Aniseikonia and visual functions with optical correction and after refractive surgery in axial anisometropia

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Abstract

PURPOSE To evaluate differences in the subjective aniseikonia and stereoacuity in patients with axial anisometropia after full correction of the refractive error with spectacles, contact lenses, and refractive surgery.

METHODS A prospective study was performed in Cairo University Hospitals on 20 patients with axial anisometropia caused by unilateral myopia > 5 D with > 4 D inter-ocular difference in spherical equivalent who were suitable candidates for excimer laser ablation (LASIK) or implantable collamer lens implantation (ICL) were included. All patients had measurement of corrected distance visual acuity (CDVA), fusion, and stereoacuity testing, and measurement of aniseikonia with spectacles, contact lenses, and after surgery.

RESULTS Mean age at time of surgery was 25.7 ± 3.1 years. There were no statistically significant differences in the CDVA or stereoacuity with spectacles, contact lenses, or after refractive surgery. Microkonia < 5%) was perceived with spectacles in 8 patients (40%) and remained unchanged in 7 of these 8 patients with contact lenses. Following LASIK (n = 11), there was macrokonia < 2% in 4 patients (36%), persistent microkonia of 3% in 1 patient (9%), and no change in image size in 6 (55%) patients. Following ICL implantation (n = 9), there was perceived macrokonia of 2% in 4 patients (44%), disappearance of microkonia in 1 patient (11%) and no change in 4 patients (44%).

CONCLUSIONS Differences in CDVA, stereoacuity, and aniseikonia after correction of anisometropia by glasses, contact lens and surgery are both clinically and statistically significant. Retinal or neural adaptation might have a role in correction for differences in image size.

Introduction

Anisometropia is a condition in which there is a difference in refractive power between the 2 eyes of a patient. The disparity between image magnifications on the 2 retinas is known as aniseikonia.[1]. Anisometropia is usually divided into axial anisometropia which is caused by a difference in the axial lengths of both eyes, and refractive type which is caused by a difference in dioptric power of the lens or cornea, or a difference in the lens position. [2-3]. Anisometropia can compromise patient's binocular function and may result in subnormal stereoacuity [1].

When spectacles are used to correct anisometropia, the retinal image is smaller in myopic eyes and larger in hyperopic eyes than that of an emmetropic eye. Each diopter of correction cause about 1.3 - 1.6% difference in image size [4]. However, according to Knapp’s law, if spectacles were placed at the anterior focal plane of the eye, the theoretical retinal image sizes will be equal in axial anisometropia [5]. Knapp postulated that in axial anisometropia, correction of the refractive error by contact lenses might induce an aniseikonia [5]. However, contrary to what Knapp’s postulated, studies that investigated the aniseikonia reported that aniseikonia was present with spectacles and got reduced with contact lenses [6]. In addition, with the increasing trend of refractive surgery, studies reported an improvement of best-corrected visual
Acuity and stereoacuity after different refractive procedures that can be explained by a reduction in aniseikonia after refractive surgery [7-10].

The aim of this study is to evaluate the differences in the subjective aniseikonia and in stereoacuity in patients with axial anisometropia after full correction of the refractive error with spectacles, contact lenses, and refractive surgery.

Methods

The study protocol was approved by Cairo University Research Ethics committee. The study and data collection conformed to all local laws and were compliant with the principles of the Declaration of Helsinki. A prospective interventional study was performed on patients with axial anisometropia during the period from January 2015 through December 2017. An informed consent was obtained from all patients.

Twenty patients with axial anisometropia caused by unilateral myopia > 5 D with > 4 D difference in the spherical equivalent between both eyes who were suitable candidates for refractive surgery; excimer laser ablation or implantable collamer lens implantation (ICL) were included in the study.

The diagnosis of axial anisometropia was confirmed if the difference in the axial length between both eyes was > 1 mm and the difference in the mean keratometric readings of both eyes was < 1 D. Patients were included if the mean spherical equivalent in the less ametropic eye was < 1 D and the mean cylindrical error in the less ametropic eye was < 2 D. Patients had to be been regularly wearing spectacles and/or contact lenses for the past 6 months. Patients with any manifest or intermittent deviation were excluded from the study.

Patients were considered a suitable candidate for refractive surgery if they were above 21 years and younger than 45 years, had a stable refraction over > 6 months, and have no other ocular or systemic diseases that might affect the visual outcome, including but not limited to ectatic corneal conditions, cataractous changes, or glaucoma. Patients were considered a suitable candidate for excimer laser ablation if the ectasia risk score is 2 points or less [11]. ICL implantation was used if the spherical equivalent was > 10 D and/or the ectasia risk score is > 2 points, and if the ACD was >= 3.2 mm.

Full ophthalmic history was taken from each patient, including history of previous ocular trauma or surgery, or history of ocular diseases. Each patient underwent full ophthalmic examination; including uncorrected (UCDVA) and corrected distance visual acuity testing (CDVA) using single crowded optotype, intraocular pressure measurement, anterior segment slit lamp examination, and a dilated fundus examination. In addition, cycloplegic refraction was done approximately 30 min after topical instillation of cyclopentolate 1% 3 times.

Axial length, and anterior chamber depth were measured using Sonomed 300A+ PacScan A Scan (Sonomed Escalon, NY, USA). Corneal topography was done using Pentacam (Pentacam HRTM, Oculus
All patients had measurement of CDVA, and evaluation of fusion and stereoacuity using spectacles, and the using contact lenses. Spectacles were checked to ensure that they were in the correct spectacle plane; approximately 12-13 mm from the corneal vertex. Refraction was checked with the patient wearing contact lens to ensure that the residual refractive error with contact lens – if present – was < 0.5 D sphere and < 1.0 D cylinder in the more ametropic eye. Fusion was evaluated using Worth 4-dot test for distance. Stereoacuity was then evaluated using TNO test (Laméris Ootech BV, Ede, Netherlands). Finally, aniseikonia was evaluated using a custom software that projects 2 equal vertical red and blue bars on a computer monitor. The patient wore red-blue anaglyphic glasses on top of spectacles or contact lenses and was asked to adjust the size of the blue bar using a keyboard pad until the patient subjectively felt that the red and blue bars were equal in size. The red and blue bars were then oriented horizontally, and the procedure was repeated. The software automatically calculated the aniseikonia as difference in the image size in percentage [12].

Patients were then divided into 2 groups according to whether laser corneal surgery or implantable collamer lens implantation was performed.

In the LASIK group, the corneal flap was performed using Moria M2 microkeratome with 90 μm head (Moria, Antony, France). The stromal bed was then dried, and excimer laser ablation was applied using Schwind Amaris 750S (Schwind eye-tech-solutions, Kleinostheim, Germany). The optical zone of the treatment was set at 6.50 mm. The system automatically calculated the transition zone according to the amount of correction needed and to the selected optical zone. For all patients, the programmed treatment consisted of the manifest refraction. All values were entered without nomogram adjustment. Proper alignment of the eye was ensured before and during the ablation with the built-in eye tracker that automatically compensated for any cyclotorsion. Fixation light was used for fixation throughout the ablation. After the ablation was completed, the interface with irrigated with balanced salt solution, any debris was removed, and the flap was repositioned. Postoperative treatment included a combination of topical antibiotic and steroid drops (Tobradex, Novartis, Basel, Switzerland) 4 times daily for 2 weeks, and artificial tears (Systane Ultra, Alcon, Fort Worth, TX, USA) 4 times daily for at least 1 month.

In the implantable collamer lens group, lens power was calculated by the manufacturer using a modified vertex formula based on the manifest refraction. The size of the IOL was chosen based on the anterior chamber depth and the horizontal corneal diameter. Two paracenteses were performed at the 6- and 12 o’clock positions followed by injection of viscoelastic substance into the anterior chamber. A 3-mm temporal clear corneal incision was then performed and a V4c ICL model was inserted into the posterior chamber. Postoperative treatment included a combination of topical antibiotic and steroid drops (Tobradex, Novartis, Basel, Switzerland) 4 times daily for 4 weeks.

All patients were examined 1 day, 1 week, 1 month, and 3 months after the surgery. Results 3 months after the surgery were analyzed in this study. Evaluation included measurement of UCDVA, CDVA,
manifest refraction, slit-lamp examination, tonometry, and fundus examination. In addition, fusion, stereoacuity, and horizontal and vertical aniseikonia was re-measured.

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 18.0, IBM Corp., Chicago, USA). Comparisons between paired and matched variables were done using Wilcoxon signed-rank test for paired 2-groups comparisons and Friedman test for comparisons between more than 2 groups. Comparisons between separate groups were done using Mann-Whitney test for 2 groups, and analysis of variance (ANOVA) repeated measures for more than 2 groups. Correlation between different parameters was done using Pearson's correlation coefficient.

Results

Twenty patients with axial anisometropia were included in the study; 11 eyes of 11 patients underwent LASIK (Group A), while 9 eyes of 9 patients underwent ICL implantation (Group B).

The mean age at the time of surgery was 25.7 ± 3.1 years. There were no statistically significant differences in the demographic characteristics of the LASIK and ICL groups (Table 1). However, the mean spherical equivalent and the mean axial length were significantly higher in the ICL group than the LASIK group (P<0.001).

There was no clinically or statistically significant improvement in the CDVA with contact lenses as compared to spectacles (P = 1.00). The mean residual spherical equivalent with contact lenses was -0.19 D ± 0.21 (range, +0.37 to -0.68 D). The mean residual astigmatic error with contact lenses was 0.36 D ± 0.22 (range, 0 to 1 D).

The mean residual spherical equivalent was less than 0.5 D in all patients in both the LASIK and ICL groups (e-supplements 1 and 2). The mean residual astigmatic error was significantly lower (P < 0.001) in the LASIK group (0.07 D ± 0.16 D) than the ICL group (0.88 D ± 0.55 D), (e-supplement 3). The refraction remained stable at the end of the third month as compared to the first month (e-supplement 4). There was an improvement in the CDVA after refractive surgery in both the LASIK and the ICL groups (e-supplement 5). However, the difference was not statistically significant in both groups (Table 2). Only 1 patient (9%) in the LASIK group and 3 patients (33%) in the ICL group showed improvement in the CDVA (e-supplement 6).

Eighteen of the 20 patients (90%) showed fusional response in Worth 4-dot test for distance with spectacles. There was no change in the fusional status with contact lenses, and after refractive surgery, both the in LASIK and the ICL groups (Table 3). None of the patients complained of diplopia with spectacles, contact lenses, or after surgery.

Near stereoacuity was subnormal with spectacles. Four patients had no measurable stereopsis with spectacles (20%). There was no correlation between the stereoacuity and the inter-ocular difference in the
spherical equivalent \((r = 0.12, P = 0.612)\). However, there was a statistically significant correlation between the CDVA in the more ametropic eye and the stereoacuity \((r = 0.45, P = 0.046)\). There was a non-significant improvement in the stereoacuity with contact lenses \((P = 0.967)\). After refractive surgery, there was improvement in the stereoacuity in both the LASIK and the ICL groups. However, the difference was statistically non-significant in both groups \((P = 0.997 \text{ and } P = 1.00 \text{ respectively})\). Of the 4 patients who had no measurable stereopsis with spectacles, one patient (9\%) in the LASIK group regained some stereoacuity after surgery (Table 4).

There was a horizontal microkonia perceived in the more ametropic eye with spectacles in 7 of the 20 patients (35\%). However, the microkonia was less than 5\% in all 7 patients. The horizontal microkonia perceived in the more ametropic eye was unchanged in 6 of these 7 patients with contact lenses and disappeared in the remaining patient. One patient in the contact lens group developed horizontal macrokonia of 2\% in the more ametropic eye with contact lenses. Results of vertical aniseikonia were quite similar. There was a vertical microkonia perceived in the more ametropic eye with spectacles in 8 of the 20 patients (40\%). However, the microkonia was less than 5\% in all 8 patients. The vertical microkonia perceived in the more ametropic eye was unchanged in 7 of these 8 patients with contact lens and disappeared in the remaining patient. None of the patients had vertical macrokonia in the more ametropic eye with spectacles or contact lenses. There was no statistically significant correlation between the mean degree of perceived aniseikonia with the CDVA \((r = 0.11, P = 0.644)\) or with the degree of anisometropia \((r = 0.10, P = 0.675)\).

In the LASIK group, there was perceived image magnification, both horizontal and vertical in 4 patients after LASIK (Figures 1 and 2). However, the magnification was 2\% or less in all 4 patients (36\%). One patient had persistent microkonia of 3\% after LASIK. The remaining 6 (55\%) patients didn't show any change in the horizontal or vertical aniseikonia.

In the ICL group, there was perceived image magnification, both horizontal and vertical in 4 patients after surgery (44\%). However, the magnification was 2\% or less in all 4 patients. One patient had disappearance of microkonia with spectacles after ICL implantation. The remaining 4 patients didn't show any change in the horizontal or vertical aniseikonia (Figures 3 and 4).

**Discussion**

The effect of full correction of anisometropia on retinal image size is influenced by many optical, retinal, and neurological factors [13-14]. According to Knapp's law, full correction of the refractive error with spectacles at the anterior focal plane in axial anisometropia will not result in aniseikonia [5]. Knapp proved mathematically that a patient with axial anisometropia will have less aniseikonia with spectacles than with contact lenses if spectacles were placed at the anterior focal plane [5].

The effectiveness of contact lenses in axial anisometropia is unclear. Although some advocated their use, others discouraged them because of Knapp's postulation that contact-lens correction induces aniseikonia in axial anisometropia [15]. When axial anisometropia is corrected by spectacles, the retinal images sizes
are approximately equal; while if contact lenses were used, the more myopic eye would have a larger image size [16]. However, contrary to what Kapp's postulated, clinical tests showed that, there is less aniseikonia with the contact lenses than with spectacle lenses [6]. Spectacles may even produce a greater degree of aniseikonia than contact lenses [17].

It is believed that Knapp's law does not accurately describe the “cortical” size of ocular images because it does not incorporate retinal and neurologic factors [18]. Using adaptive optics retinal camera, it was shown that the foveal cone density decreases and the cone spacing increases as the axial length increases [19]. This can be explained by the relatively fixed number of photoreceptors that get more spaced with the stretch of the myopic eye. Thus, while the retinal image might not be minified according to Knapp’s law, the retinal image will stimulate a smaller number of retinal photoreceptors as compared to the fellow eye of normal axial length [13]. Another factor that can influence the retinal image size is the neural interpretation of the image size. A change in the image size would imply a change in the size of the visual field. The interpretation of the retinal image size might be compensated for by the brain as alerted to by the change in the size of the visual field [14].

In our study, no clinically or statistically significant changes in vertical and horizontal aniseikonia were observed between glasses, contact lenses, or after refractive surgery. The normal limit for fusion by the visual system is a difference in retinal image size of 3–5% [18]. In the few patients in this study were aniseikonia was detected, the perceived aniseikonia was less than 4%. We hypothesize that while optically changing the size of the retinal image result in non-congruous retinal images to both eyes, a process of neural adaptation occurs in most patients to ensure that aniseikonia is reduced [7, 13]. Nevertheless, we were not able to include in this study patients who did show fusional response with the aniseikonia test. Thus, patients included in this study reflect only one end of the spectrum of anisometropia with relatively good preoperative fusion.

The improvement of visual acuity with contact lenses and following refractive surgery in our study was statistically insignificant (P = 0.78). This is contrary to some studies which reported improvement in the BCVA after refractive surgery [8-10]. We believe that it might related to selection bias in our study. as we included only patients who were wearing spectacles regularly for the past 3 months who might have reached their plateau for visual acuity improvement. Numerous studies have shown improvement of visual acuity in amblyopic and anisometropic eyes only with regular wearing of spectacles [21-23]. The improvement of BCVA in other studies might have achieved without refractive surgery if the patient had been wearing spectacles on a regular basis.

Moreover, there was no difference in the fusional status or stereoacuity with the 3 modalities of treatment. Stereoacuity tended to correlate with the BCVA in the more ametropic eye rather than with the degree of anisometropia. This was in accordance to studies that reported no statistically significant relationship between the severity of the anisometropia and the level of stereopsis [24].
Many tests exist to measure aniseikonia and each has its pros and cons. A space eikonometer is probably that most precise tool for measuring aniseikonia [25]. The original model had 5 square feet viewing area. The reduced table version has size lenses to measure the aniseikonia in different meridians [26]. However, the reduced table-version can measure aniseikonia up to 5% difference only. This limits its use in measurement of larger aniseikonia. Moreover, the space eikonometer is not available commercially anymore. The New Aniseikonia Test (NAT, Awaya) was designed to determine both horizontal and vertical aniseikonia [27-28]. However, individual measurements on the NAT also cannot be rescaled to true size difference [29]. The Aniseikonia Inspector is a software used to measure the degree of aniseikonia [30]. In this study we used a custom-made software based on the same principles of aniseikonia inspector.

In conclusion, our study showed although there were some differences in in visual acuity, stereoacuity, and aniseikonia between the different modalities of anisometropia correction, these differences were both clinically and statistically insignificant.

**Declarations**

**Funding:** None

**Conflicts of interest/Competing interests:** None

**Ethics approval:** The study protocol was approved by Cairo University Research Ethics Committee. The study and data collection conformed to all local laws and were compliant with the principles of the Declaration of Helsinki.

**Consent to participate:** Written informed consent was obtained from the patients included in the study.

**Consent for publication:** All authors approved the final version of the manuscript.

**Availability of data and material (data transparency):** Data are available from the corresponding author upon request.

**Code availability (software application or custom code):** Not applicable

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Tables

Table 1: Mean preoperative characteristics of the studied patients
|                                | Total       | LASIK Group | ICL Group | P-value |
|--------------------------------|-------------|-------------|-----------|---------|
| Mean age ± SD in years         | 25.7 ± 3.1  | 25.4 ± 3.7  | 26.1 ± 2.1| 0.540   |
| (range)                        | (range, 21 to 33 years) | (range, 21 to 33 years) | (range, 22 to 28 years) |         |
| Male Sex (%)                   | 8 (80%)     | 5 (45.4%)   | 3 (33.3%) | 0.670   |
| Mean spherical equivalent in   | -0.17 ± 0.42| -0.25 ± 0.38| -0.07 ± 0.48| 0.357   |
| the less ametropic eye ± SD in | (range, -0.88 to 0.63) | (range, -0.88 to 0.25) | (range, -0.75 to 0.63) |         |
| D (range)                      |             |             |           |         |
| Mean cylindrical error in the  | -0.47 ± 0.44| -0.41 ± 0.41| -0.72 ± 0.54| 0.172   |
| less ametropic eye ± SD in D   | (range, -1.5 to 0) | (range, -1.00 to 0) | (range, -1.50 to 0) |         |
| (range)                        |             |             |           |         |
| Mean spherical equivalent in   | -10.88 ± 2.87| -8.60 ± 0.47| -13.65 ± 1.88| <0.001* |
| the more ametropic eye ± SD in | (range, -7.75 to -16.50) | (range, -7.75 to -9.38) | (range, -10.63 to -16.50) |         |
| D (range)                      |             |             |           |         |
| Mean cylindrical error in the  | -1.60 ± 0.64| -1.48 ± 0.79| -1.75 ± 0.40| 0.358   |
| more ametropic eye ± SD in D   | (range, -0.50 to -2.75) | (range, -0.50 to -2.75) | (range, -1.50 to -2.75) |         |
| (range)                        |             |             |           |         |
| Mean best-corrected visual acuity in the less ametropic eye in logMAR ± SD (range) | -0.03 ± 0.05 | -0.01 ± 0.03 | -0.05 ± 0.08 | 0.21 |
|                                | (range, 0 to -0.18) | (range, 0 to -0.08) | (range, 0 to -0.18) |         |
| Mean axial length in the less ametropic eye in mm ± SD (range) | 23.63 ± 0.28 | 23.66 ± 0.29 | 23.59 ± 0.27 | 0.563 |
|                                | (range, 23.22 to 24.13) | (range, 23.22 to 24.17) | (range, 23.22 to 24.17) |         |
| Mean axial length in the more ametropic eye in mm ± SD (range) | 27.73 ± 1.16 | 26.78 ± 0.49 | 28.88 ± 0.41 | <0.001* |
|                                | 9 (range, 25.92 to 29.51) | (range, 25.92 to 27.4) | (range, 28.11 to 29.51) |         |
| Mean keratometric              | 43.91 ± 0.70| 43.84 ± 0.73| 43.99 ± 0.70| 0.641   |
D, diopters; ICL, implantable collamer lens; LASIK, laser in-situ keratomileusis; logMAR, logarithm of the minimum angle of resolution; SD, standard deviation

* statistically significant difference

**Table 2: Mean logMAR best corrected visual acuity in the more ametropic eye with spectacles, contact lenses, and 3 months after refractive surgery**

|                  | Spectacles          | Contact lens        | After refractive surgery | P-Value |
|------------------|---------------------|---------------------|--------------------------|---------|
| **Total**        | 0.29 ± 0.21 (range, 0.10 to 0.60) | 0.29 ± 0.21 (range, 0.10 to 0.60) | 0.24 ± 0.20 (range, 0.0 to 0.60) | 0.711   |
| **LASIK Group**  | 0.19 ± 0.17 (range, 0.10 to 0.52) | 0.19 ± 0.17 (range, 0.10 to 0.52) | 0.17 ± 0.13 (range, 0.10 to 0.52) | 0.945   |
| **ICL Group**    | 0.45 ± 0.17 (range, 0.20 to 0.60) | 0.45 ± 0.17 (range, 0.20 to 0.60) | 0.34 ± 0.26 (range, 0.0 to 0.60) | 0.954   |

**Table 3: Fusion in Worth 4-dot test with spectacles, contact lenses, and 3 months after refractive surgery**
|                  | Spectacles (%) | Contact lens (%) | After refractive surgery (%) | P-Value |
|------------------|----------------|------------------|-----------------------------|---------|
| Total            | 18 (90%)       | 18 (90%)         | 18 (90%)                    | 1.00    |
| LASIK Group      | 9 (82%)        | 9 (82%)          | 9 (82%)                     | 1.00    |
| ICL Group        | 9 (100%)       | 9 (100%)         | 9 (100%)                    | 1.00    |

Table 4: Mean seconds of arc of near stereoacuity as measured with TNO test with spectacles, contact lenses, and 3 months after refractive surgery

|                  | Spectacles     | Contact lens    | After refractive surgery   | P-Value |
|------------------|----------------|-----------------|---------------------------|---------|
|                  | Mean ± SD (range) | Mean ± SD (range) | Mean ± SD (range)     |         |
| Total            | 1573 ± 1043 (range, 240 to 3000 seconds of arc) | 1560 ± 1062 (range, 120 to 3000 seconds of arc) | 1461 ± 1046 (range, 120 to 3000 seconds of arc) | 0.997   |
| LASIK Group      | 1156 ± 1092 (range, 240 to 3000 seconds of arc) | 1135 ± 1113 (range, 120 to 3000 seconds of arc) | 924 ± 991 (range, 120 to 3000 seconds of arc) | 0.997   |
| ICL Group        | 2228 ± 527 (range, 1920 to 3000 seconds of arc) | 2228 ± 527 (range, 1920 to 3000 seconds of arc) | 2228 ± 527 (range, 1920 to 3000 seconds of arc) | 1.00    |

Figures
Figure 1

Box and whisker plot showing the distribution of percentage of horizontal aniseikonia with spectacles, contact lenses and 3 months after LASIK.
Figure 2

Box and whisker plot showing the distribution of percentage of vertical aniseikonia with spectacles, contact lenses and 3 months after LASIK.
Figure 3

Box and whisker plot showing the distribution of percentage of horizontal aniseikonia with spectacles, contact lenses and 3 months after implantable collamer lens implantation.
Horizontal aniseikonia with spectacles, contact lenses, and 3 months after ICL implantation

Figure 4

Box and whisker plot showing the distribution of percentage of vertical aniseikonia with spectacles, contact lenses and 3 months after implantable collamer lens implantation.

Supplementary Files

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- esupplement1.tif
- esupplement2.tif
- esupplement3.tif
- esupplement4.tif
- esupplement5.tif
- esupplement6.tif