Validity and Repeatability of a New Test for Aniseikonia

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PURPOSE. The Aniseikonia Inspector 1.1 (AI) is a new software product to measure aniseikonia using red-green anaglyphs. The purpose of this study was to test whether the AI is a valid and reliable test.

METHODS. There were two groups of sample subjects: one at risk of aniseikonia, with anisometropia greater than or equal to 1.00 D (n = 29), and a control group (n = 45). The validity was studied by comparing the measured aniseikonia with the aniseikonia simulated with size lenses. The reliability was estimated by the Bland-Altman statistical method.

RESULTS. The results showed that the AI underestimated aniseikonia and that the underestimation was greater in the horizontal than in the vertical direction. The reliability was low, with biases that were clinically insignificant, but the 95% limits of agreement were around ±2%. The behavior of the test was similar in both groups of subjects.

CONCLUSIONS. The reliability of the AI is only moderate, and professionals are therefore warned to use the results of this test with caution. (Invest Ophthalmol Vis Sci. 2007;48:58-62) DOI:10.1167/iovs.05-0575

Aniseikonia is considered to be clinically significant when a patient’s visual system has difficulty combining two images of different size and/or shape in a single perceived image.1-4

The largest prevalence of this anomaly is observed in patients with anisometropia greater than 1.00 D, corrected with lenses. A very high percentage of anisometropias are axial (as are most anisomyopias) and to a lesser extent, they are refractive (usually related to hyperopia). In general, aniseikonia higher than 2% is considered to be mainly associated with a difference in the axial length of both eyes.5 A difference in the corneal power between the two eyes indicates that at least one part of the aniseikonia has a refractive origin. In addition to size differences between retinal images, other factors, such as differences in retinal photoreceptor density and cortical rescaling of the images may influence the size of the perceived image.6,7

Aniseikonia was initially studied in the 1940s and 1950s. Today, there is renewed interest in this visual anomaly because of the considerable increase in the number of patients who have aniseikonia.8 The large number of patients with symptoms attributable to aniseikonia7 make this condition a significant public health problem. The greatest prevalence occurs among patients with anisometropia greater than 1.00 D—between 5% and 10% of the population.9 Among those at risk of aniseikonia are people with anatomic differences between eyes, patients who have had refractive surgery (e.g., LASIK or photorefractive keratectomy [PRK]) and those with pseudophakic eyes. After refractive surgery or cataract surgery, there are frequently residual refractive differences between the eyes.6,10,11 In recent years, refractive surgery to correct myopia, hyperopia and astigmatism has become increasingly popular. Also, with the progressive aging of the population and constantly improving surgical methods, there are more operations for cataract, and most of the patients receive implants of intraocular lenses. Kramer et al.12 established that ~40% of patients with pseudophakic eyes present symptoms associated with aniseikonia.

The asthenopic symptoms associated with aniseikonia are not specific to this anomaly. Hence, we need an efficient, precise clinical instrument, to identify aniseikonia easily and prescribe appropriate treatment. The traditional estimation methods have low reliability from a clinical point of view and are not adequate for using in the treatment of aniseikonia (Schreiber P et al. IOVS 1994;35:ARVO Abstract 2543).13,14

There are two systems of measuring aniseikonia: stereoscopic techniques and direct-comparison methods. Stereoscopic eikonometers cannot be used in patients who lack binocular vision; direct-comparison eikonometers, however, provide measurements of aniseikonia in many of these cases. The best reference test for methods of evaluating aniseikonia is the Space Eikonometer (American Optical Company, New York, NY). However, this system for measuring aniseikonia is the most precise, has not been produced for several decades. Of the direct-comparison tests for measuring aniseikonia currently available, the New Aniseikonia Test (NAT) (Handaya Co., Tokyo, Japan) is one of the best known, but various studies have shown it to underestimate aniseikonia.15,16 The Aniseikonia Inspector 1.1 (AI) (Optical Diagnostics, Culemborg, The Netherlands) computer software has recently appeared on the market. It is based on the same principles as the NAT, but it is more complete, as it provides data for the calculation of the prescription. The only published study to assess the validity of this test included only four subjects and reports that the measurement of the aniseikonia is not significantly underestimated.17

To attempt to determine the diagnostic value of the AI, in this study the following specific objectives were set: (1) to estimate its validity through a comparison between the aniseikonia measured and the aniseikonia simulated through calibrated size lenses; (2) to determine its reliability; and (3) to study the correlation between subjective refraction and aniseikonia.

METHODS

Subjects

The study adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained after the nature of the study had been fully explained. The experiment was performed in 74 subjects recruited from students and teachers of the School of Optics at the Complutense University in Madrid. Those subjects who did not have fusion were excluded. The Randot Stereotest and TNO were used to ensure that all the subjects had some degree of stereopsis. Also, we

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confirmed that all the subjects were able to see simultaneously the red and green parts of the aniseikonia test.

The age range of the sample was 19 to 44 years. The range of ametropia was from −9.00 to +6.00 D for the sphere and up to −4.50 D of astigmatism. The sample was divided into two groups: one group of anisometropes (n = 29 with 1.00 D or more of anisometropia in one or more of the meridians of vectorial notation of spherical-cylindrical refraction (see more information at the end of methods section), and a control group (n = 45) with less than 1.00 D of anisometropia.

The range of anisometropia in the study population was 1.00 to 4.00 D. All the subjects in the control group had corrected visual acuity (VA) greater than or equal to 20/20, stereopsis greater than or equal to 30 minutes of arc, and no ocular disease. The group of anisometropes had a corrected VA greater than or equal to 20/25.

Test for Aniseikonia

The Aniseikonia Inspector 1.1 (Optical Diagnostics, Culemborg, The Netherlands) is a software program that includes a direct-comparison test that presents the stimuli on the computer screen. The dissociation is performed with anaglyphic filters. The test is composed of two semicircles of different sizes (one red and one green) one of which the subject can vary in size with the keyboard or mouse until the circles are perceived as having the same dimensions. It is measured in the vertical and horizontal directions and, in each direction, the measurement is performed two times: once with a starting value for aniseikonia of +25% and then with a starting value of −25%. The aniseikonia measurement for each batch is the mean of the two measurements.

Before the first aniseikonia measurements were recorded, the subjects were given time to familiarize themselves with the methodology of the test. Also, we took a test measurement to verify whether the subjects had understood the task and to verify that each measure was consistent when the starting value varied from +25% to −25%. Most of the subjects agreed that the test was easy to perform.

Preliminary Tests

First, a questionnaire was completed to record age, sex, and ocular history of each subject. Next, their optometric characteristics were established through refraction and binocular vision tests.

We measured the corneal radii and the objective refraction by means of an autorefractometer (SRW 5000; Shin Nippon, Tokyo, Japan). The subjective refraction was performed according to the usual methodology, with Snellen optotypes projected at 6 m and a manual phoropter. Different binocular vision tests were administered: accommodative facility and horizontal phoria with the technique of von Graefe, horizontal fusional vergence range and stereopsis (Randot and TNO).

Measurements of Aniseikonia

According to Bland and Altman, the best way to study the reliability of an instrument is to take various measurements in a series of subjects. For this reason, measurements of aniseikonia were taken on two separate occasions with an interval of at least 24 hours between them. At the start of the first visit, all the subjects were given a brief explanation of their role in the study and their informed consent was obtained. The data from the first batch of measurements were not reviewed until the second batch had been completed. The tests were administered in random order, and for all the measurements the subjects had their distance corrections inserted in the trial frame. The aniseikonia was measured separately in horizontal and vertical directions. In the control group that did not have significant aniseikonia, it was induced with afocal magnifying lenses (generously donated by Essilor-Espa{	extntilde}{\textntilde}a, Madrid, Spain). The distance between the eyes and the computer screen was 40 cm.

Trial Lens Magnifiers

The percentage of induced magnification was +3%, +1.5%, 0%, −1.5%, and −3%. To check the accuracy of the trial lens magnifiers, we measured all the parameters that determine the shape factor and the power factor of an ophthalmic lens. We verified, by means of a very good approximation, that the size lenses were correctly manufactured, that is, the power factor was zero, independent of the distant vertex, and the shape factor was equal to the magnification of the lens. These lenses were inserted in front of the right eye in the most external groove of the trial frame and were applied in random order. Thus, the subject could not see which lens had been used. To avoid vertical maladjustments (deviation) of the two semicircles, it is important that the trial frame be adjusted correctly and that the subject remain directly in front of the test when the measurements of aniseikonia are taken through the simulation lenses.

Vectorial Notation of Spherical-Cylindrical Refraction

During the data analysis, vectorial notation of spherical-cylindrical refraction was used, according to the criteria of Harris. This notation allows a direct comparison to be made of the subject’s refraction in different meridians. In particular, it allowed us to calculate the anisometropia separately for the horizontal and vertical meridians. Depending on the degree of anisometropia, the subjects were classified as the control group or the anisometropic group.

Data Analysis

Once the data had been collected for the whole sample, they were processed statistically. The data analysis was performed with a commercial statistical program (Analyze-it for Microsoft Excel; Analyze-it Ltd., Leeds, UK). To evaluate the test validity, we applied a linear regression analysis to the aniseikonia data and compared the slope with −1. A test reliability analysis was also performed using the Bland and Altman method. To evaluate the reliability, the numerical difference between the measurements obtained on two different occasions was calculated, and an analysis was performed of the distribution of the differences between the two visits (initial and final) extracting the bias and the 95% limits of agreement for this distribution. From the clinical point of view, the advantage of this method is that the reliability of the test is expressed in the same units of measurement as the test itself and allows the clinician to establish his or her own criteria as to whether a change is significant.

Sign Convention

To interpret the signs correctly, it is important to remember that the simulation lenses must always be inserted in front of the right eye. The +3% and +1.5% lenses increase the size of the image and the −3% and −1.5% lenses reduce it. Taking into account the sign convention that was adopted in the study, definitions were as follows: negative aniseikonia, image perceived by the right eye (RE) greater than that of the left eye (LE)—simulated with +3% and +1.5% lenses; positive aniseikonia, image perceived by the RE as smaller than that perceived by the LE—simulated with −3% and −1.5% lenses.

RESULTS

Validity

This part of the experiment was designed to determine whether the aniseikonia test studied estimates adequately the degree of aniseikonia simulated in normal subjects.

When aniseikonia was induced through afocal lenses of known magnification, the AI measured less aniseikonia than was expected. Figure 1 represents the mean values of aniseikonia measured relative to the induced magnification in the control group. The dotted line, with a slope −1.0 represents the location of the expected values in a normal subject (without aniseikonia). The continuous line represents the least-squares adjustment of the data, with the equation shown in the
lower left corner of each graph. The offset bars correspond to ±1 SD. It can be seen that the slope differs significantly from −1.0, which is interpreted as underestimated aniseikonia. The slope was −0.07 less in the vertical direction (P = 0.0002) and −0.31 less in the horizontal (P = 0.0001; that is, the underestimation is greater in the horizontal direction). The intersection with the y-axis does not differ significantly from 0. The intersection with the y-axis represents any aniseikonia inherent in the subjects (0% induced magnification) and, as this refers to the control group, it is natural to expect them not to display any significant inherent aniseikonia (>1%).

Reliability

The data differences are distributed approximately according to a normal distribution. The skewness and the kurtosis of the histograms show that they generally conform to normality. It is thought that the existing small deviations occur because the aniseikonia is not measured in a continuum but rather that there are only certain difference percentages that can be chosen. In contrast, when we observe the points distribution graphics of the difference between the initial and the final measurement, compared with the mean of both, there is no evidence of correlation between the values of the difference and their mean. For this reason, we consider the two conditions necessary to estimate the 95% limits of agreement for each case have been met.

Table 1 shows the reliability coefficient (range of the central interval within the 95% limits of agreement) and the mean difference or bias for the measurements with the AI. The data were categorized according to the subject group (control, anisometropes), and the direction of measurement (vertical, horizontal). Although the details are commented on in more detail later in the article, in this table it can be seen that there were no substantial differences in the reliability coefficients of the different situations.

There is no uniform tendency toward augmentation or diminution of the measured aniseikonia in the final evaluation (F) compared with the initial one (I). All the reliability coefficients are relatively high, so that we can say that the reliability is low. The 95% difference intervals in repeated measurements range from ±1.5% (control group, vertical 0%) to ±2.65% (anisometropic group, vertical). No significant differences were found between the control group and the anisometropic group.

Two-factor ANOVA with repeated measures for the factor direction was used to analyze a possible interaction in the measurement of reliability between the direction of aniseikonia (horizontal/vertical) and the group (control/anisometropic). The results did not show significant differences in the reliability between the horizontal direction and vertical direction (F(1,72) = 0.417, P = 0.520) or between the control group and the anisometropic group (F(1,72) = 0.977, P = 0.326). Finally, there was no interaction between both factors, direction and group (F(1,72) = 0.853, P = 0.359).

Correlation between Subjective Refraction and Aniseikonia

A study was performed to test the hypothesis that a greater degree of anisometropia corresponds to a greater degree of aniseikonia. For the total subject group (N = 74) the correlation study showed that there was a moderate positive correlation between these two parameters for the vertical direction, without simulation (0%) of aniseikonia (r = 0.69, P < 0.0001). However, for the horizontal direction, there was a notable discrepancy between both (r = 0.03, P = 0.79). If we consider only the anisometropic group, the result was similar (see Fig. 2) for the vertical (r = 0.72, P < 0.0001) and the horizontal (r = 0.15, P = 0.49) directions.

Comparison of Vertical and Horizontal Aniseikonia Measurements in the Control Group

This behavior led us to think that the precision of the test is different for the two directions. To study this hypothesis a comparison was made of the aniseikonia measurements obtained in the vertical and the horizontal direction in the control group. For this part of the experiment we decided to study only the control group data, as these were subjects in whom differences were not expected in the aniseikonia measured in

| TABLE 1. Mean Difference (Bias) and Reliability Coefficient (95% Interval) for the AI |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                | Control Group (n = 45)          | Anisometropic Group (n = 29)    |
|                                | Bias 95% interval P*           | Bias 95% interval P*            |
| Vertical                       | 0.01% (I > F) ±1.48% 0.53      | 0.19% (I > F) ±2.66% 0.47       |
| Horizontal                     | −0.11% (F > I) ±1.64% 0.40     | 0.18% (I > F) ±2.21% 0.40       |

* By t-test.
the horizontal and the vertical directions because they did not have clinically significant anisometropia (Table 2). The bias corresponds to the mean difference (horizontal − vertical). Those cases in which the aniseikonia measurement in the vertical direction was greater than in the horizontal are marked with an asterisk. The results demonstrate that in many of the percentages of induced aniseikonia there were statistically significant differences between the vertical and the horizontal directions, according to the *t*-test for paired samples.

In Table 2, it can be seen that there was a greater number of cases, including all those that were statistically significant, in which the vertical aniseikonia was greater than the horizontal. This result was coherent with the fact that the underestimation found in the measurement of the aniseikonia was greater in the horizontal direction than in the vertical, as we mentioned when discussing the validity of the test. This behavior may be linked to the greater precision in the measurements of aniseikonia in the vertical direction also found by other authors.\(^{16,17}\)

**DISCUSSION**

**Validity**

Because there is no good gold standard method available to compare with the validity of the Aniseikonia Inspector, the decision was made to simulate different levels of known aniseikonia with size lenses and compare the measured percentage of aniseikonia with the simulated percentage. Our validity results indicate that if the test behaves in the same way in patients as it did with the sample subjects, patients with a substantial real difference between the size of the images of both eyes (2%−6%; i.e., subjects with fusion but with asthenopic symptoms linked to aniseikonia) can be expected to display clinically insignificant aniseikonia with this test (<2%) due to the underestimation associated with it in the horizontal direction.

The work by Bradley et al. (\textit{IOVS} 1990;31:ARVO Abstract 493) on the chromatic magnification of ocular images indicates that the anaglyphs used in the measurements can only account for a small part of the underestimation of the aniseikonia (<0.25%). The study by McCormack et al.\(^{16}\) speculates that the main factor causing the underestimation is a sensorial fusion response that leads to a rescaling of the image. This argument was suggested by Awaya et al.\(^{22}\) in the early 1980s. However, if the surroundings are relatively weakly illuminated, as is recommended for measurement with the AI, the fusion response and rescaling should have less effect. Only if the surroundings are lit and clearly visible to both eyes, can binocular vision cues leading to the mental rescaling be given.

The only study with which we can compare our results for the AI is the one by De Wit.\(^{17}\) In this study, aniseikonia was simulated with size lenses in four subjects with normal vision, and the degree of magnification was compared with the aniseikonia measured. De Wit found that the average slope for the linear regression was −0.98 for the vertical direction and −0.89 for the horizontal. Thus, as in our study, the AI test measured less well in the horizontal direction; however, his results do not show the degree of underestimation we found. Although in the vertical direction there is quite good agreement in the average slope: −0.93 in versus −0.98; in the horizontal direction there is a notable discrepancy in the average slope: −0.69 versus −0.89 in our study and De Wit’s, respectively. This discrepancy may be explained by the small size of the sample, with only four subjects, compared with the 45 in our experiment.

One possible justification for the lower validity of the tests of aniseikonia in the horizontal direction compared with the vertical is the higher incidence of heterophorias and fixation disparity on the horizontal plane, which may generate instability of the images\(^{23}\) and make it difficult to compare the size of the semicircles. Although the AI includes the possibility of moving one semicircle with respect to the other to compensate for the effect of uncompensated phorias, the width of the displacement area permitted by the test (4 min arc) is clearly insufficient for many of the subjects. For this reason, we decided not to displace the two semicircles, but rather to compensate for it by giving prisms inserted in front of the left eye of all subjects who needed them.

**Reliability**

Of interest is whether the reliability of the test varies significantly between a control group and an anisometropic group, one of the groups with a high risk of aniseikonia. The results obtained demonstrate that there are no significant differences in the reliability of the test between both groups of subjects.

*Aniseikonia measured in the vertical direction greater than in the horizontal.*

**TABLE 2.** Comparison between the Measurements of Aniseikonia in Vertical and Horizontal Directions of the Control Group

<table>
<thead>
<tr>
<th>Difference (%)</th>
<th>Agreement 95% Limits</th>
<th><em>P</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>+3%</td>
<td>0.68%*</td>
<td>±1.81%</td>
</tr>
<tr>
<td>+1.5%</td>
<td>0.24%*</td>
<td>±1.52%</td>
</tr>
<tr>
<td>0%</td>
<td>−0.06%</td>
<td>±1.49%</td>
</tr>
<tr>
<td>−1.5%</td>
<td>−0.24%*</td>
<td>±1.66%</td>
</tr>
<tr>
<td>−3%</td>
<td>−0.89%*</td>
<td>±2.05%</td>
</tr>
</tbody>
</table>

N = 45. Mean difference (horizontal-vertical). Bold: statistically significant difference.
in the degree of aniseikonia measured. This conclusion is based on the fact that most subjects with aniseikonia-related symptoms show size differences of between 2% and 5%. Furthermore, only aniseikonia measurements with AI greater than 2% can be considered a reliable indicator of a visual problem (see mean reliability coefficient of ±2.00%, Table 1).

We compared our reliability estimation with the results of a study by Corliss et al. They analyzed average data from two trials obtained by the method of adjustment of the AI (one measure starts from ±25% and another from −25%), and found no significant bias (vertical: 1.9% and horizontal: −1.7%), but large concordance intervals (vertical: ±5.65% and horizontal: ±10.1%). De Wit, the designer of the AI, recommends using the average of the latter setting to reduce the variability in the data. In our study we followed this recommendation, and yet our 95% limits of agreement are still quite large (close to ±2.00%).

**Conclusions**

To sum up, we can say that an underestimation of aniseikonia occurred in the simulated cases (+1.5% and ±3%) and that this underestimation was greater in horizontal measurements than in vertical ones. That is to say, the validity of the vertical direction was greater than the horizontal. Similarly, it was found there were more cases in the control group where the aniseikonia measured in the vertical direction was greater than in the horizontal.

Although the biases between repeated clinical measurements were not statistically significant, the 95% limits of agreement were high. For this reason, it can be concluded that the reliability of the test is not very high, and only changes greater than ±2% fall outside the margin of error of the measurements at 95%. The test does not perform better in anisometropic subjects than in normal control subjects.

Although reliability is not the only criterion to be taken into account when judging a test, in general high reliability is considered necessary (although not sufficient alone) for a test to discriminate well. As a result, a test with only moderate reliability such as the one studied herein should be used with caution to measure aniseikonia.

The possibility of comparing our results with those of other studies is limited and points out to a need for further studies to confirm the conclusions reached in this one.

**References**