

Effect Of Pupil Size On Visual Performance Of Presbyopes With Small-Aperture Corneal Inlay

AcuFocus[®]
THE SMALL APERTURE COMPANY™

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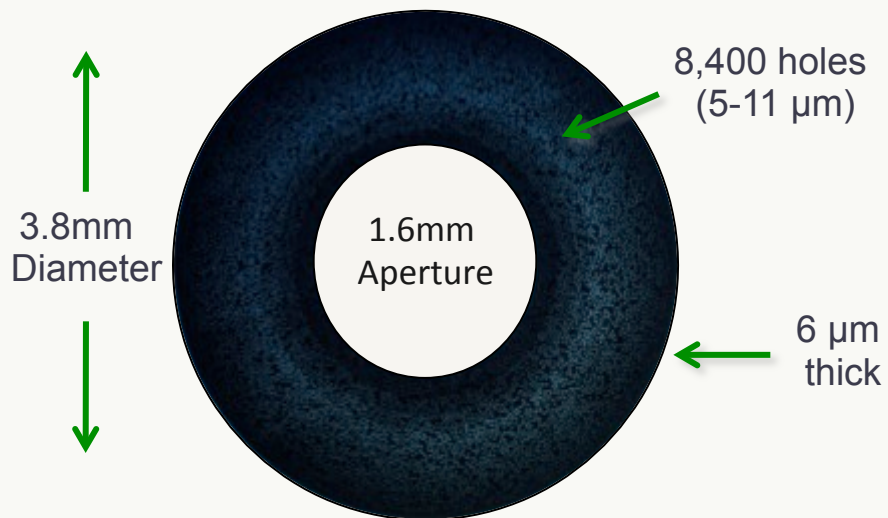
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Wavefront Congress - 03/05/16

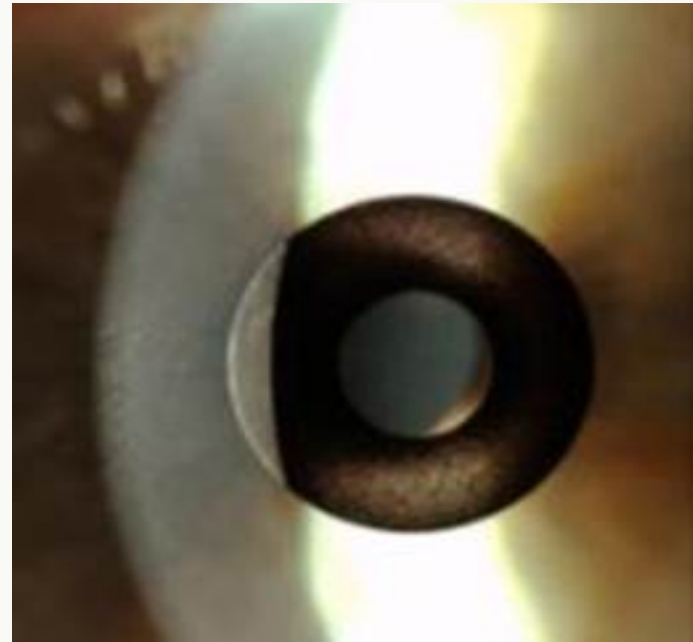
KAMRA[®] Inlay Design

- Inlay improves near vision by extending depth-of-focus
- Central aperture is a hole in the inlay and has no power
- Inlay provides an unobstructed pathway for focused light to reach the retina

Inlay Design



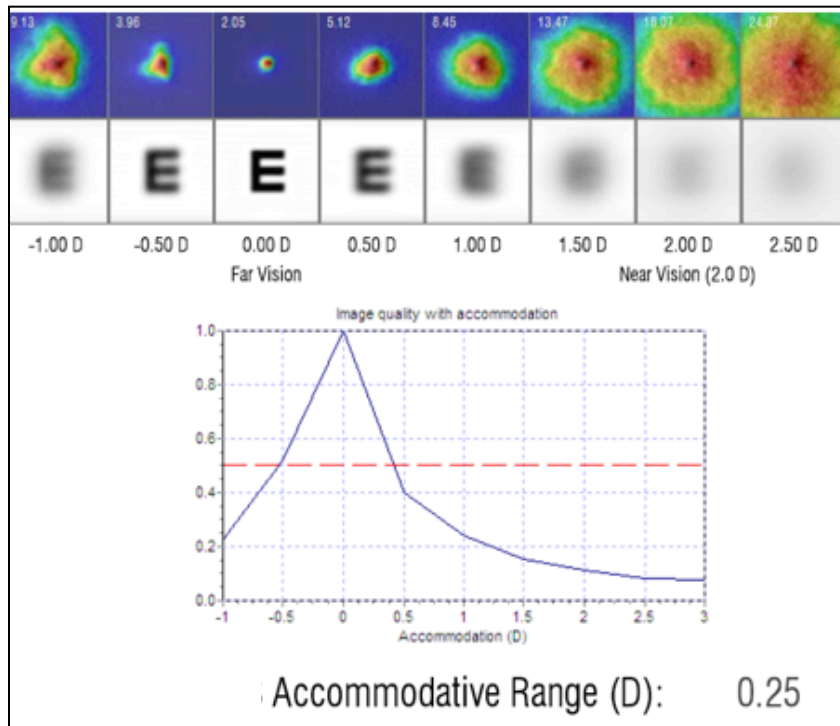
Made from Polyvinylidene fluoride (PVDF)



Depth-of-Focus Pre-op and Post-op

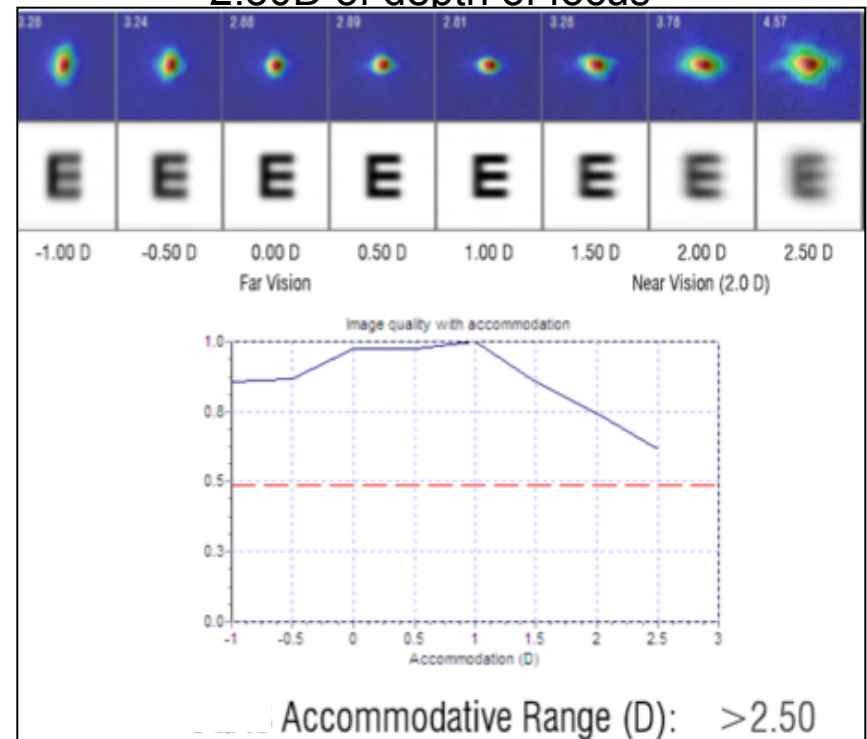
Pre-op

0.25D of depth of focus



Post-op

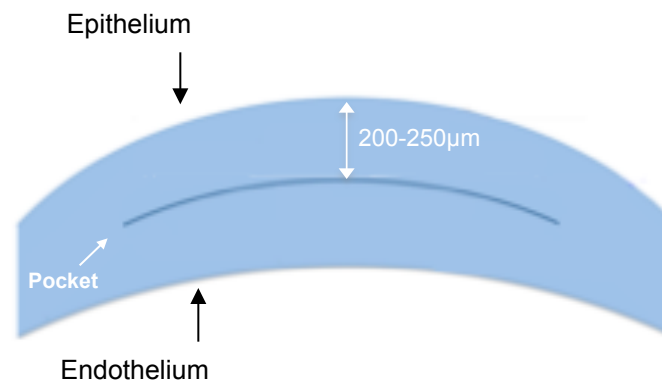
2.50D of depth of focus



Surgical Procedure

- **Description:** A femtosecond laser created pocket in the stroma at a depth of 200-250 μ m with femtosecond laser spot/line settings of $\leq 6 \times 6$ or equivalent is recommended.

Pocket Emmetropic KAMRA (PEK)



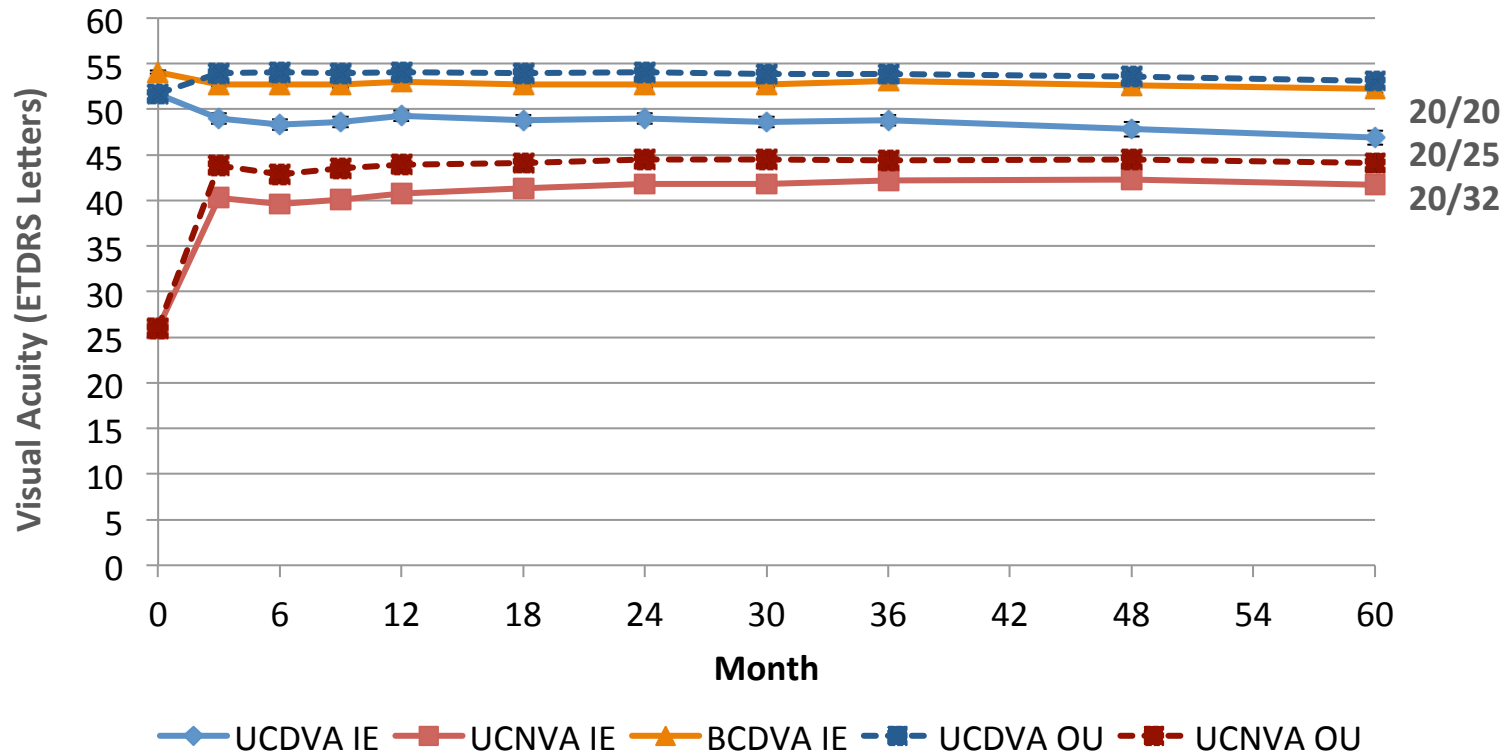
US IDE - Study Design

- 24 Sites (US, Europe & Asia-Pacific)
- Prospective, non-randomized clinical trial
- Subjects:
 - 507 enrolled and implanted in non-dominant eye
 - Naturally occurring presbyopic emmetropes
 - 45 - 60 years old
 - Spherical equivalent between + 0.50 D to -0.75 D
 - Uncorrected Near VA
 - Worse than 20/40 (0.5), and
 - Better than 20/100 (0.2)
 - Best Corrected Distance VA \geq 20/20 (1.0) in both eyes

US IDE Clinical Study

Long-Lasting Visual Performance

- Improvements in near acuity over the 5 year duration of the study
- Essentially no change in binocular UCDVA at any time point versus pre-op



Clinical Study Outcomes

Resection Groups Stratification

- Stratification by femtosecond laser settings demonstrates improved results when a $\leq 6 \times 6$ spot/line settings are used

	Study Endpoint	6x6 (N=154/175)	7x7 (N=118/149)	8x8 (N= 135/156)
Primary Endpoints				
Efficacy - % 20/40 or better UCNVA	$\geq 75\%$	94.8%	83.8%	78.5%
Safety – persistent BCDVA loss ≥ 2 lines	$< 5.0\%$	0.0%	0.0%	3.0%
Additional Outcomes				
Refractive Stability – change in MRSE (D) per month (24 month consistent cohort)	0.04D per month	-0.019 D per month	-0.005 D per month	-0.006 D per month
Refractive Stability - % within ± 1.00 D (24 month consistent cohort)	$\geq 95\%$	96%	93%	94%

Introduction

- Theoretical and ray tracing modelling of the optical effects of inlay annulus on retinal image and retinal illumination over a range of pupil sizes and visual field angles showed¹:
 - In an eye with an extremely small pupil, the reduction in retinal illumination has the potential to produce a relative scotoma.
 - In an eye with a very large pupil and/or a decentered annulus, the retinal image formed through the annulus and around the outside of the annulus may degrade the quality of the retinal image.

¹ Raasch TW. Optical effects of an intracorneal annulus as a treatment for presbyopia. Investigative Ophthalmology & Visual Science June 2015, Vol.56, 2987.

Purpose

Describe the effects of photopic and mesopic pupil sizes on visual acuity, visual symptoms and contrast sensitivity in a series of natural emmetropic presbyopes implanted with a small-aperture inlay in the non-dominant eye.

Methods

- Sub-group of 154 patients in the 6x6 pocket group
- 12-month post-operative visit
- Photopic and mesopic pupil sizes were measured using a pupillometer to the nearest half-millimeter
 - **Photopic:** Measure pupil size in full room illumination
 - **Mesopic:** Reduce overhead lighting to simulate a mesopic light level and dark adapt the subject for 10 minutes prior to measurements

Methods

- Uncorrected and best-corrected visual acuities were measured with the OPTEC® 6500 Vision Tester (ETDRS)
- Contrast sensitivity (CS) was measured in a subgroup of 76 of the 154 patients with the F.A.C.T. chart (OPTEC 6500 Vision Tester)
 - Subjects were measured monocularly and binocularly under photopic and mesopic conditions
- Visual symptoms were rated by subjects from 0 (none) to 7 (very severe)

Analyses One: *Average Pupil Size*

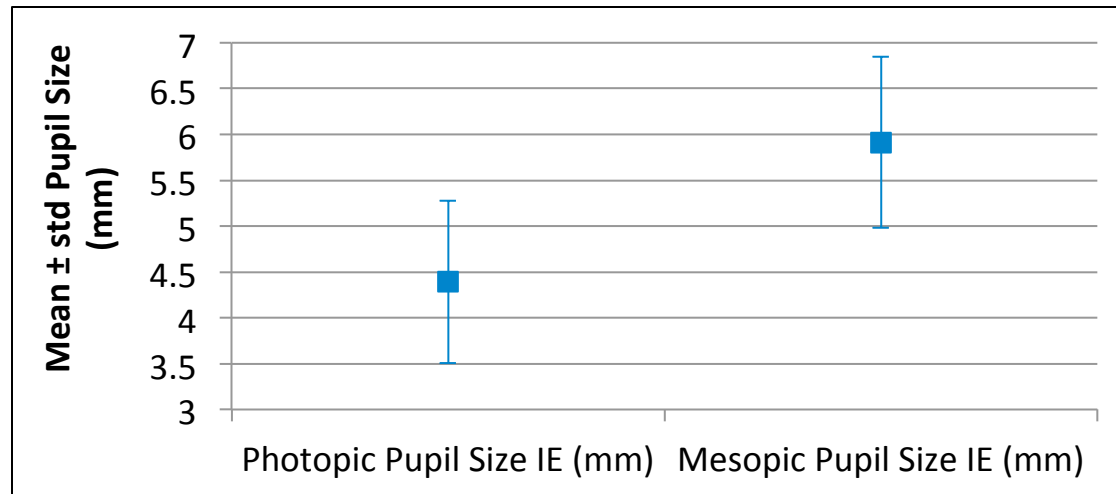
- **COMPARISON I:** Photopic and mesopic pupil sizes from the subjects in the 6x6 cohort were divided into two groups and compared:
 - **Group 1:** Above average pupil size
 - N = Photopic: 65 and Mesopic: 76
 - **Group 2:** Equal to or below average pupil size
 - N = Photopic: 89 and Mesopic: 78
- Statistical analyses: Nonparametric Wilcoxon-Mann-Whitney rank sum tests were done to compare between-groups

Analysis Two: *Large Pupil*

- **COMPARISON II:** between the largest pupil group and the rest
 - **Largest pupil group:**
 - 5% of subjects with pupils greater than 2.0 or more standard deviations (SDs) above mean were considered to be outliers.
 - N = Photopic: 5
 - N = Mesopic: 3
 - **The rest:**
 - 95% of subjects with pupils no greater than 2.0 standard deviations (SDs) above mean
 - N = Photopic: 149
 - N = Mesopic: 151
- Statistical analyses: Nonparametric Wilcoxon-Mann-Whitney rank sum tests were done to compare between-groups

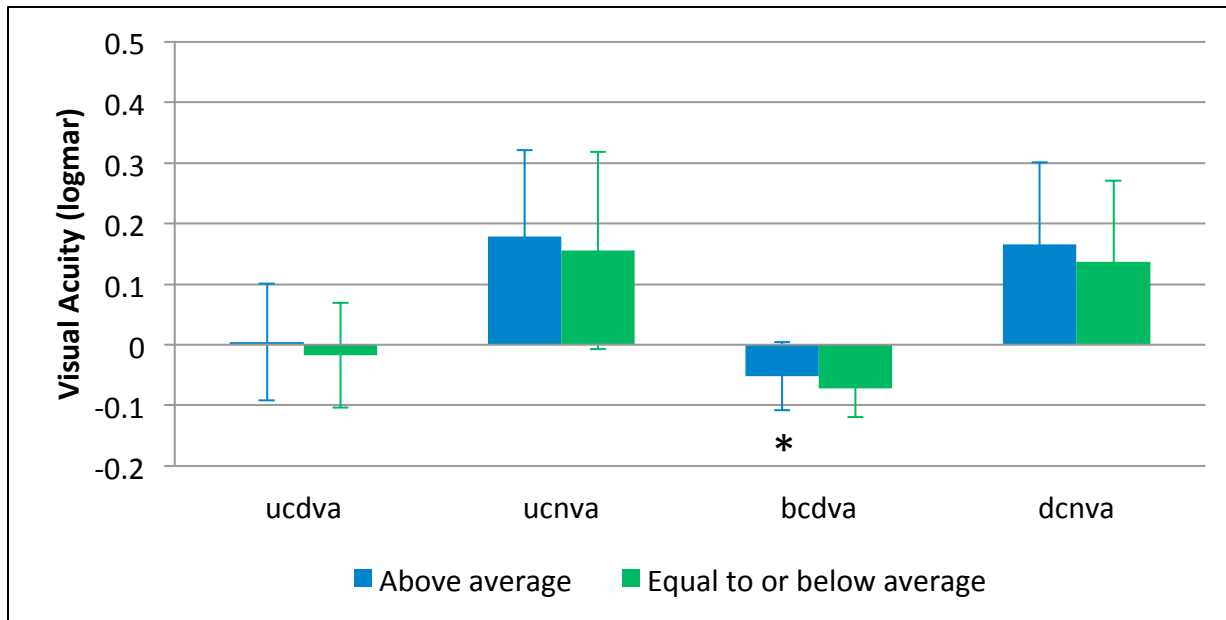
Average Pupil Size

(IDE Pivotal Trial- 6x6 subgroup)



- KAMRA® Inlay IDE study:
 - Photopic pupil size was 4.4 mm and it did not vary with age.
 - Mesopic pupil size varied from 6.1 to 5.7 mm between 45 to 60 years of age (p = 0.106)

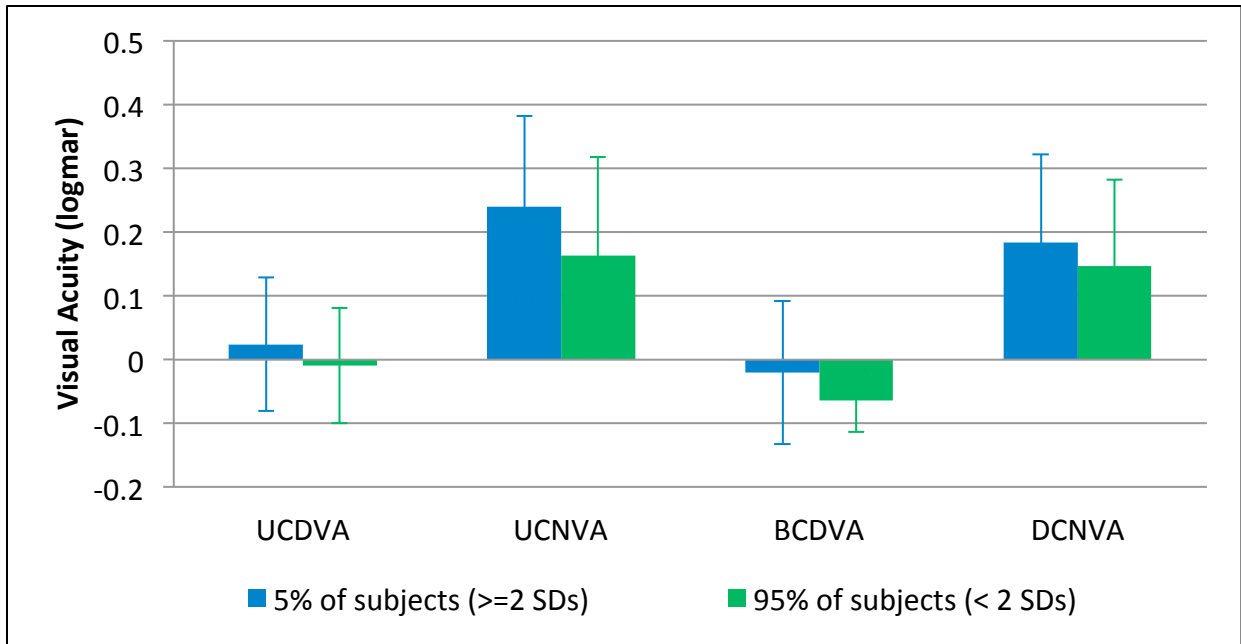
Average Pupil Size Group: *Photopic Pupil Size vs. Visual Acuity*



Pupil size categories (p = 0.7467)	MRSE (Diopters)
Above average (n=65)	0.19 ± 0.58 D
Equal to or below average (n=89)	0.21 ± 0.52 D

- The between-group differences on UCDVA (p = 0.1498), UCNVA (p = 0.1207) and DCNVA (p = 0.7453) were not statistically or clinically significant.
- The between-group differences on BCDVA (p = 0.0037) showed a statistically significant difference. However, this difference was only 2-3 letters which is not clinically significant.

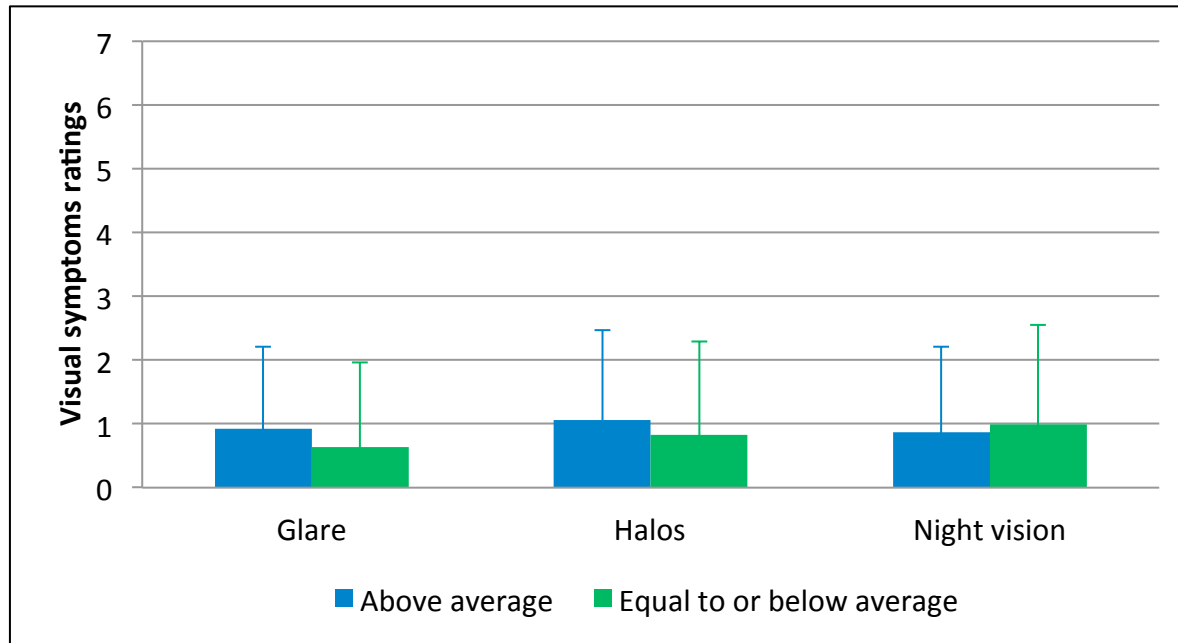
Large Pupil Group: *Photopic Pupil Size vs. Visual Acuity*



Pupil size categories ($p = 0.3236$)	MRSE (Diopters)
5% of subjects (≥ 2 SDs, $n = 5$)	0.50 ± 0.57 D
95% of subjects (< 2 SDs, $n = 149$)	0.19 ± 0.54 D

- The between-group differences on UCDVA ($p = 0.3746$), UCNVA ($p = 0.2186$), BCDVA ($p = 0.4830$) and DCNVA ($p = 0.4904$) visual acuities were not statistically or clinically significant.

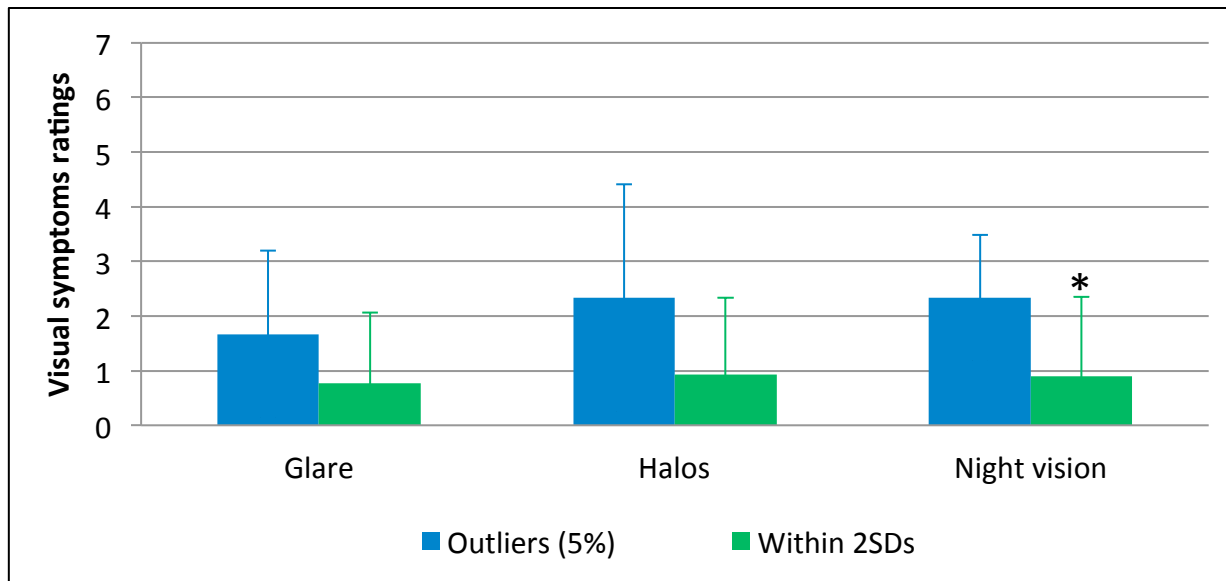
Average Pupil Size Group: *Mesopic Pupil Size vs. Visual Symptoms*



Pupil size categories (p = 0.6900)	MRSE (Diopters)
Above average (n=76)	0.19 ± 0.58 D
Equal to or below average (n=78)	0.21 ± 0.52 D

- The between-group differences on symptoms ratings for glare (p = 0.2990), halos (p = 0.5390) and night vision (p = 0.2520) were not statistically significant.

Large Pupil Group: *Mesopic Pupil Size vs. Visual Symptoms*

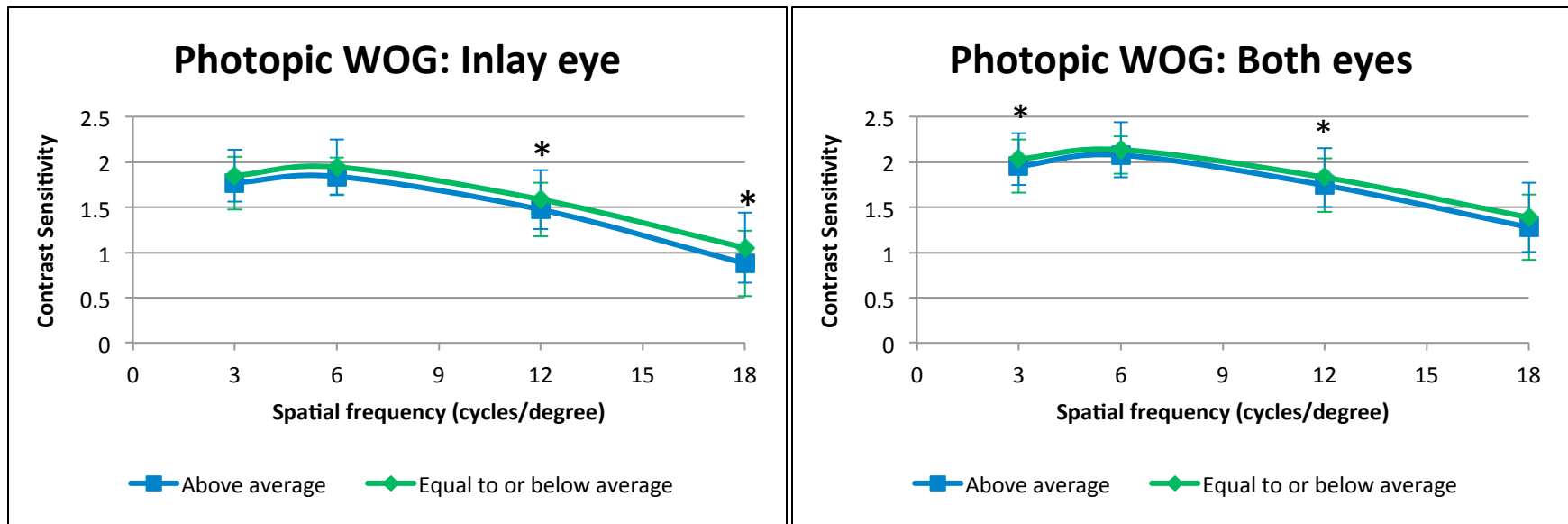


Pupil size categories (p = 0.1527)	MRSE (Diopters)
5% of subjects (>= 2SDs, n= 3)	-0.25 ± 0.54 D
95% of subjects (< 2SDs, n= 151)	0.21 ± 0.54 D

- The between-group differences on glare (p = 0.1361) and halos (p = 0.1878) were not statistically significant.
- The between-group differences on night vision problems (p = 0.0329) was statistically significant.

Average Pupil Size Group:

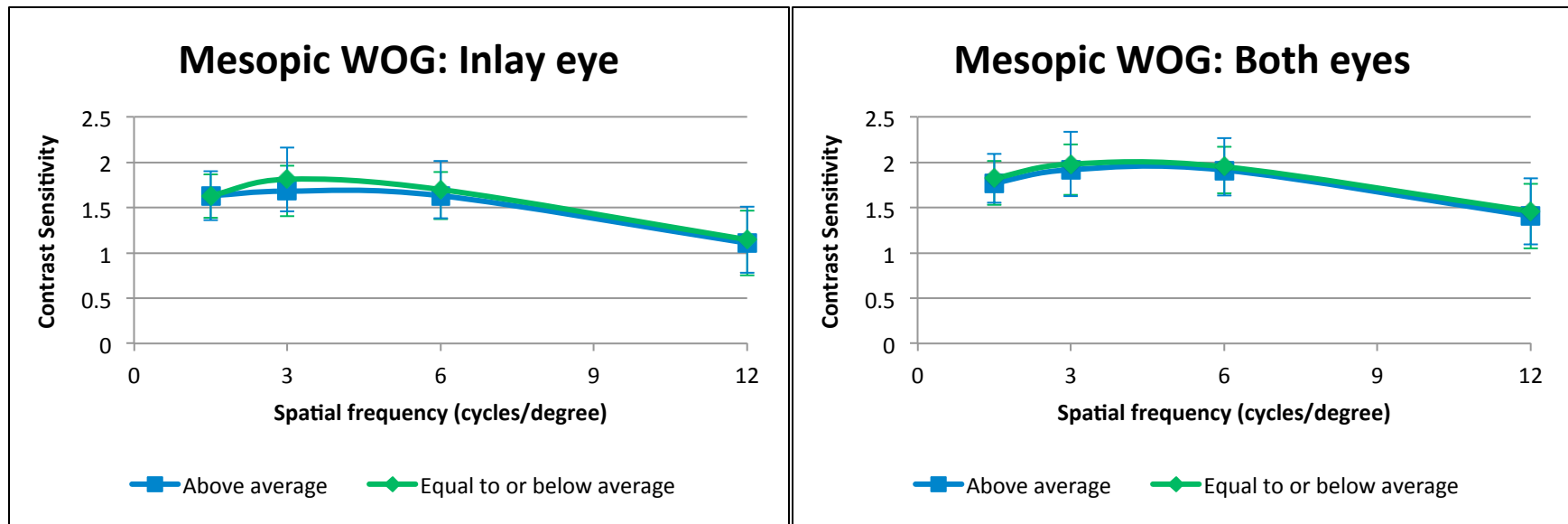
Photopic Contrast Sensitivity Without Glare (12 Months)



- The between-group differences on for photopic without glare condition in the inlay eye ranged from 0.07 to 0.17 log units.
- The between-group differences on for photopic without glare condition in both eyes ranged from 0.07 to 0.10 log units.
- The between-group differences did not reach clinical significance level of 0.30 log units.

Average Pupil Size Group:

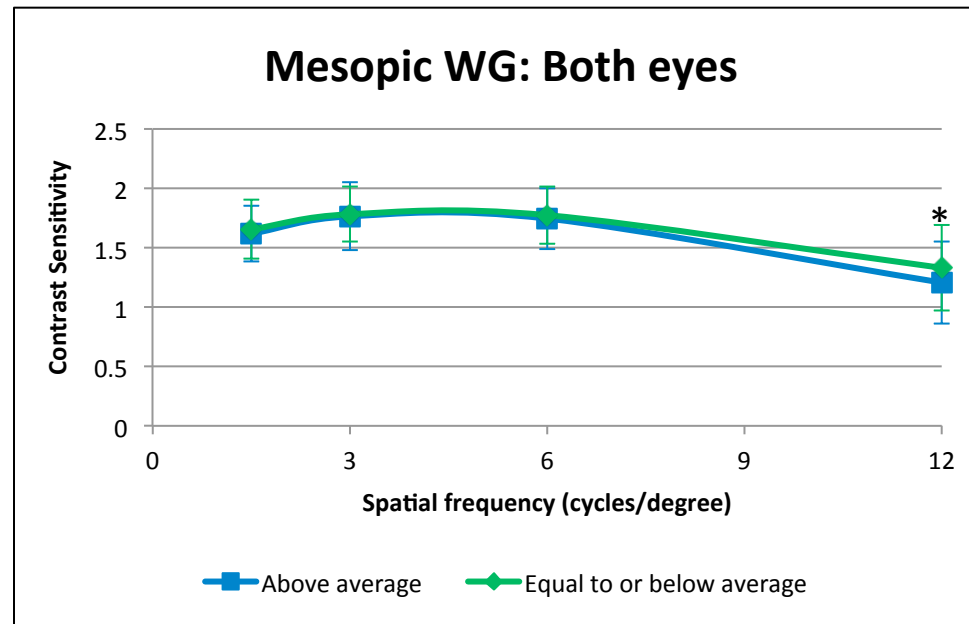
Mesopic Contrast Sensitivity Without Glare (12 Months)



- The between-group differences for mesopic without glare condition in the inlay eye ranged from 0.00 to 0.13log units.
- The between-group differences on for photopic without glare condition in both eyes ranged from 0.03 to 0.06 log units.
- The between-group differences did not reach clinical significance level of 0.30 log units.

Average Pupil Size Group:

Binocular Mesopic Contrast Sensitivity With Glare (12 Months)



- The between-group differences for binocular mesopic with glare condition ranged from 0.02 to 0.12 log units.
- The between-group differences on for photopic without glare condition in both eyes ranged from 0.03 to 0.06 log units.
- The between-group differences did not reach clinical significance level of 0.30 log units.

Summary

- Subjects in the **large** pupil group (5%) showed 2-3 letter difference in uncorrected and best-corrected visual acuities compared to the **rest** of the subjects (95%).
- Similarly, the **large pupil** groups rated their symptoms 1 level worse than the **rest** subjects.
- There was a small difference in contrast sensitivity between the above average and the equal to or below average pupil groups under photopic and mesopic contrast testing conditions. However, these differences were not clinically significant.

Conclusion

- Pupil size has minimal impact on visual acuity, visual symptoms and contrast sensitivity in eyes implanted with a small-aperture corneal inlay.
- The impact is only observable in the largest 5% pupil size study population.

