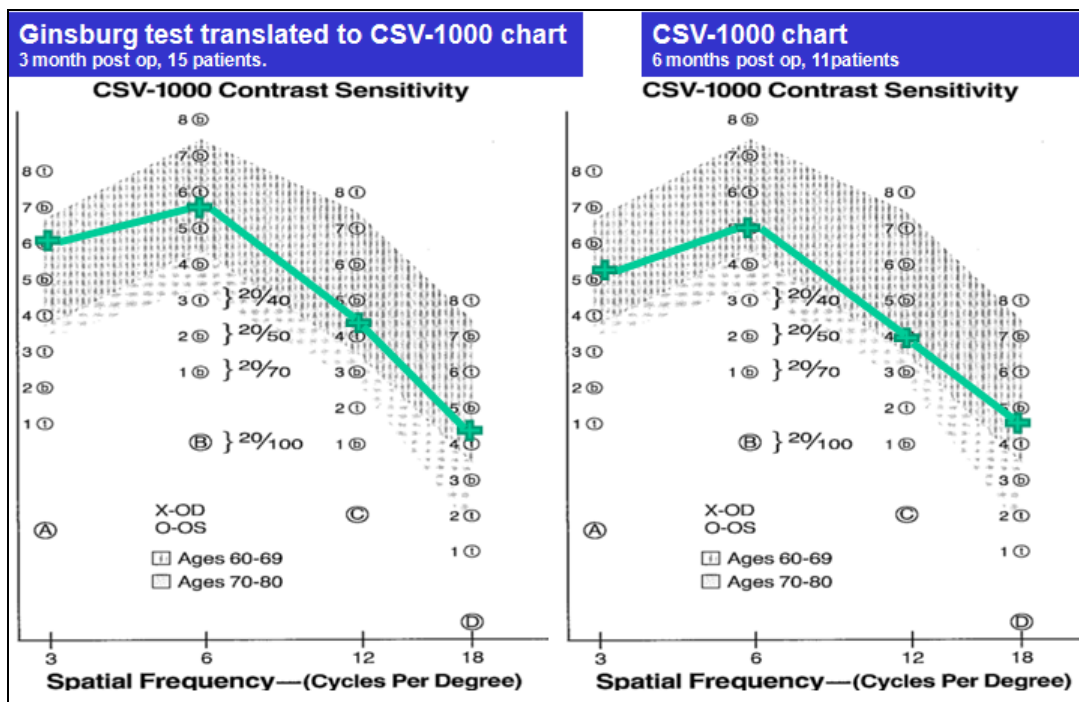
The functional evaluation of SA was performed in a group of 15 patients using same light conditions, 3 months post operatively. The evaluation was done using functional vision pupil. Measured pupil size ranged from 2.7 to 4.5 with average of 3.51. The results are presented below.

- Total SA (measured using WASCA aberrometer minus): $-0.01\mu\text{m}$
- Average Corneal SA (measured using Pentacam): $+0.26\mu\text{m}$

Functional IOL asphericity (in the functional pupil size) was estimated to be: $-0.27\mu\text{m}$.

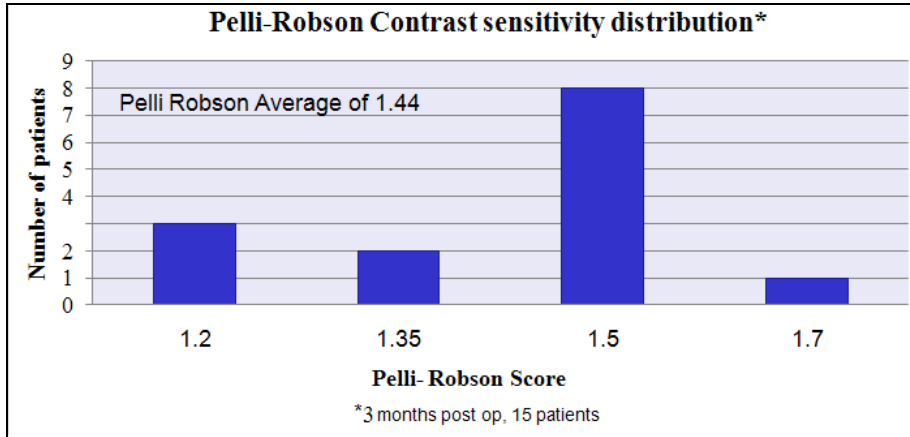
Clinical results of SeeLens AF Contrast Sensitivity performance are presented in Graphs 7-8.

Graphs 7-8: Contrast Sensitivity 3 and 6 months Post Operatively



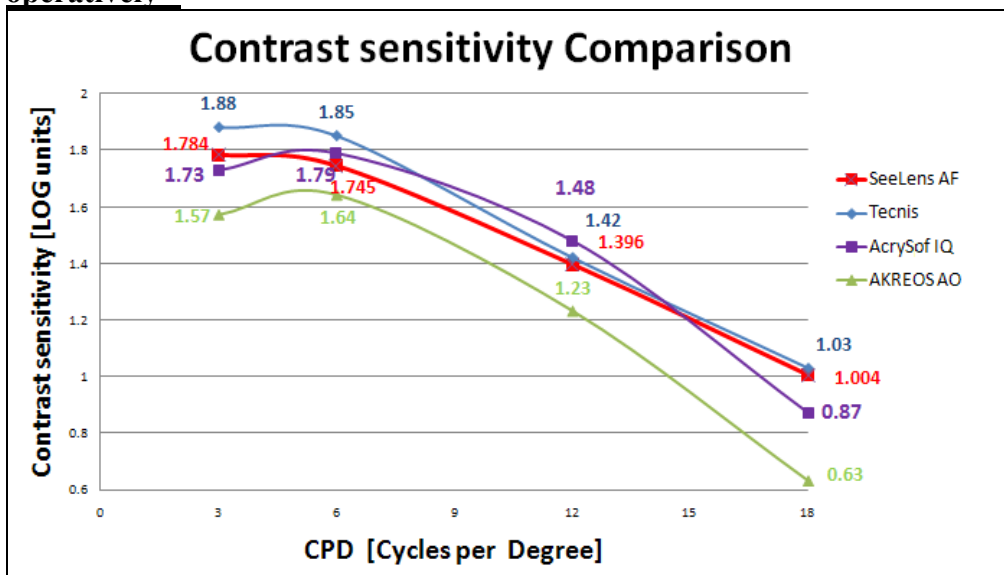
Pelli-Robson Contrast sensitivity distribution between 15 patients 3 months post operatively is presented in graph 9.

Graph 9: Pelli-Robson Contrast Sensitivity Distribution



The comparison of Contrast Sensitivity between SeeLens AF and other IOLs available in the market is presented in Graph 10:

Graph 10: Comparison of Contrast Sensitivity between Different IOLs, 3 months post operatively⁵⁶



As can be seen in graph 10, SeeLens AF demonstrated excellent contrast sensitivity, similar and superior to some aspheric IOLs available in the market. Since the BunnyLens AF IOL has the same optical design as the SeeLens AF, this conclusion is applicable for both IOLs.

⁵ Dr. Ralph Chu research as presented in the AAO Nov. 2007

⁶ Clinical Performance of New Aspheric Single-Piece IOL Design, Prof. Dr. Manfred Tetz, ASCRS, Boston 2010

Conclusions:

All surgeons reported that the BunnyLens AF handling, folding and injection are easy and smooth. IOL unfolded gently and no difficulties in IOL positioning and centration were reported.

Optical performance of the lens is in accordance to ISO 11979-7 2006 requirements.

For 100% of the examined eyes, IOP remained within the normal range.

BunnyLens AF IOL is rotationally stable and therefore, can be used as a platform for toric IOL.



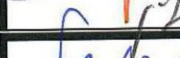

No intra-operative complications related to the IOL were reported.

Safety of the lens is in accordance to the ISO 11979-7 2006.

Similarly to SeeLens AF IOL, functional vision quality of the BunnyLens AF is similar or superior to other aspheric IOLs available in the market as estimated in terms of contrast sensitivity.

Signature page:

Revision	Date	Change description	Name
1.0	28-March-2011	Document formation	Alex Maliarov

Title	Name	Signature	Date
Autor	Alex Maliarov		28/3/11
Hanita Lenses Executive VP	Dorit Kelner		10/4/11
R&D Director	Yakir Kushlin		10/4/11
RA/QA VP	Roni Frenkel		13/4/11