Measuring aniseikonia tolerance range for stereoacuity – a tool for the refractive surgeon

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ABSTRACT.

Objective: No method exists to measure aniseikonia tolerance in stereoacuity. The brain can compensate for 2%–3% aniseikonia (i.e. 2–3 dioptres of anisometropia) without impairing stereoacuity; however, a substantial proportion of anisometropic patients experience problems caused by disruptions of sensory fusion due to surgically induced aniseikonia. We hypothesized that individual differences in tolerance to aniseikonia exist and sought to develop a method to measure aniseikonia tolerance.

Methods: A total of 21 eye-healthy phakic individuals older than 50 years of age and 11 patients awaiting clear lens extraction were included. Patients were tested with best corrected near and distance visual acuity, cover/uncover test, eye dominance test, stereoacuity threshold (TNO test), slit lamp examination and ocular coherence tomography. The stereoacuity threshold was determined with aniseikonia induced by different size lenses ranging from 1% to 9% magnification of both eyes in increments of 1%. The aniseikonia tolerance range (ATR) was defined as the percentage aniseikonia in which the stereoacuity threshold was maintained.

Results: We examined 32 patients with a median age of 65 (95% CI: 62–66 years), CDVA better than 6/7.5 (0.1 logMAR), and median near visual acuity better than 6/6 (0.0 logMAR). The median stereoacuity threshold was 60 arcsec (maximum 30, minimum 120). We observed large inter-individual differences in ATR: 6/31 (19%) participants had an ATR of ≤1%, 1/31 (3%) had an ATR of 1-5%, 7/31 (22%) had an ATR of 5-10%, and 17/31 (54%) had an ATR of >10%.

Conclusion: We present a reliable method for measuring the amount of aniseikonia that a person can tolerate without impairing stereopsis. We report large inter-individual differences in tolerance of aniseikonia.

Key words: cataract surgery – anisometropia – aniseikonia – rule of thumb – ametropia – aniseikonia tolerance – size glasses

Introduction

Some refractive or cataract procedures involve deliberate introduction of anisometropia, either because only one eye needs cataract surgery or as a remedy for presbyopia (monovision or mini-monovision) (Labiris et al. 2017; Mahrous, Ciralsky & Lai 2018; Boissonnot, Risse & Ingrand 1990).

Surgical induced anisometropia can lead to aniseikonia, a difference in the size (or shape) of the retinal images in the two eyes. Aniseikonia can disrupt fusion and thereby impair the binocular vision reducing the binocular depth perception, also called stereopsis or stereoacuity, in which the two eyes can fixate at an object while locating other objects as being closer or farther away, solely on the basis of retinal disparity (Ogle 1950; Levin & Adler 2011). Furthermore, if anisometropia is corrected with spectacles of unequal optical powers the patient may experience prismatic effects during oblique gaze through the lenses, a condition labelled dynamic aniseikonia (Remole 1989). If the amount of optical aniseikonia exceeds the patient's tolerance, it can lead to clinical aniseikonia with symptoms related to disturbances in binocular vision such as reading difficulties, double vision, asthenopia or nausea under binocular viewing conditions (Burian 1943; Bannon & Textor 1948).

The primary cause of aniseikonia is anisometropia, which can have either a refractive, axial or surgical origin. While refractive and axial differences

are seen in children with likeliness of suppression due to binocular confusion, surgical induced anisometropia in adults is more likely to become symptomatic as adults have less ability to develop suppression (Tomaç & Birdal 2001; Levi, Knill & Bavelier 2015; Webber et al. 2019). In patients with equal axial lengths, the relationship between spectacle-corrected anisometropia and aniseikonia is approximately linear, and 1% of aniseikonia occurs as a result of a 1% difference in retinal image size (Ogle 1950; Linksz & Bannon 1965; Brown & Enoch 1970; Hillman & Hawkswell 1985; Lubkin et al. 1999). Psychophysical studies have suggested that the threshold for compromising the binocular system is approximately 3% aniseikonia (Katsumi, Tanino & Hirose 1986; Oguchi & Mashima 1989). The clinical threshold of 3% aniseikonia and the correlation between aniseikonia and anisometropia have led to the commonly used rule of thumb in cataract surgery in which a patient can tolerate 3 dioptres of anisometropia without experiencing binocular problems. However, several clinical studies have shown large variability in the tolerance of aniseikonia and described patients with a high degree of aniseikonia with maintained fusion and stereoacuity without clinical manifestations, as well as patients with aniseikonia below 3% with clinical symptoms (Lubkin, Stollerman & Linksz 1966; Lubkin, Linksz & Chamby 1969; Highman 1977; Lovasik & Szymkiw 1985; Katsumi, Tanino & Hirose 1986; Kramer et al. 1999; Bharadwaj & Rowan Candy 2011). These equivocal results indicate that the threshold for aniseikonia relies heavily on the plasticity of the brain and has large inter-individual variability.

To test a patient's tolerance of anisometropia, the patients can wear contact lenses with the desired anisometropia. This method is time consuming, includes blurring the vision on one eye and excludes the magnification/minification effect produced by the use of spectacle. There lacks a clinically preoperatively screening method that can assess tolerance of spectacle-corrected anisometropia in cataract patients. The clinical consequences for an ametropic patient undergoing unilateral cataract surgery can be either second eye surgery in the other healthy eye if the patient is sensitive towards aniseikonia, or it can be an undesirable postoperative refraction. A tool that can assess a patient's tolerance towards aniseikonia could thus help identify which patients can tolerate monovision, and it could prevent second eye surgery in healthy eyes and improve refractive outcome in ametropic patients undergoing unilateral surgery.

Intraocular lens (IOL)-induced anisometropia cannot readily be manipulated other than during cataract operations. Aniseikonia, in contrast, can be induced artificially by afocal size lenses. Because the adverse effect of anisometropia stems from the induced aniseikonia, the effects of various degrees of induced aniseikonia can be studied as a surrogate for the effects of IOL-induced anisometropia. The quality on binocular function can be assessed by determining stereoacuity. It is likely that patients with high cerebral plasticity can maintain the stereoacuity threshold in high amounts of aniseikonia induced by afocal size lenses compared to patients with low plasticity where stereoacuity threshold is impaired by low amounts of aniseikonia.

Aniseikonia Inspector version 3.5c (Optical Diagnostics, Beusichem, the Netherlands) (de Wit & De Wit 2003) is a software program for measuring aniseikonia. The purpose of the software is to examine whether patients with anisometropia or asthenopia have aniseikonia and, if needed, to calculate iseikonic prescriptions. Earlier versions have been reported to underestimate aniseikonia. In this paper, we validate the latest version of Aniseikonia Inspector and examine if the amount of optical aniseikonia induced by the afocal size lenses also equals the aniseikonia perceived by the patient.

The aim of this paper was to examine whether afocal size lenses and stereoacuity cards can be used to examine patients' aniseikonia tolerance, defined as aniseikonia tolerance range (ATR) and to determine the variance in ATR in an eye-healthy population. For ATR to serve as a potential screening method, it is important to ensure that the method is unaffected by surgery, and therefore, the second aim was to examine consistency of ATR before and after cataract surgery with induced isometropic refractive changes.

Methods

All participants volunteered to be included in the trial, and informed consent was obtained. The study adhered to the Declaration of Helsinki and was approved by the Regional research ethics committee H-16020057 and the Danish Data Protection Agency and registered at clinical trials.gov under NCT03832335. Power calculation for sample size could not be performed due to lack of data, and this study is therefore a pilot study. Sample size of 21 was chosen as this was feasible and believed to be enough patients to examine variation of tolerance in a normal distribution.

This study consisted of two parts.

Study 1 was performed to determine whether ATR might be measurable in an elderly eye-healthy phakic population. In addition, Aniseikonia Inspector version 3.5c was validated.

Study 2 examined the reproducibility of ATR before or after cataract surgery and dilation.

Study 1

Patients

Study 1 was a case study involving 21 phakic individuals with no previous eye disease.

The inclusion criteria were age >60 years old and visual acuity (VA) better than 6/7.5 (0.1 logMAR) in each eye.

The exclusion criteria were lack of fusion determined by plate IV in TNO chart, stereoacuity threshold >120 seconds of arc (arcsec), axial anisometropia with an axial length difference ≥0.3 mm, and a history of eye diseases: severe dry eye, corneal scars, history of herpetic keratitis, signs of keratoconus, history of uveitis, pseudoexfoliation syndrome, glaucoma, visually significant maculopathy, vitreomacular traction or tremor, previous ocular surgery or lack of cooperation.

Ophthalmic examination

The examination included autorefraction, corrected distance visual acuity (CDVA) on a logarithmic scale, distance CDVA measurement with an ETDRS VA chart, corrected near VA

(CNVA) by an ETDRS VA chart, cover/uncover test, dominance test with the Miles test, axial length measured by the IOL master (Carl Zeiss Meditec AG, Jena, Germany) and slit lamp evaluation including corneal status, fundus status with ophthalmoscopy, aniseikonia measurement and measurement of ATR with TNO stereopsis tests (Laméris Ootech, Ede, the Netherlands).

All patients underwent ocular coherence tomography to exclude macular pathology and vitreomacular traction.

Aniseikonia, afocal size lenses and fusion
Afocal size lenses magnify without using refractive powers. The lenses are used to induce artificial aniseikonia. The magnifying effect is independent of the vertex distance, because the lens is afocal. In this study, we used size lenses from 1% to 9% magnification with increments of 1%, thus making it possible to induce 1%–9% aniseikonia.

Aniseikonia values are calculated relative to the right eye. Positive values indicate that the image from the left eye is perceived as larger than that from the right eye, and the aniseikonia is corrected by placing a magnifying lens in front of the right eye. Negative values indicate that the left eye image is perceived as smaller than the right eye image, and the aniseikonia is corrected by placing a minifying lens in front of the right eye.

Fusion was tested using plate IV in the TNO stereopsis test, in which three round figures are seen through red/green glasses. A patient will see all three figures only if simultaneous perception is present.

The stereoacuity threshold was defined as the best possible stereoacuity with optimal spectacle correction.

Aniseikonia tolerance range (ATR)
Aniseikonia tolerance range (ATR) is the percentage of induced optical aniseikonia that a patient can endure without impairing the stereoacuity threshold and is measured using afocal size lenses and stereoacuity tests. Aniseikonia tolerance range (ATR) is measured separately for the right and left eyes and is calculated by adding the sum of the aniseikonia tolerance for the left and right eyes. ATR = $ATR^{OD}+ATR^{OS}$; thus, if a patient experienced deterioration of stereoacuity threshold with 4% size lens before the right eye and with 3% size lens before the left eye, the ATR was 5 (3 + 2) as stereoacuity threshold was maintained up to and including 3% size lens before the right eye and 2% size lens before the left eye.

Aniseikonia tolerance range (ATR) was measured with patients seated with their head fixed in a headrest integrated with a trial frame with appropriate refraction at a 40 cm distance from the stereoacuity cards. A good light source was applied above the headrest, with a colour rendering index of 97 Ra and colour temperature 5000 K.

The stereoacuity tests used were the TNO stereoacuity test and RANDOT stereo test (Stereo optical company INC, Chicago, USA). All test cards were cut into individual single cards so that each card could be shown in a blinded randomized order to the patient.

The patients were informed of stereoacuity cards would be presented in different difficulty level and that magnifying glasses would be placed in front of the right and left eyes. The patients were unaware of what effect the afocal size lens could have on the stereoacuity testing. The procedure started by showing plates I–III of the TNO stereo cards to the patient. The following procedure was then explained to the patients, and the patients were shown that stereoacuity cards of different difficulty would be displayed in randomized order, and afocal size glasses would be placed randomly. The first measurement was the maximal possible stereoacuity when only optimal correction was added and is denoted the stereoacuity threshold. There was no time for adaptation allowed before measurement was taken.

Demonstration of stereoacuity cards. Stereoacuity cards were shown in a stepwise manner. For example, with TNO cards, the first showing comprised 480 arc of seconds (arcsec), 240 arcsec, 120 arcsec, 60 arcsec and 30 arcsec, and the lowest result observed was considered the stereoacuity threshold. For each stereoacuity step, there were two different cards displaying different figures, and they were demonstrated in randomized order to avoid learning effect. The patient was unaware of the stereoacuity level.

Adding afocal size lenses. After the stereoacuity threshold was determined, size lenses were added in a stepwise manner at 3%, 6% and 9% size lenses (Fig. 1). The size lenses were added in steps of 3% to avoid learning response with a stepwise testing of 1%. The right eye was always examined first. If the patient had unaffected stereoacuity when a 3% size lens was added, then the 3% was replaced by a 6% size lens, and if 6% had no effect on stereoacuity, then a 9% size lens was added. If the patients experienced any deterioration in stereoacuity when a 3% size lens was added, then measurements with 1% and 2% size lenses were conducted to determine when stereoacuity was impaired. If 3% had no effect, but an effect was observed with a 6% size lens, then measurements with 4% and 5% size lens were collected, and so forth. This was done to find the exact magnification that provided deterioration of stereoacuity.

When a deterioration of the stereoacuity threshold was measured, stepwise retesting with higher and lower stereoacuity cards was performed to avoid false negatives.

Afocal lenses were first added to the right eye, and then, the procedure was repeated with afocal lenses in front of the left eye. The entire procedure was then repeated with the Randot stereo test.

Aniseikonia measurement
Aniseikonia was measured with Aniseikonia Inspector™ version 3.5c. Aniseikonia Inspector is a software using a direct comparison method to examine whether a patient experiences aniseikonia. The patients look through red/green glasses, and the software shows a series of red and green rectangles of different sizes. The task is to identify which of the two rectangles is larger.

The software offers the possibility of examining aniseikonia in different field angles, that is visual field angles 1°, 2°, 3°, 4° and 8°. The visual field is the angular distance from a peripheral point to the centre of the fovea in object space, that is, how large an area/close to the macula is stimulated. Visual field should not matter in optical aniseikonia, because the aniseikonia should be the same in all fields; however, in retinal aniseikonia, the aniseikonia can present in one visual field but not the other, depending on where the retinal disruption exists (de Wit 2007).

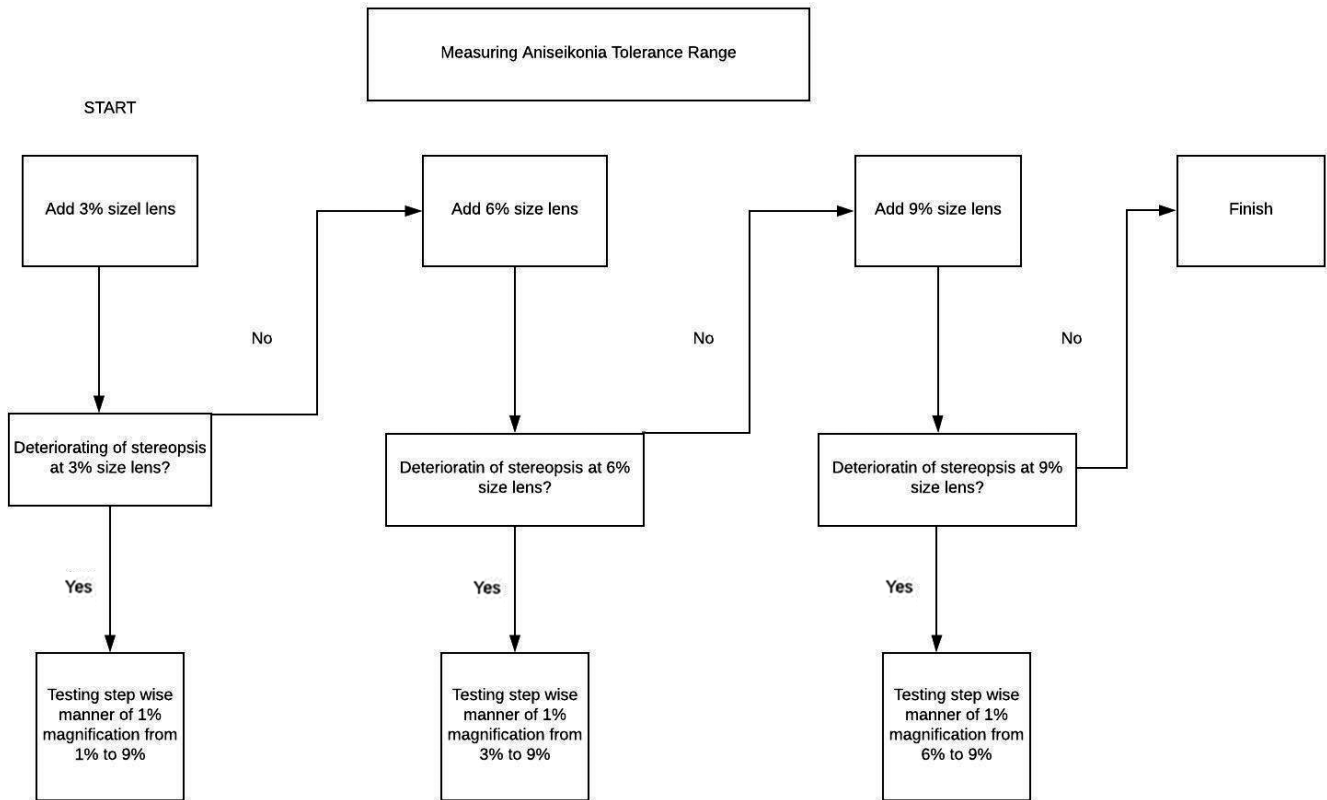The patients were informed of the purpose and function of Aniseikonia

Fig. 1. Diagram of measuring aniseikonia tolerance range using a stepwise manner of magnification.

Inspector and instructed to fixate on the centre of the screen and choose the longer of the two figures. Afterwards, the procedure was demonstrated, and when the patients understood the principle of the examination, they were seated and placed in a fixation headrest in front of a computer screen at the recommended distance of 52 cm. The examination was performed with optimal optical correction for the distance. The software provided an inconsistency value, and in cases with inconsistencies above 3, the test was redone, as recommended by the manufacturer.

The viewing time was set at short, and measurements were performed in horizontal and vertical directions in visual fields 4° and 8°. All examinations were performed in a dimly lit room.

$$\text{Mean aniseikonia vertical} = \frac{(\text{Aniseikonia vertical field } 4 + \text{Aniseikonia vertical field } 8)}{2}$$

$$\text{Mean aniseikonia horisontal} = \frac{(\text{Aniseikonia horisontal field } 4 + \text{Aniseikonia horisontal field } 8)}{2}$$

We used the latest version of Aniseikonia Inspector and validated this version compared with earlier used versions to ensure that the amount of optical aniseikonia induced by the afocal size lens reflected the amount of aniseikonia experienced by the patient. All patients had a baseline measurement, and afterwards, we validated Aniseikonia Inspector by masking the patients with 2% and 4% afocal size lenses in randomized order in front of the left or right eye, and then measured aniseikonia.

Calibrations of afocal size lenses and adjustments according to the right and left eyes were performed according to instructions from the manufacturer (de Wit 2008). Calibration indicated that the 2% lens magnified by 2.35% and the 4% lens magnified by 3.38%.

Study 2

Patients
Study 2 was a case study of 11 patients who were offered clear lens extraction (CLE) in both eyes at a private eye hospital, Scandinavian Eye Hospital in Hellerup, Denmark.

The inclusion and exclusion criteria were identical to those in study 1.

Ophthalmic examinations
Preoperatively, the same examinations as study 1 were performed, except that distance VA was determined with an ETDRS VA chart. In study 2, ATR was examined with both a random dot stereo test and a contour stereo test to compare the two tests for ATR testing. The tests used were TNO stereo test and Randot stereo tests supplemented in two patients with the Titmus Stereo Fly Test (Stereo Optical Company, Chicago, USA) as the patients were unable to perceive the stereoscopic in the Randot stereo test. The procedure for measuring ATR was the same as in study 1.

Aniseikonia tolerance range (ATR) was measured by the same examiner preoperatively, in dilated condition and postoperatively. The preoperatively and dilated ATR results were masked after examination until the postoperative measurement was performed.

The density of the cataract was based on the Lens Opacities Classification System (LOCS III) (Chylack et al. 1993). All patients underwent ocular coherence tomography to exclude macular pathology and vitreomacular traction.

Dilated ATR
After the preoperative measurements were performed, one drop of metaoxedrine x3 (Skanderborg Pharmacy,

Skanderborg, Denmark), one drop of mydriacyl 10 mg/ml × 3 (Novartis, Basel, Switzerland) and one drop of cyclopentolate 1% × 3 (Alcon Novartis, Forth West, Texas, USA) were instilled in both eyes every ten minutes until three doses of each drug have been administered. A cycloplegic subjective refraction was then performed to ensure a VA of 6/6 (0.00 logMAR) or better in both eyes, and then, ATR^{RANDOT} and ATR^{TNO} were re-measured to examine reproducibility.

Postoperative ophthalmic examinations
All study two patients were re-examined 6–10 weeks after the cataract surgery was performed on both eyes. The following measurements were collected: uncorrected distance VA (UDVA), CDVA with subjective refraction performed by an optometrist, autorefraction, CNVA with an ETDRS VA chart, and measurements of ATR^{RANDOT} and ATR^{TNO}.

Statistics
For validation of Aniseikonia Inspector, a linear regression model was used with slope values, to determine the extent to which the slope deviated from 1.

Results

Study 1

We included 21 patients in study 1. All patients had VA better than 6/7.5 (0.1 logMAR). For baseline values, see Table 1.

ATR
In total, five patients had an ATR^{TNO} below or equal to 1, seven patients had ATR^{TNO} between 5 and 10 and nine patients had an ATR^{TNO} above 10. We retested five of the patients and found 100% reproducibility.

Fig. 2A shows the distribution of ATR in the population, Fig. 2B shows an example of a patient with ATR^{TNO} equal to ATR > 10, and Fig. 2C shows an example of a patient with ATR^{TNO} equal to 1.

There was no difference between the ATR of the right or left eye or between the ATR of the dominant or the non-dominant eye (Paired t-test p-values 0.3 and 0.8).

Aniseikonia inspector
Results for validation of Aniseikonia Inspector are summarized in Table 2.

Table 1. Baseline values for study 1.

Baseline characteristics study 1 $N = 21$	
Age (y)	64 (SD ± 3.3)
Gender	12 females
Mean SEQ OD (D)	0.13 (SD ± 2.1)
Mean SEQ OS (D)	0.09 (SD ± 2.01)
Distance visual acuity logMAR/(Snellen decimal)	−0.08/(1.13) (SD ± 0.04/(0.09))
Near visual acuity logMAR/(Snellen decimal)	−0.02/(1.05) (SD ± 0.04/(0.09))
Median TNO stereopsis (arcsec)	60 (range: 30–120)
Mean aniseikonia angles 4 and 8 vertical direction (%)	−0.36 (SD ± 1.16)
Mean aniseikonia angles 4 and 8 horizontal direction (%)	0.34 (SD ± 2.08)

Arcsec = arc of second; SEQ = spherical equivalent.

Data are presented with a regression coefficient for field 4 and field 8 in both horizontal and vertical meridian. A slope of 1.0 signifies that each afocal size lens consistently produced a change in achieved aniseikonia exactly equal to the afocal size lens magnification. A p-value > 0.05 indicated that the regression coefficient did not differ from 1.00.

Aniseikonia Inspector version 3.5c underestimated aniseikonia in both meridians in field 8. The underestimation was below 10%. In field 4, there was less underestimation, and in the vertical meridian, a regression coefficient of 0.98 was found. None of the slopes differed significantly from 1.0. However, when plotted, there still seemed to be some variation in correlation (Fig. 3).

Study 2

We included 11 patients in study 2.

Baseline characteristics are shown in Table 3. The first two patients were tested with only TNO stereoacuity tests, because we had not received the Randot test yet. The ATR^{TNO} was below 1 for one patient and equal to 2 for another patient, whereas the ATR^{TNO} for the remaining nine patients was above 9. In the two patients with ATR^{TNO} < 2, the ATR^{RANDOT} was above 9. The remaining six patients all had ATR^{RANDOT} above 10.

After dilation, the ATR^{TNO} increased in one patient from 14 to 16 with no change in the stereoacuity threshold. Similarly, ATR^{RANDOT} increased from 16 to 18 in one patient, also with no change in the stereoacuity threshold. Postoperatively, the same patient had an ATR^{RANDOT} of 18 and an increase in ATR^{TNO} from 17 to 18, but, with a deterioration in the Randot stereoacuity threshold from 100 to 200 arcsec. The difference in measurements pre- and postoperatively as well as before and after dilation is shown in Fig. 4.

Discussion

The aim of this study was to examine whether a patient's tolerance to aniseikonia can be measured using afocal size lenses and stereoacuity cards. Furthermore, the aim was to describe the variance in tolerance towards aniseikonia with special regard to patients with low sensitivity.

In recent years, the frequency of refractive surgery and cataract surgery has increasingly lead to more patients with iatrogenic anisometropia (Achiron et al. 1997; Solborg Bjerrum, Mikkelsen & la Cour 2015; Kessel et al. 2016). Despite general agreement that a clinical threshold of 3 dioptres of anisometropia should be tolerable, many reports have indicated that patients with lower ranges of anisometropia still may experience symptoms associated with aniseikonia (Burian & Ogle 1943; Bannon & Textor 1948; Burian 1962; Katsumi et al. 1992; Kramer et al. 1999). Burian has reported that clinically significant aniseikonia depends on the patient's subjective complaints and can be as low as a 0.75% image difference between the eyes. Some patients can tolerate large amounts of aniseikonia without having subjective symptoms, whereas some patients are sensitive to minor size differences (Burian 1943; Burian, Walsh & Bannon 1946).

In monovision and mini-monovision where the focus point is deliberately different between the eyes, there is an
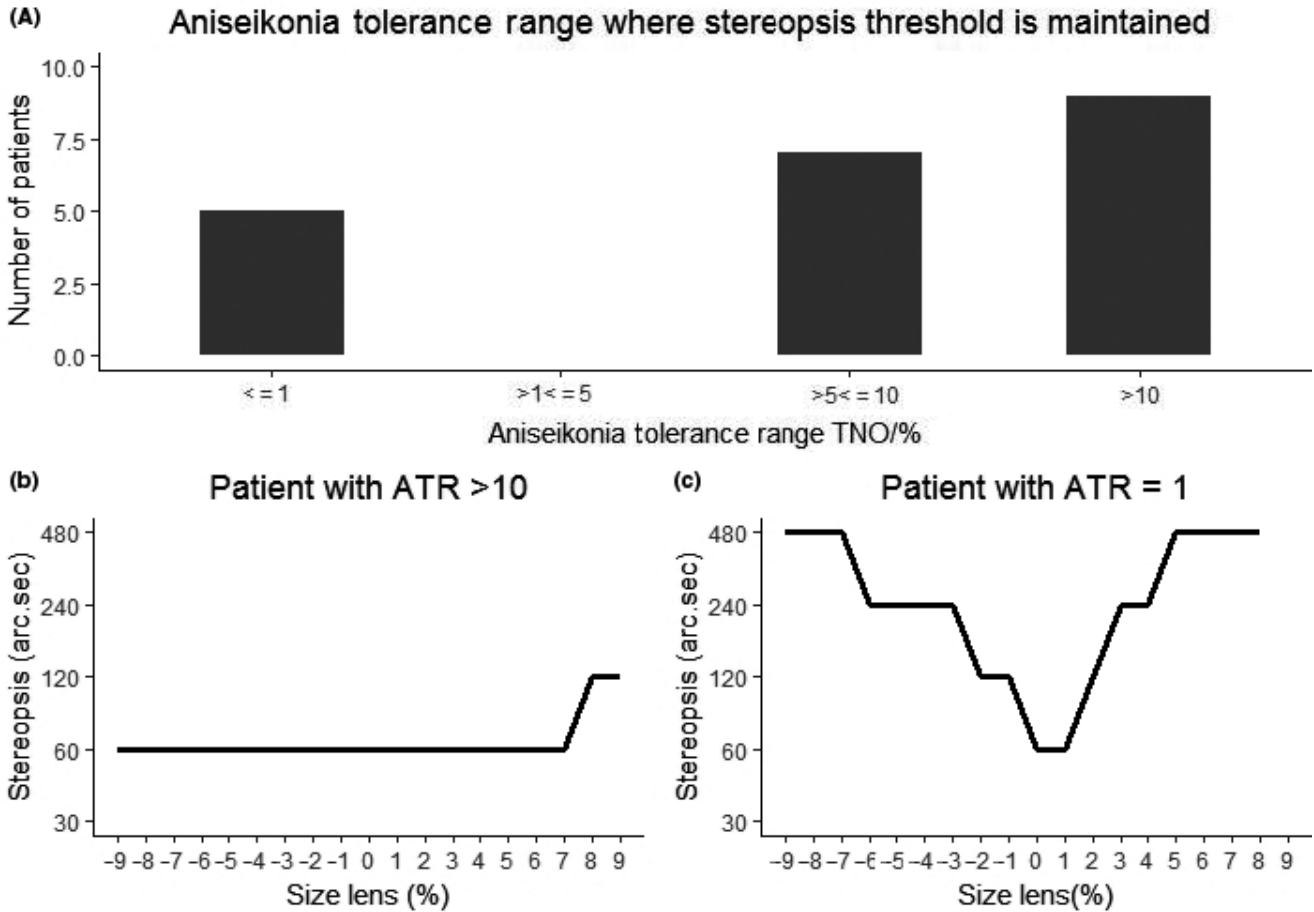
Fig. 2. A: Distribution of aniseikonia tolerance range in study 1. Aniseikonia tolerance range (ATR) is the amount of aniseikonia the patient can tolerate while maintaining optimal stereoacuity threshold. B: A patient with ATRTNO = 16. This patient had high ATR, and stereoacuity was impaired when a size lens of more than seven per cent was placed in front of the left eye. C: A patient with ATRTNO = 1. In this case, only 1% aniseikonia is tolerated. Positive values on the x-axis indicate size lenses placed in front of the right eye, and negative values indicate size lenses placed in front of the left eye. ATR, aniseikonia tolerance range

Table 2. T, Student's value, confidence interval: 2.5–97.5, p-value: whether the slope of the regression line for achieved aniseikonia versus induced aniseikonia differs significantly from 1.0.

Meridian	Field	Regression coefficient	Standard error	Confidence interval	Slope R^2	Intercept	T	p-value
Vertical	4	0.98	0.089	0.80-1.15	0.57	-0.13	10.98	0.84
Horizontal	4	0.94	0.11	0.73-1.15	0.48	1.23	8.77	0.57
Vertical	8	0.94	0.076	0.79-1.10	0.65	-0.12	12.44	0.49
Horizontal	8	0.91	0.09	0.72-1.09	0.50	0.74	9.714	0.31

expected small decrease in stereoacuity due to aniseikonia and anisometropic blur (Naeser, Hjortdal & Harris 2014), and it is possible that the anisometropic blur makes it more acceptable for the patients to fuse the images.

We used afocal size lenses to mimic the effects of IOL-induced anisometropia. Afocal size lenses magnify without using refractive power and should therefore be an acceptable surrogate for the retinal magnification of a refractive correction of IOL-induced

anisometropia without blurring the vision. A patient with clinically significant aniseikonia could experience symptoms due to impaired binocular vision such as headache, double vision and asthenopia. If a method can assess a patient's tolerance towards aniseikonia, it might be possible to estimate which patients can endure aniseikonia and, more importantly, which patients that cannot tolerate aniseikonia. Binocular vision can be assessed by measuring stereoacuity, and we

therefore measured the effects of artificial IOL-induced anisometropia on binocular vision as a surrogate for aniseikonic symptoms. The retinal disparity steps in TNO cards were large with a halving in the arcsec at each step (480, 240, 120, 60, 30 and 14 arcsec). Although disparity steps of the same magnitude are preferable when testing methodology, we chose this large disparity for multiple reasons. First, the commercially available stereoacuity tests are produced on this logarithmic
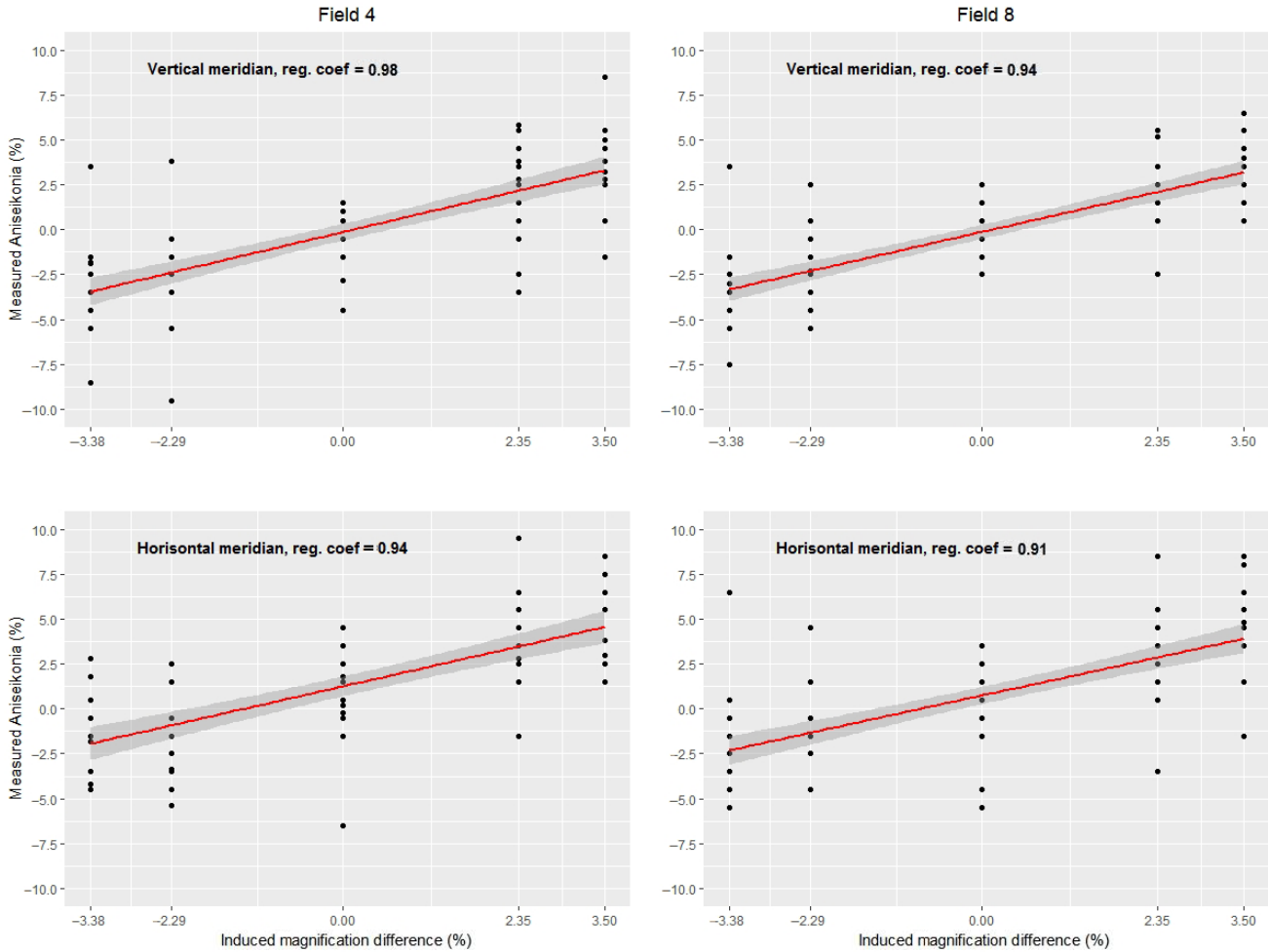
Fig. 3. Regression slopes for validation of Aniseikonia Inspector version 3.5c in field 4 and field 8 in both horizontal and vertical meridian. Induced aniseikonia and measured aniseikonia on x- and y-axes, respectively.

scale, and although testing in steps of 60 arcsec might have been possible by changing the viewing distance of the stereoacuity cards, doing so would have introduced another layer of uncertainty. Second, we observed patient tiredness with the current test, and adding additional testing would have been strenuous for the patients.

Based on the findings of a bimodal distribution of ATR in population, we hypothesize that ATR can be divided into two categories: high or low ATR. In a clinical setting, a surgeon would most likely be hesitant to intentionally induce more anisometropia than 3 dioptres due to the risk of clinical aniseikonia, 3 D anisometropia results in approximately 3%–5% optical aniseikonia (Ogle 1950). We therefore defined low ATR as ≤5 and high ATR as >5 and hypothesize that patients with low ATR are at risk of experiencing clinical aniseikonia due to IOL-induced anisometropia. However,

this remains to be confirmed in future studies.

Previous studies (Crone & Leuridan 1975; Isomura & Awaya 1980; Lovasik & Szymkiw 1985; Stewart & Whittle 1996) using the same methodology with size lenses and stereoacuity tests examine young persons with good stereoacuity, and they report mean values of loss of stereoacuity and describe the generalized relationship between induced aniseikonia and loss of stereoacuity. The focus in the present article is the variation in aniseikonia tolerance among the presbyopic population, especially the proportion of patients that have low tolerances towards aniseikonia. We found low ATR^{TNO} (<1) in 24% (5/21) of patients in study 1, while 76% (16/21) could tolerate optical aniseikonia >5%, which we assume reflects the general consensus that most patients can tolerate 3 dioptres of anisometropia (Lubkin, Linksz & Chamby 1969; Miyake, Awaya &

Miyake 1981; Tomaç & Birdal 2001). Our findings support the results of Isomura & Awaya (1980) in a similar study examining aniseikonia tolerance by using afocal size lenses and measuring stereopsis in a study population of 20 eye-healthy young phakic individuals with stereoacuity threshold of 30 arcsec or better, in which only the inter-variability in stereoacuity threshold was examined. Calculation of ATR in the study population revealed 12 (60%) patients with an ATR < 1, representing more than 50% of the patients. Lovasik & Szymkiw (1985) also examined aniseikonia tolerance towards stereoacuity in the dominant eye using afocal size lenses in 50 patients aged 20–32 years with a stereoacuity threshold of 40 arcsec. Their results demonstrated a curvilinear relationship between aniseikonia and loss of stereoacuity with large inter-variability in the tolerance towards aniseikonia with stereoacuity

Table 3. Baseline characteristics of study group 2.

Baseline characteristics preoperative study 2 N = 11 Randot N = 9	
Age (y)	70 (SD ± 7.9)
Gender	4 men/6 females
Cataract grade (LOCS)	I
Distance visual acuity logMAR/Snellen	0.04/ (0.93) (SD ± 0.05/0.1)
Subjective refraction SEQ OD (D)	0.099 (SD ± 1.29)
Subjective refraction SEQ OS (D)	0.39 (SD ± 1.27)
Near visual acuity (logMAR/Snellen)	0.0/1.0 (SD ± 0/1.0)
Median TNO and range (arcsec)	60 (60–120)
Median Randot and range (arcsec)	60 (40–100)
Mean aniseikonia vertical angles 4 and 8 (per cent)	0.54 (SD ± 1.28)
Mean aniseikonia horizontal angles 4 and 8 (per cent)	0.4 (SD ± 1.04)

AFTER DILATION N = 11 Randot N = 9	
Distance visual acuity logMAR/Snellen	0.04/0.93 (SD ± 0.05/0.1)
Near visual acuity ETDRS logMAR/Snellen	0.0/1.0 (SD ± 0/0)
Change in optimal TNO	0/11
Change in optimal Randot	0/9
Change in aniseikonia tolerance range TNO	1/11 (range 14–16)
Change in aniseikonia tolerance range Randot	1/9 (range 16–18)

POSTOPERATIVE N = 11 Randot N = 9	
Mean distance visual acuity logMAR/Snellen	−0.02/1.05 (SD ± 0.07/0.20)
Mean near visual acuity logMAR/Snellen	−0.03/1.07 (SD ± 0.04/0.12)
Change in stereoacuity threshold TNO	0/11
Change in stereoacuity threshold Randot	1/9 (100–200)
Change in aniseikonia tolerance range TNO	1/11 (17–18)
Change in aniseikonia tolerance range Randot	1/9 (16–18)

The first two patients were only examined with TNO stereoacuity test.
ETDRS = Early Treatment Diabetic Retinopathy Study, OD = oculus dexter, OS = oculus sinister, SEQ = spherical equivalent.

level of 40 arcsec associated with aniseikonia value between 0 and 16%. Unfortunately, their data did not demonstrate the proportion of patients with low sensitivity towards aniseikonia.

The current paper describes the inter-individual variance in aniseikonia tolerance in an elderly presbyopic population. The variance found in ATR might describe the individual tolerance towards aniseikonia that we experience in the cataract population. Therefore, ATR might be a future clinical parameter to screen patients individually for their sensitivity towards aniseikonia, before inducing surgical anisometropia. Our study population were older, and the stereoacuity threshold was higher than Lovasik et al. and Isomura et al. with 60 arcsec for 15 patients and 120 for the remaining six patients. The difference in age could explain the difference in stereoacuity threshold, because stereoacuity appears to decline with age (Haegerstrom-Portnoy, Schneck & Brabyn 1999). The higher values of stereoacuity in the present study could indicate that elderly patients might be less sensitive towards induced aniseikonia and thus explain the lower proportion of low ATR in the present study.

In the clinical setting, refractive surgeons are unaware of whether patients are sensitive to aniseikonia. Kramer et al. (1999) have found that 40% of patients with pseudophakic anisometropia present symptoms associated with aniseikonia. Rutstein et al. (2015) have examined stereopsis, aniseikonia and aniseikonic symptoms in patients awaiting bilateral cataract operation. Measurements were taken preoperatively, in between the operation of the first and second eyes, and postoperatively after both eyes had been operated on. The authors found no significant differences in symptoms between the preoperative and follow-up results in between surgeries in which anisometropia was most pronounced. Our results indicate that most patients have a large ATR; if Rutstein et al. had only one or two patients with low ATR, the group statistics would not be substantially affected.

If patients at risk of surgically induced clinically significant aniseikonia are assumed to have low aniseikonia tolerance, our method presents a possible measurement to screen patients preoperatively for a low ATR and thereby identify patients at risk of clinically significant aniseikonia due to IOL-induced anisometropia. For the method to be a potential preoperative screening method, we need to ensure that the endpoint is reproduceable and not affected by the surgical procedure in itself with induced isometropic refractive changes. In study 1, we retested five patients and found 100% reproducibility in ATR^{TNO}. In study 2, we retested the patients twice in both ATR^{TNO} and ATR^{RANDOT}; after dilation and postoperatively after surgery. We found that 10 ATR^{TNO} out of 11 and 8 ATR^{RANDOT} out of 9 showed 100% reproducibility of ATR after dilation and surgery, whereas one patient in each ATR group changed by a small amount, from 16 to 18, a result likely to be clinically insignificant. These findings indicate that ATR is a robust measure and is not affected by the surgical procedure. The patients included in this study were eye-healthy individuals with a visual acuity of 0.80 (logMAR 0.1) or better. For the method to be clinically useful, stereoacuity must be measurable in patients with a low VA. Donzis et al. (1983) have established that despite a visual acuity of 0.5 in both eyes, stereoacuity of 60 arcsec was possible. In addition, Levy and Glick have shown a linear relationship between VA and SA, demonstrating a stereopsis of 100 arcsec with Snellen VA at 0.3 (Levy & Glick 1974). These findings indicate that measuring ATR should be feasible for most of the cataract population.
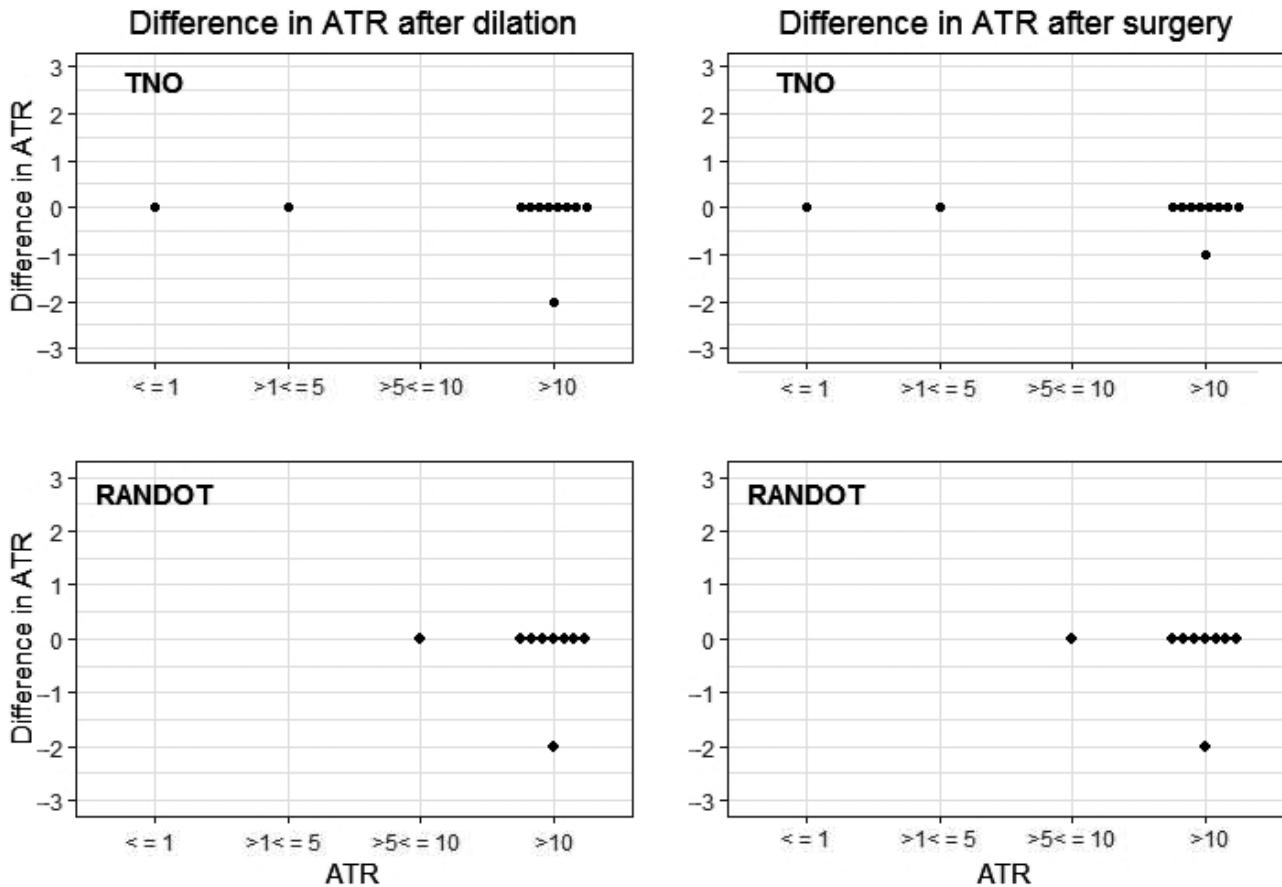
Fig. 4. Change in ATR between preoperative and postoperative and before and after dilation of both eyes. Patients were re-refracted after dilation to ensure maximum visual acuity. Negative values on y-axis indicate that ATR became bigger, and positive values indicate that ATR became smaller. ATR, aniseikonia tolerance range.

In study 2, we found a difference in stereoacuity threshold with Randot and TNO stereopsis tests. The patients had better stereoacuity with TNO than Randot, possibly because of the larger stimulus size of the TNO test than Randot (Pageau, de Guise & Saint-Amour 2015).

We found an underestimation of aniseikonia by using Aniseikonia Inspector. Our results were best in field 4 in the vertical meridian. Underestimation of the afocal size lens-induced aniseikonia has been confirmed by others and found to be primarily a result of free viewing time, full light during examination and decisional bias due to wear of red/green glasses (Rutstein, Corliss & Fullard 2006; Antona et al. 2007; García-Pérez & Peli 2015). We used the recommended short viewing time, dim lightning and a fixed head position to eliminate these biases but still found an underestimation. This result might have been due to decisional bias from the red/green glasses, which could not be avoided. However,

plasticity of the brain might also have affected the outcome of lens-induced aniseikonia, so that a person with high plasticity would produce smaller aniseikonia values than a person with low plasticity. The largest measured values of aniseikonia were in patients with low ATR; however, our sample size was too small to support further conclusions on the matter. In concordance with previous studies, we also found a larger underestimation in the horizontal meridian than the vertical meridian, albeit, to a lesser degree than previously reported. Another reason for the lesser underestimation might have been changes in stimulus in Aniseikonia Inspector version 3 used in our study with correction of fixation disparity and two rectangles instead of two haploscopic figures.

None of our regression slopes were significantly different from 1.00, thus indicating that the tests were able to measure afocal size lens-induced aniseikonia with a minor underestimation of 2%–9%. We observed no tendency to

any systematic error. Our results indicated that the current version of Aniseikonia Inspector is more accurate than previous versions (McCormack, Peli & Stone 1992; de Wit & De Wit 2003; Barra et al. 2005; Antona et al. 2007; Fullard, Rutstein & Corliss 2007; Children et al. 2014; García-Pérez & Peli 2015).

The study is limited by our examination of only patients with clear intraocular lenses with no prior eye disease and good VA. The method must still be tested in a true cataract population with clinically significant opacity. Furthermore, our patients wore the afocal size lenses for only the duration of the examination and were not given time to adapt to the aniseikonia. Aniseikonia tolerance range (ATR) might possibly have increased if the patients had been given longer time to adapt to the aniseikonia; therefore, our findings might not represent the real postoperative results. In addition, we tested stereoacuity as an outcome in ATR but not other binocular endpoints and we only tested in

one gaze and at one distance which could affect the results. In study 2, the same examiner rated the patients pre-operatively, in dilated condition and postoperatively. This procedure might have affected the results, because the examiner was not blinded towards previous findings. Despite most patients needed spectacle correction after dilatation, it seems unlikely to expect accommodation in this patient cohort, and therefore, the effect of accommodation on ATR requires further studies. Lastly, titmus test was used as supplement in two patients that could not perceive the randot test stereoscopic. The study is strengthened by its good reproducibility, as confirmed in both study 1 and study 2, regardless of whether the comparison was test–retest or pre- versus post-cataract surgery. Finally, determining the ATR is an inexpensive and easily feasible method that could be used in a clinical setting and, if validated in a cataract population, might serve as a tool to prevent surgical induced clinically significant aniseikonia.

Conclusion

We present a method to evaluate patient's tolerance for aniseikonia and thus tolerance to anisometropia. This method shows good reproducibility; however, further studies are needed to examine the clinical relevance of ATR in an anisometropic cataract population.

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