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ORIGINAL PAPER

Prediction of pupil size under binocular open-view settings using the new CASIA2 device

Tsukasa Satou · Sayaka Kato · Akihito Igarashi · Misae Ito · Shuntaro Tsunehiro · Manabu Koshimizu · Takahiro Niida · Kimiya Shimizu

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Abstract
Purpose Pupillometry should be performed under conditions as close to natural viewing as possible. The present study aimed to determine whether pupil size in binocular open-view settings can be predicted based on pupil size measured using the CASIA2 device.
Methods The present study included 61 participants (25 men and 36 women; mean age, 49 ± 15 years; age range, 22–69 years) with no history of ophthalmic disease other than refractive errors and cataract. We measured pupil size using the new CASIA2 device and a binocular open-view digital pupillometer (FP-10000II, TMI Co., Ltd., Saitama). Intra-class and inter-class reliabilities were evaluated by measuring pupil times three times with each device (two independent examiners) in 21 of the 61 participants. Reproducibility was analyzed using intra-class and inter-class correlation coefficients (ICCs). Regression formulae for calculating FP10000II pupil size based on CASIA2 pupil size were developed via simple linear regression analyses.
Results Both devices exhibited high ICC values (> 0.80). The regression formulae for calculating the FP10000II pupil size for the distant and near views based on CASIA2 pupil size were $y = 0.5702x + 0.4611$ (determination coefficient, 0.67) and $y = 0.502x + 0.445$ (determination coefficient, 0.64), respectively.
Conclusions Pupil size under binocular open-view settings can be predicted based on simultaneous measurement of pupil size during evaluation of the anterior segment using the CASIA2 device. The calculated pupil size may represent a useful index for determining the most appropriate treatment strategy in candidates for cataract and refractive surgery.

Keywords CASIA2 · Binocular open-view digital pupillometer · Pupil size · Prediction

T. Satou (✉) · M. Ito · T. Niida
Department of Orthoptics and Visual Sciences, School of Health Sciences, International University of Health and Welfare, 2600-1, Kitakanemaru, Ohtawara, Tochigi 324-8501, Japan
e-mail: tsukasa@iuhw.ac.jp

T. Satou · S. Kato · A. Igarashi · M. Ito · S. Tsunehiro · M. Koshimizu · K. Shimizu
Eye Center, Sanno Hospital, Tokyo, Japan

T. Satou · A. Igarashi · M. Ito · S. Tsunehiro · M. Koshimizu · T. Niida · K. Shimizu
International University of Health and Welfare, Tochigi, Japan

Introduction

An adequate understanding of pupil size is important for ensuring improvements in the quality of vision following cataract and refractive surgery. In a previous study involving a laboratory model of pseudophakic monovision, binocular visual acuity for near vision in

the non-dominant eye was maintained over 0.8 by using an entrance pupil size of 2.5 mm and refractive error of − 1.50 D [1]. Furthermore, clinical studies have revealed that near visual acuity of 0.8 can be achieved in patients with pupil diameters < 2.5 mm using a target refraction of − 1.00 to − 1.50 D (slight myopia) for the non-dominant eye [2]. Pupil size has also been associated with decreases in patient satisfaction following multifocal intraocular lens surgery for pseudophakic presbyopia [3, 4], while treatment with brimonidine tartrate has been shown to reduce halo and pupil size in patients with night vision symptoms following laser in situ keratomileusis (LASIK) surgery [5, 6]. Therefore, pupil size should be evaluated prior to surgery to ensure that the patient can provide informed consent based on the predicted quality of vision following surgery.

There are several simple methods for the assessment of pupil size, such as the Colvard pupillometer [7] or Haab scale [8], although these methods are associated with low accuracy due to the subjective nature of measurements and scale of 1 mm. To obtain an accurate measurement of pupil size, routine examinations should include assessment during head fixation using dedicated instruments, although multiple tests prior to cataract or refractive surgery may increase the overall test burden on patients.

However, several recent studies have indicated that anterior segment optical coherence tomography (AS-OCT) is useful for clinical evaluation of the anterior segment prior to cataract and refractive surgery [9–11]. The CASIA2 device—a recently developed AS-OCT device with a swept-source laser wavelength of 1310 nm (Tomey, Nagoya, Japan)—has demonstrated improved measurement accuracy and functionality relative to traditional, commercially available instruments [12]. The CASIA2 device allows for simultaneous measurement of pupil size during examination of the anterior segment. However, the pupil size obtained using the CASIA2 is distinct from that measured under routine conditions in that patients must gaze into the instrument through a monocular lens. Therefore, the present study aimed to determine whether pupil size under binocular open-view examination can be predicted based on pupil size measured using the CASIA2 device.

Materials and methods

Participants

The present cross-sectional study included 61 participants (25 men and 36 women; mean age, 49 ± 15 years; age range, 22–69 years). The number of participants in each age-group was as follows: 20–29 years old (n = 11), 30–39 years old (n = 10), 40–49 years old (n = 9), 50–59 years old (n = 9), and 60–69 years old (n = 22).

The procedures used in the present study were approved by the Institutional Review Board of Sanno Hospital (approval number, 17-S-6) and conformed to the tenets outlined in the Declaration of Helsinki. Written informed consent was obtained from each of the volunteers following an explanation of the purpose, risks, potential discomfort, and steps associated with the study.

Measurement of pupil size

We measured pupil size using the CASIA2 device and a binocular open-view digital pupillometer (FP-10000II, TMI Co., Ltd., Saitama) in a room with constant illuminance (300 lx). During measurement, participants gazed at a fixation target inside the CASIA2 device through a monocular lens and on distant (5 m) and near (33 cm) fixation targets near under binocular open-view in the FP-10000II. The luminance of the target was 2.7 cd/m^2 for the CASIA2 device and 20.0 cd/m^2 for the FP-10000II device. For CASIA2 assessments, the anterior segment was measured once the pupil had been stabilized on the monitor. For FP-10000II assessments, the average pupil size was measured over 5 s. While both instruments measure the size of the entrance pupil, the entrance pupil size is automatically converted to the actual pupil size by the FP10000II software. Refractive errors were uncorrected for both measurements.

Reproducibility

We investigated the reproducibility of pupil size measurements obtained using the CASIA2 and FP-10000II devices. Pupil size was measured three times using each instrument by two independent examiners for a total of 21 participants (mean age, 32 years; age range, 22–48 years) among the study population of 61

individuals. Intra-class and inter-class reliabilities were then calculated.

Statistical analysis

The reproducibility of pupil measurements was examined using intra-class and inter-class correlation coefficients (ICCs). Pupil measurements obtained using the two instruments were compared via using one-way analyses of variance with Bonferroni post hoc testing. (CASIA2 vs. FP10000II with distant vision; CASIA2 vs. FP10000II with near vision). Ratios of pupil sizes obtained using the two instruments were calculated (FP-10000II/CASIA2), along with the mean ± standard deviation (95% prediction intervals). In addition, the correlations between the pupil size ratio (FP-10000II/CASIA2) and participant age, refraction, and pupil size were determined using Pearson's product moment correlation coefficients. Simple linear regression analyses were used to obtain regression formulae for calculating the FP10000II pupil size based on the CASIA2 pupil size. The level of statistical significance was set at $P < .05$.

Results

The ICC values for each instrument are shown in Table 1. High ICC (> 0.80) was observed for both instruments. The mean pupil size obtained using the CASIA2 device was 4.4 ± 1.0 mm, which was significantly higher than that obtained using the FP-10000II for distant vision (3.0 ± 0.7 mm) and near vision (2.7 ± 0.6 mm) ($P < .05$; Fig. 1). The mean ± standard deviation (95% prediction intervals) of the pupil size ratio (FP-10000II/CASIA2) was 0.681 ± 0.091 (0.503–0.858) for distant vision and 0.610 ± 0.094 (0.425–0.795) for near vision. Although no significant correlation was observed between the pupil size ratio and age or refraction ($P > .05$), the pupil size ratio was significantly correlated with CASIA2 pupil size [$P < .05$; $r = -0.27$ (distant FP10000II view) and − 0.31 (near FP10000II view); Fig. 2]. The regression formulae for calculating the FP10000II pupil size for the distant and near views based on CASIA2 pupil size were $y = 0.5702x + 0.4611$ (determination coefficient, 0.67) and $y = 0.502x + 0.445$ (determination coefficient, 0.64), respectively.

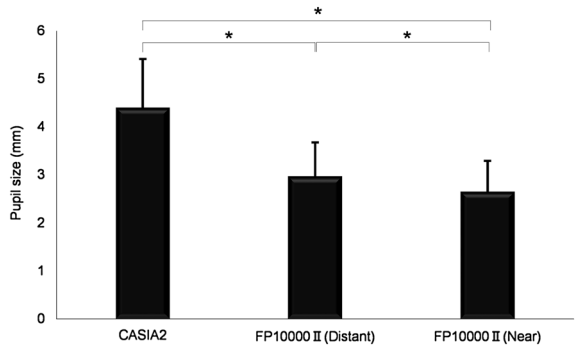

Fig. 1 Comparison of pupil sizes obtained using each instrument according to measurement condition. Pupil sizes differed significantly based on the device used and condition of measurement. Values are presented in the bar graph as the mean ± standard deviation. *$P < .0001$

Discussion

In the present study, we evaluated pupil size using both the CASIA2 and FP10000II devices and calculated regression formulae for the prediction of FP10000II pupil size based on CASIA2 measurements. Differences in pupil size obtained using these instruments may have depended in part on the luminance of the target [13]. Pupil sizes obtained using the FP10000II device were smaller than those obtained using the CASIA2 device because the luminance of CASIA2 target was greater than that of the FP10000II target. The entrance pupil size (113% of

Table 1 Results of intra- and inter-class correlation coefficients in each measurement of pupil size

	Intra-class correlation coefficient	Inter-class correlation coefficient
CASIA2	0.92	0.95
FP10000II with distant vision	0.94	0.81
FP10000II with near vision	0.97	0.98

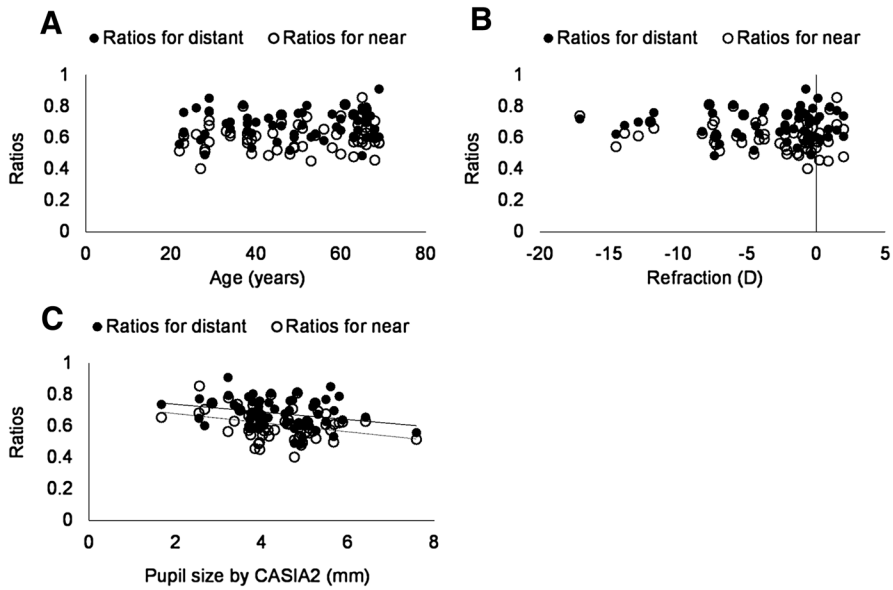

Fig. 2 Correlations between pupil size ratios (FP-10000II/CASIA2) and age, refraction, and pupil size. **a** Correlation between pupil size ratios and age. **b** Correlation between pupil size ratios and refraction. **c** Correlation between pupil size ratios and pupil size by CASIA2. No significant correlation was observed between the pupil size ratio and age or refraction. $P < .05$: correlation coefficient between pupil size ratio (FP10000II distant view) and CASIA2 pupil size, − 0.27. $P < .01$: correlation coefficient between pupil size ratio (FP10000II near view) and CASIA2 pupil size, − 0.31

actual pupil size) measured using the FP10000II was automatically converted to the actual pupil size based on measurements of the corneal radius, anterior chamber depth, and refractive index of the aqueous humor by software located within the instrument. In accordance with our findings, previous studies have reported that pupil size measured under binocular view is smaller than that measured in monocular settings [14, 15]. Given that daily activities generally involve bright environments in binocular open-view settings, pupillometry should be performed under conditions as close to natural viewing as possible [16]. In the present study, high ICC (> 0.80) values were observed for both instruments. In addition, pupil size obtained using the FP10000II device was smaller than that obtained using the CASIA2 device, even after adjusting for the effect of difference between entrance and actual pupil size, suggesting that these measurements accurately reflect pupil size under natural conditions (Fig. 3).

Our findings further indicated that the pupil size ratio (FP-10000II/CASIA2) was significantly correlated with the pupil size measured using the CASIA2 device. As the determination coefficients for the regression formulae were approximately 0.65 each,

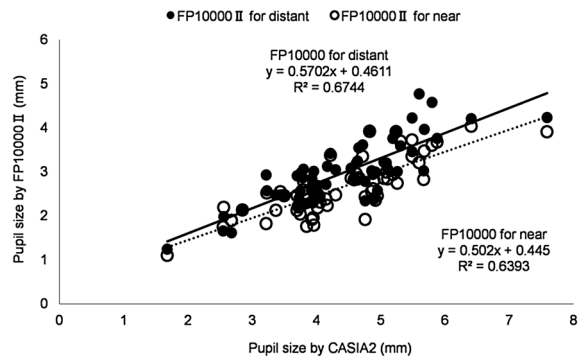

Fig. 3 Simple linear regression analysis between CASIA2 and FP10000II pupil size. CASIA2 pupil size was regarded as the explanatory variable (i.e., *x*-axis), while FP10000II pupil size was regarded as the criterion variable (i.e., *y*-axis). The regression formulae for calculating the FP10000II pupil size for the distant and near views based on CASIA2 pupil size were $y = 0.5702x + 0.4611$ (determination coefficient, 0.67) and $y = 0.502x + 0.445$ (determination coefficient, 0.64), respectively

these findings indicate that CASIA2 measurements may be able to predict pupil size within a certain range under binocular open-view settings. Thus, our findings suggest that pupil size should be calculated from the regression formula rather than from the pupil size

ratio. Such calculation may decrease the overall test burden on patients prior to cataract or refractive surgery.

Despite our findings, the present study possesses some limitations of note. First, we did not assess pupil size following cataract and refractive surgery. Previous reports have suggested that pupil size decreases slightly following cataract surgery [17, 18], yet rarely changes following refractive surgery involving implantable collamer lenses (ICL) [19, 20]. As these studies did not measure pupil size with an open-view pupillometer, we would have been unable to compare findings between the present and previous studies. However, our findings indicate that pupil size may decrease after cataract surgery, based on the regression formulae obtained in the present study. Thus, these formulae may be useful in prediction pupil size following ICL surgery. Second, pupil size was assessed under constant illuminance only (300 lx), indicating that regression formulae must be specific to each clinic due to differences in measurement conditions. Nonetheless, our findings indicate that these regression formulae will exhibit high determination coefficients and be useful in clinical settings. In conclusion, the results of the present study demonstrate that pupil size under binocular open-view settings can be predicted based on simultaneous measurement of pupil size during evaluation of the anterior segment using the CASIA2 device. The calculated pupil size may represent a useful index for determining the most appropriate treatment strategy in candidates for cataract and refractive surgery.

Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements) or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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