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# Comparison of perceptual eye positions among patients with different degrees of anisometropia

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**Abstract**

The aim of this study is to compare the perceptual eye positions (PEPs) among patients with different degrees of anisometropia.

A total of 157 patients were recruited into this retrospective study. A detailed ophthalmic examination was conducted on each patient. The degree of refractive errors in the presence of astigmatism was converted into the degree of spherical equivalent (SE). Patients were divided into 3 groups according to the interocular SE difference: severe anisometropia group with interocular SE difference ≥2.50D, mild anisometropia group with interocular SE difference ≥1.00D and <2.50D, and non-anisometropia group with interocular SE difference <1.00D. The vertical and horizontal PEP were measured by a computer-controlled perceptual examination evaluation system. The results obtained from the 3 groups were compared and analyzed.

A total of 157 patients were enrolled including 32 patients in the severe anisometropia group, 37 patients in the mild anisometropia group, and 88 patients in the non-anisometropia group. The quartiles of vertical PEP pixels were as follows: 7.50 (5.00, 16.75) in the severe anisometropia group, 5.00 (2.00, 7.50) in the mild anisometropia group, and 5.00 (3.00, 9.00) in the non-anisometropia group, respectively. The vertical PEP pixel was much higher in the severe anisometropia group than that in the other two groups ($P < .05$). The quartiles of horizontal PEP pixels were as follows: 27.50 (10.75, 67.50) in the severe anisometropia group, 17.00 (7.00, 54.50) in the mild anisometropia group, and 21.50 (11.00, 60.75) in the non-anisometropia group. There were no statistically significant differences among the 3 groups ($P > .05$).

There was an obvious deviation of vertical PEP in patients with anisometropia ≥2.50D, indicating that the instability of vertical PEP might be associated with the development of severe anisometropia.

**Abbreviations:** 3D = 3 dimension, FMNS = fusion maldevelopment nystagmus, MST = medial superior temporal, MT = medial temporal, PEP = perceptual eye position, SE = spherical equivalent.

**Keywords:** anisometropia, computer-controlled perceptual examination, perceptual eye position

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## 1. Introduction

Anisometropia, a relative difference in the refractive state of the eyes, is one of the most commonly seen refractive abnormalities. The incidence of anisometropia ranges from 3.79% to 21.8% in different regions.[1–10] In a number of studies, anisometropia has been defined as the bilateral difference of refractive error in spherical equivalent (SE) ≥1.00 diopter (D).[11–13] It is believed that when the interocular SE difference is ≥2.50D, the retinal image size difference of the eyes will exceed 5%, resulting in binocular fusion disability and aniseikonia. The association between increasing anisometropia and decreasing binocular function has been convincingly shown by artificially induced anisometropia in normal subjects.[14–22]

Perceptual eye position (PEP) is a new concept describing binocular alignment raised by Zhao et al in 2014.[23] It is one of the indicators used to evaluate fixation disparity and binocular function measured by a computer-controlled perceptual examination evaluation system. Normal fixational eye movements, such as microsaccades, drift, and tremor, do not preclude binocular fusion.[24] Patients with a fixation disparity may not experience diplopia or obvious strabismus, but they may present with binocular misalignment. People with normal apparent eye position may manifest a PEP abnormality.[25] Different from the traditional definition of eye position using the Hirschberg test, cover test, or synoptophore, PEP is measured under a dichoptic vision condition, and the PEP pixels are recorded by a computer so that binocular misalignment can be quantified precisely. There are several kinds of diseases that lead to binocular misalignment. By traditional tests, the misalignment can only be qualified, but not accurately quantified. The minimum unit of binocular misalignment checked by computer-controlled ocular misalignment software is 1 pixel, whereas the synoptophore is 1 prism, equaling 25 pixels. Based on a more precise quantification, the relationship of PEP and refraction correlated diseases can be detected. There have been some studies on the characteristics of PEP in young people. In children with normal visual acuity and eye position, the mean vertical PEP is 1 to 3 pixels and the mean horizontal PEP 4 to 8 pixels.[23] The deviation pixels of PEP in amblyopic children are much higher compared with normal children. The more severe the degree of amblyopia is, the more serious the abnormality becomes.[26]

However, whether PEP deviation is associated with severity of anisometropia has not yet been reported in the literature as far as we are aware. In the present study, PEP pixels were measured and compared among patients with severe anisometropia, mild anisometropia, and non-anisometropia to establish the relationship between PEP deviation and the development of anisometropia.

## 2. Patients and methods

### 2.1. Patients

This retrospective study included ametropic patients seeking treatment at the Ophthalmology Department of Guangdong General Hospital from June 1, 2014 to December 31, 2015. For all subjects, a detailed ophthalmic examination was conducted, including measurements of unaided and best-corrected visual acuity, a slit-lamp examination, a fundus examination, intraocular pressure, manifest and cycloplegic refractions, and ocular movement. All refraction procedures were performed with the same experienced optometrist. The degree of refractive errors in the presence of astigmatism was converted into the degree of SE. Patients with myopia, hyperopia, or a combination of both were all included. Patients were excluded if they had a history of obvious strabismus, amblyopia, nystagmus, severe trachoma, corneal disease, glaucoma, cataract, retinal or optic nerve disease, media opacities, ocular trauma, or mental retardation. Patients who underwent ocular surgeries or binocular vision therapies were also excluded. Children under 6 years were not enrolled in case they were unable to understand the procedure of the PEP measurement test.

In the present study, anisometropia was defined as a bilateral difference of a refractive error in SE ≥1.00D. The types of anisometropia were classified into the severe anisometropia group (interocular SE difference ≥2.50D), mild anisometropia group (interocular SE difference ≥1.00D and <2.50D)[27] and non-anisometropia group (interocular SE difference <1.00D).

Finally, 32 patients were enrolled in the severe anisometropia group, 37 in the mild anisometropia group, and 88 in the non-anisometropia group (see Table 1 for summary demographics). Written informed consent was obtained from all patients or their guardians before data collection commenced. All study protocols were approved by the Ethics Committee of Guangdong General Hospital and carried out in adherence to the Declaration of Helsinki with regard to ethical principles for research involving human subjects.

**Table 1**

**Summary demographics of patients in the study.**

| | Non-anisometropia | Mild anisometropia | Severe anisometropia | *P* value |
|---|---|---|---|---|
| Patients* | 88 | 37 | 32 | |
| Gender* (male:female) | 41:47 | 18:19 | 14:18 | .52† |
| Age‡ | 15.03±9.73 | 15.52±9.61 | 14.51±9.50 | .40§ |
| Mean SE Difference (D) | 0.31±0.28 | 1.48±0.40 | 5.04±2.92 | |

D=diopters, SE=spherical equivalent.
* Numbers of patients.
† From the $\chi^2$ test.
‡ Average years of age at first diagnosis.
§ From the One Way ANOVA.

### 2.2. Measurement of perceptual eye position

The devices used to measure PEP included: Windows XP system PC host, LG2342p polarized 3 dimension (3D) monitor with a resolution power of 1920×1080 and refresh frequency of 120 Hz, and 3D polarized glass. A visual and perceptual examination evaluation system invented by the National Engineering Research Center for Healthcare Devices was used. The stimulating template was generated by MATLAB.

All tests were conducted at a constant room luminance, and all patients wore their spectacle corrections and 3D polarized glasses for the clinical measurement. PEP was measured by the cross-into-circle test, which allowed the left eye to see a cross and the right eye to see a circle (Fig. 1). The midpoint of the monitor was held 80 cm away and at the same height as the patients' eyes, with the average light source of 80 cd/m$^2$ in white, attenuating to 50 cd/m$^2$ when wearing 3D polarized glasses, and 30 cd/m$^2$ in black, attenuating to 3 cd/m$^2$ when wearing 3D polarized glasses. The stimulating template was 51 × 29 cm in size and 38×18° in visual angle. The size of the circle was 0.4° × 0.4°, whereas the size of the cross was 0.33° × 0.33° (1° fixation test-object). Patients used a computer mouse to place within what they perceived to be the circle's center, and were then instructed to click the mouse. The system automatically recorded vertical and horizontal bias by the 360° test-object to observe any ocular misalignment. The minimum unit of ocular misalignment observed by this computer-controlled ocular misalignment system was 1 pixel, which equals 0.04 prism. To distinguish from conventional eye position, we defined this bias pixel as PEP.

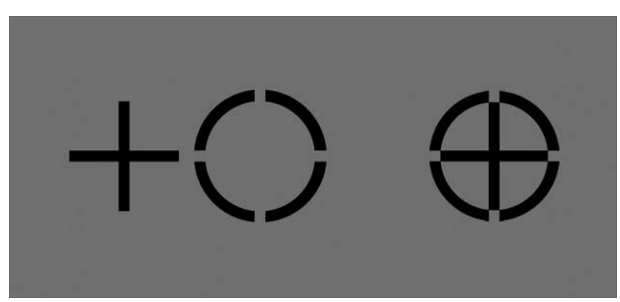

Figure 1. Example of a cross-into-circle test. By wearing 3D polarized glasses, patients should see a cross in their left eye and a circle in their right eye. They were asked to use a computer mouse to place the cross into their subjective view of the circle's center and then click the mouse. The system automatically recorded horizontal and vertical bias pixels. 3D = 3 dimension.

### 2.3. Statistical analysis

Statistical analysis was performed using SPSS Statistics for Windows (ver. 22.0. IBM Corp, Armonk, NY). Normally distributed data were presented as with mean ± standard deviation. Abnormally distributed data were presented as median (P25, P75). Comparison of gender among the 3 groups was made using the $\chi^2$ test with $P$ value <.05 being considered statistically significant difference. Comparison of age among the 3 groups was made using the One Way ANOVA with $P$ value <.05 being considered statistically significant difference. Comparison of PEP pixels among the 3 groups was made using the Kruskal-Wallis test, with $P$ value <.05 being considered statistically significant difference. Comparisons of PEP pixels between 2 independent groups were made using the Wilcoxon rank-sum test, with $P$ value <.0167 being considered statistically significant.

## 3. Results

### 3.1. Demographics of patients

A total of 157 patients from 6 to 52 years old in age were enrolled in the study and divided into 3 groups: 32 in the severe anisometropia group (including 12 myopes, 8 hyperopes, and 12 combinations of both), 37 in the mild anisometropia group (including 22 myopes, 8 hyperopes, and 7 combinations of both), and 88 in the non-anisometropia group (including 64 myopes, 22 hyperopes, and 2 combinations of both), respectively. The mean age was 14.51 ± 9.50 years old in the severe anisometropia group, 15.52 ± 9.61 years old in the mild anisometropia group, and 15.03 ± 9.73 years old in the non-anisometropia group. There were no statistically significant differences in gender ($P$=.52) and age ($P$=.40) of the patients among the 3 groups. The mean interocular SE differences of the 3 groups were as follows: 5.04 ± 2.92 in the severe anisometropia group, 1.48 ± 0.40 in the mild anisometropia group, and 0.31 ± 0.28 in the non-anisometropia group (Table 1).

### 3.2. Comparison of vertical PEP among the groups

The quartiles of vertical PEP pixels in the 3 groups were as follows: 7.50 (5.00, 16.75) in the severe anisometropia group, 5.00 (2.00, 7.50) in the mild anisometropia group, and 5.00 (3.00, 9.00) in the non-anisometropia group. There were significant differences among the 3 groups ($H$=13.324, $P$=.001). As shown in Figure 2, the vertical PEP pixel was much higher in the severe anisometropia group compared with the mild anisometropia group ($Z$=−3.308, $P$=.001) and the non-anisometropia group ($Z$=−3.211, $P$=.001). No statistically significant difference was found between the mild anisometropia group and the non-anisometropia group ($Z$=−0.853, $P$=.394).

### 3.3. Comparison of horizontal PEP among the groups

The quartiles of vertical PEP pixels in the 3 groups were as follows: 27.50 (10.75, 67.50) in the severe anisometropia group, 17.00 (7.00, 54.50) in the mild anisometropia group, and 21.50 (11.00, 60.75) in the non-anisometropia group. As shown in Figure 3, there were no significant differences among the 3 groups ($H$=2.134, $P$=.344).

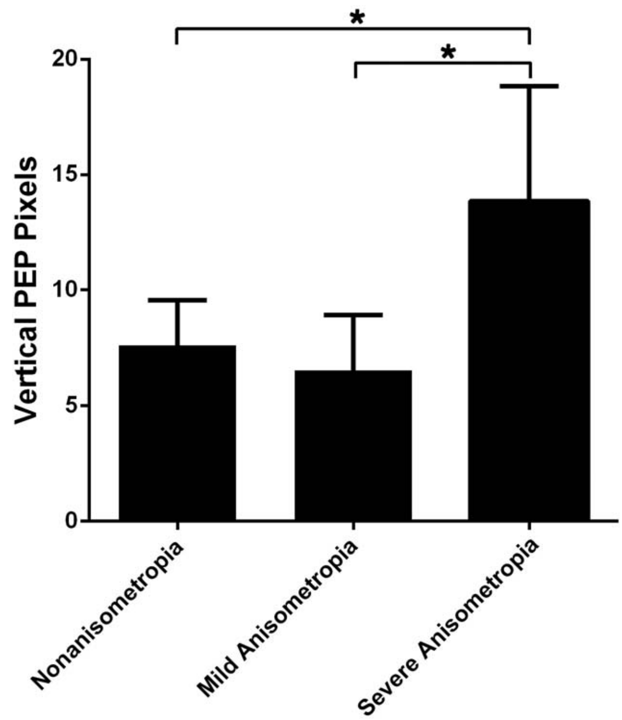


**Figure 2.** Bar graph showing the vertical PEP pixels in the 3 groups. Error bars showed the 95% confidence interval (CI). * = statistically significant difference, PEP = perceptual eye position.

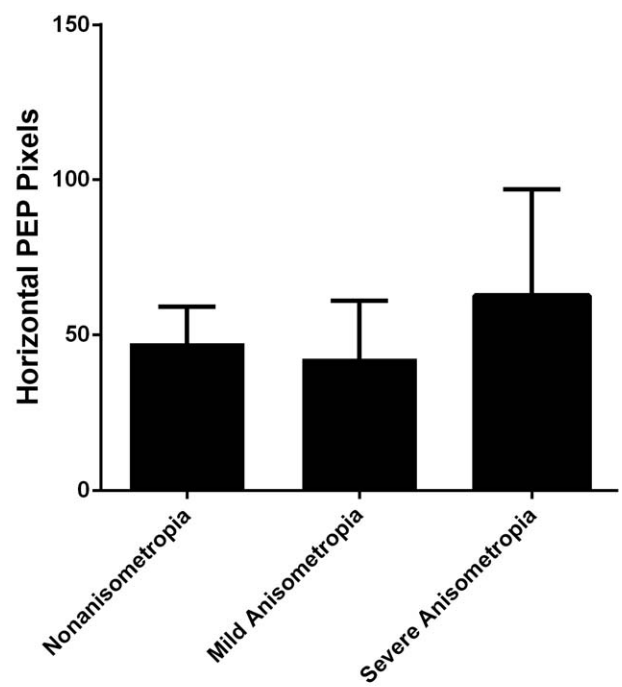


**Figure 3.** Bar graph showing the average horizontal PEP pixels in the 3 groups. There was no statistically significant difference among the 3 groups. Error bars showed the 95% CI. Note: PEP = perceptual eye position, CI = confidence interval.

## 4. Discussion

There have been many studies on binocular visual function in anisometropes. Most of the investigations focused on the stereoacuity, contrast sensitivity, accommodation and convergence, and interocular suppression of anisometropic patients.[14–22] In this retrospective study, the PEP among patients with different degrees of anisometropia were compared to elucidate whether PEP deviation was associated with the development of anisometropia. We found that the deviation of vertical PEP in patients with interocular SE difference ≥2.50D was much higher than that in patients with interocular SE difference <2.50D. However, no statistically significant differences were found in the deviation of horizontal PEP among the different degrees of anisometropic patients. The results indicate that the instability of vertical PEP may be associated with the development of severe anisometropia.

Perception, which is the result of sensation and thus different from it, represents not only the reflecting image, but also the integration of a variety of substances in the human brain after they act upon the sensory organs directly. Therefore, in a broad sense, perception is the result of all of the coordinated activities synthesized by human brain.[23] When an object is visualized for the first time, the brain not only perceives the size, shape, and color of the object using the eyes, but also the smell, sound, and tactility of the object using the other sensory organs. When the same object is visualized again, the brain will unconsciously integrate information from all of the senses without the need to smell, hear, or touch it. This is sensory perception.

The traditionally defined normal eye position, measured by the Hirschberg test and cover test, describes the apparent eye position. PEP, measured by a computer-controlled perceptual examination evaluation system under a dichoptic vision condition, shows the eye position when an object is seen and integrated by the brain. People with normal apparent eye position might manifest a PEP abnormality. Compared with the eye position measured by synoptophore, it shows a more precise result. As one of the indicators used to evaluate fixation disparity and binocular function, it can be measured by several types of sensory approaches. The basic method of measurement is under a dichoptic vision condition using a polarized monitor and glass. There have been different stimulating templates and tests of sensory approaches including Turville Infinity Balance test, pointer test, rectangle test, cross test, cross-into-circle test, and so on.[28] In the present study, the cross-into-circle test was chosen as it is easily understood and manipulated, and also showed the results clearly. A relatively smaller fixation test-object of 1° was chosen rather than 3° in this study because it could reveal subtler changes of ocular misalignment in nonamblyopic and nonstrabismic patients.

Zhao et al have listed standard data of normal PEP pixels in children with normal visual acuity and normal conventionally defined eye position. The mean vertical PEP was 1 to 3 pixels, whereas the mean horizontal PEP was 4 to 8 pixels.[23] However, in amblyopic children, the deviation of PEP pixels was much higher and was amblyopic severity dependent.[26] Based on this result, anisometropes with amblyopia were excluded from our study to maintain the homogeneity of PEP tests among the patients.

Birch et al investigated fixation instability and binocular misalignment in hyperopic anisometropic children using the microperimeter and cover test to measure eye movements.[29] Their findings supported the hypothesis that the binocular decorrelation caused by anisometropia could disrupt ocular motor development. This abnormality may result in fusion maldevelopment nystagmus (FMNS). The main feature of FMNS was a nasalward slow drift, with a temporalward fast-phase microsaccade. The data suggested that FMNS were seen in many of the anisometropic children, but only in small-amplitude and intermittent bursts.[29] These results were consistent with the model of FMNS proposed by Tychsen et al in which correlated visual experience was necessary for the development of stereopsis and balanced gaze.[30] In a primate model of strabismus, it was demonstrated that a decorrelated visual experience during visual development, such as strabismus, uniocular high ametropia in hyperopia or myopia (severe anisometropia), monocular congenital cataract, uniocular neonatal vitreous hemorrhage, and uniocular corneal clouding caused stereoacuity deficits and the fixation instability of FMNS. Besides FMNS, there were other findings, including interocular suppression, strabismus, and small vertical oscillations of the eyes, with the most necessary and sufficient factor being binocular decorrelation.[30] The mechanisms of all these findings may be the lack of connectivity and suppression of temporalward neurons of major visual areas V1, V2 (prestriate cortex), medial temporal (MT), and medial superior temporal (MST) of the cerebral cortex.[30,31]

In the present study, we found a high deviation of vertical PEP in severe anisometropes without amblyopia. The finding is consistent with the small vertical oscillations of primate models reported by Tychsen et al.[30] In our opinion, the results indicate that in nonamblyopes, the deviation of vertical PEP is associated with the severity of anisometropia. Based on previous studies, this deviation may be due to the binocular decorrelation or foveal suppression caused by severe anisometropia during visual development. It may also be a result of aniseikonia, a perceived retinal image size difference, caused by severe anisometropia.[32–34] However, there were no differences in the deviation of horizontal PEP among different degrees of anisometropic patients without amblyopia, which did not concur with the temporalward refoveating "flicks" of small eye movements reported by Birch et al[29] and Tychsen et al.[30] The reason for this inconsistency may be due to the different criteria of patient enrollment in our study. We chose anisometropic patients without amblyopia or strabismus, which partially ensured a relatively more stable fixation than amblyopic or strabismic patients. However, PEP is a distinctive concept that describes binocular misalignment after objective substances act on several sensory organs and then are integrated by the brain. The PEP measurement approach differs from the methods used by previous researchers to detect eye movements or apparent eye positions. The intermittent, small-amplitude bursts may not be detected by this approach. We also assumed there may be another hypothesis that vertical PEP and horizontal PEP are controlled by different pathways in visual areas. Any deficits in the pathway controlling vertical PEP may lead to the development of severe anisometropia. This hypothesis still needs further experiments to confirm its validity.

The limitation of the study is that this was a retrospective study with a sample size not large enough to classify different types of anisometropia (for example, myopia, hyperopia, or a combination of both). However, the study center was one of the biggest optometry centers in South China with a large population, and the PEP test could provide representative data for clinical anisometropic patients in general. This study was expected to yield an understanding of the relationship between PEP and anisometropia preliminary. Based on the result of this study, a further study of PEP characteristics in ametropic patients is in progress, with a more specific classification of ametropia and a larger sample size.

In conclusion, the deviation of vertical PEP in patients with interocular SE difference ≥2.50D was much higher than that in patients with interocular SE difference <2.50D, indicating that the instability of vertical PEP may be associated with the development of severe anisometropia.

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