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LABORATORY INVESTIGATION

Corneal displacement during tonometry with a noncontact tonometer

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Abstract

Purpose To measure the extent of corneal displacement during the early phase of tonometry using a noncontact tonometer and to determine the factors that affect the extent of the displacement.

Methods The cornea was photographed in profile by use of a high-speed camera during tonometry with a noncontact tonometer. The frame rate of the camera was 5,000 frames/s. The extent of the displacement of the central corneal area at 13.2 ms after application of the air puff was measured in 115 healthy volunteers. The factors that affected the extent of the corneal displacement were determined by stepwise multiple linear regression analysis.

Results The subjects' age, sex, intraocular pressure (IOP), central corneal thickness, anterior chamber depth, and axial length were selected by the stepwise method. The results of the multiple linear regression analysis showed that subjects with low IOP, of older age, and of male sex had significantly greater displacement of the central cornea.

Conclusions High-speed photography can be used to evaluate the degree of corneal displacement during tonometry with a noncontact tonometer. The amount of corneal displacement is affected by the individual's IOP, age, and sex.

Keywords Noncontact tonometer · High-speed camera · Corneal displacement · Ocular bioproperty

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Introduction

Because tonometry is used to assess the effectiveness of glaucoma treatments, accurate intraocular pressure (IOP) measurements are crucial for the successful management of glaucoma [1]. Regardless of whether the tonometer is an indentation or an applanation type, the IOP is measured by deforming the eye by applying force to the outside of the globe. The tonometric reading is affected by the biophysical properties of the ocular shell: when the cornea is thick or the corneal curvature steep, the IOP readings will be higher than the true IOP [2–5]. It is also well known that IOP readings are low after refractive surgery [6]. Differences in the ocular rigidity of the eye globe can also decrease the accuracy of the IOP values.

Ocular biomechanics are becoming increasingly important to ophthalmologists, especially to those in the glaucoma and corneal fields. Several studies have measured the biomechanical properties of the eye [7, 8]. Pallikaris et al. [8] studied 79 eyes in situ during cataract surgery. They measured the IOP continuously with a pressure transducer while injecting balanced salt solution into the anterior chamber. Because the IOP and the injected volume had a simple linear relationship, they defined the slope of the line as the coefficient of rigidity. However, this invasive method cannot be used in the clinic. Two other studies measured Young's modulus of the cornea and quantified age-related biomechanical changes of the human cornea using eye-bank eyes [9, 10]. They reported that Young's modulus of the cornea increased with age.

Kempf et al. [11, 12] developed a noninvasive method using a high-speed camera to observe corneal displacement during tonometry with a noncontact tonometer. Using the methods developed by Kempf et al., we photographed corneal displacement during tonometry with a noncontact tonometer. We measured the magnitude of the corneal displacement at a designated time after an air puff had been applied to the eye.

The aim of this study was to determine the effects of age, sex, intraocular pressure (IOP), central corneal thickness (CCT), corneal curvature, axial length, and anterior chamber depth on the extent of the corneal displacement. Our findings indicate that corneal displacement can be used as a new biophysical parameter for assessing the bioproperties of the eye.

Methods

This study was approved by the institutional review board of Hiroshima University, and the procedures conformed to the tenets of the Declaration of Helsinki. Informed consent for the examination was obtained from all subjects. The subjects comprised 115 healthy volunteers (61 men and 54 women); their left eyes were examined. Tables 1 and 2 show the subjects' demographics. Figures 1 and 2 show their age and IOP distributions. Subjects with a history of ocular surgery or of any type of eye disease other than mild cataracts or refractive errors were excluded. This study was conducted between January 2005 and March 2007.

Table 1 Subjects' background (*N* = 115)

	Mean ± SD	Range
Age (years)	41.8 ± 21.9	20.0–86.0
Intraocular pressure (mmHg)	14.4 ± 2.4	9.0–20.0
Central corneal thickness (μm)	535.6 ± 31.6	459.0–629.0
Corneal curvature radius (mm)	7.76 ± 0.27	7.15–8.55
Axial length (mm)	24.81 ± 1.70	21.36–29.11
Anterior chamber depth (mm)	3.49 ± 0.46	2.06–4.62

Before beginning the experiments, the visual acuity for each patient was measured, and slit-lamp biomicroscopy and ophthalmoscopy were carried out. The CCT was measured with a specular microscope (SP-2000p; Topcon Corporation, Tokyo, Japan). The corneal curvature, anterior chamber depth, and axial length of the eye were measured with an IOLMaster (Carl Zeiss, Oberkochen, Germany).

The IOP was measured with a noncontact (air puff) tonometer (CT-80A; Topcon Corporation). Before beginning this study, we confirmed that our noncontact tonometer applied an air puff to each subject's cornea with the same pressure distribution [12]. The average peak air puff pressure from five continuous measurements was 11323.7 ± 869.5 Pa.

During tonometry, the cornea was photographed in profile with a high-speed camera arranged perpendicular to the geometrical axis of the eye (Fig. 3). Fifteen minutes after photographing the cornea, we measured the IOP with a Goldmann tonometer three times, and the average of these IOPs was taken as the standard IOP.

A high-speed camera allows images to be captured more frequently within 1 s than does a normal camera (30 frames/s). A high-speed camera (Phantom V7.1; Vision Research, Wayne, NJ, USA) with a field of 512 × 1,024 pixels was used to photograph the corneal profile at 5000 frames/s (1 frame/0.2 ms). The cornea was illuminated by two infrared light sources to assure high optical quality images at this high frame rate. The high-speed camera shutter was synchronized to the noncontact tonometer switch, and the photographic system was designed to allow the camera to photograph the cornea from the onset of the air jet for 40 ms.

Table 2 Subjects' sex and age distribution (*N* = 115)

	N	Ratio (%)	IOP (mmHg)	CCT (μm)	Corneal curvature radius (mm)	Axial length (mm)	Anterior chamber depth (mm)
Sex							
Male	61	−53.00	14.5 ± 2.5	539.5 ± 34.4	7.86 ± 0.25	25.3 ± 1.59	3.55 ± 0.43
Female	54	−47.00	14.2 ± 2.3	531.2 ± 27.8	7.65 ± 0.26	24.3 ± 1.69	3.41 ± 0.43
P value			0.735	0.337	<0.001	0.004	0.046
Age group							
Younger (<50 years)	66	−57.40	14.5 ± 2.3	530.2 ± 34.2	7.86 ± 0.26	25.7 ± 1.31	3.69 ± 0.34
Older (>50 years)	49	−42.60	14.2 ± 2.5	539.5 ± 29.3	7.62 ± 0.26	23.6 ± 1.46	3.20 ± 0.45
P value			0.459	0.174	<0.001	<0.001	<0.001

IOP intraocular pressure, *CCT* central corneal thickness

To examine the corneal surface in detail, the photographed images were processed to obtain a binary format of the image that depended on the threshold value. From these edge data, the corneal surface was fitted to circles of different radii by the least squares method. This made it possible for us to find the center coordinate of the circle in the image and the radius of curvature of the corneal surface. The coordinate of the top of the corneal edge was defined as the intersection of the corneal edge with the line along the x axis from the center coordinate of the cornea. The amount of corneal displacement from the initial position was computed from the edge of the cornea frame by frame (Fig. 4) [11, 12].

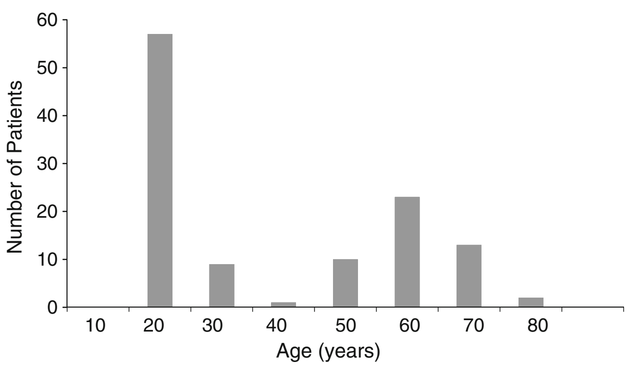


Fig. 1 Subjects' age distribution

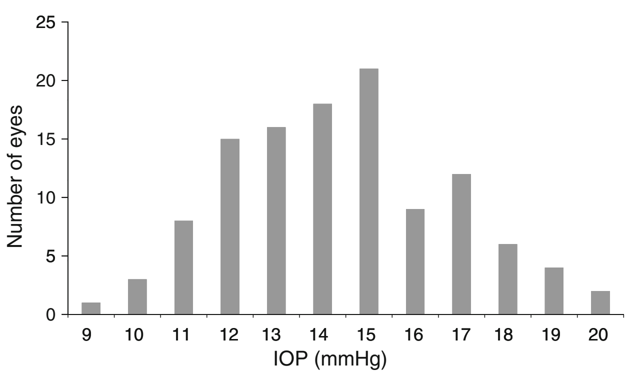


Fig. 2 Subjects' intraocular pressure (IOP) distribution

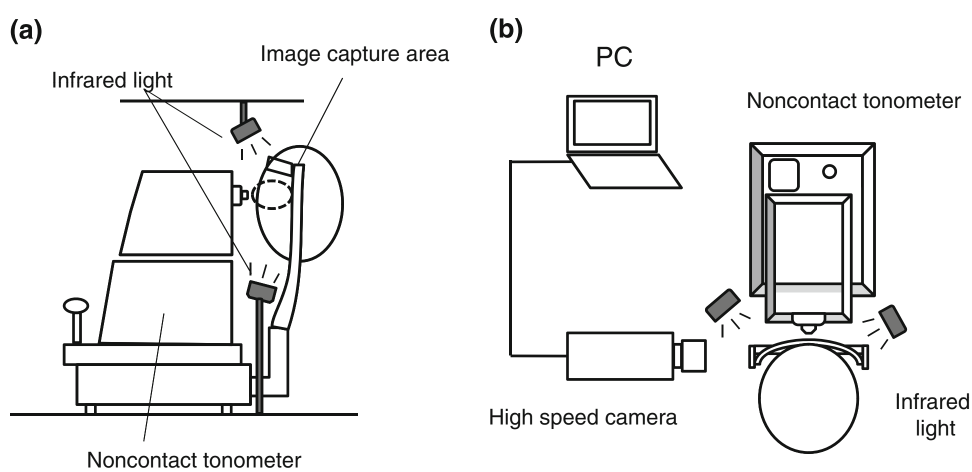
After the cornea was displaced to produce a flat surface, its center had a concave shape. However, our system could not observe whether the cornea was indented owing to the camera's location perpendicular to the cornea. In our subjects, the earliest time to observe a flat surface was at 13.2 ms after the beginning of the measurements. This indicated that the deformation of the cornea into a concave shape did not occur before 13.2 ms. We therefore measured the displacement of the corneal apex in the image at 13.2 ms after the onset of the air puff to avoid quantifying the degree of corneal displacement during the "inversion" phase of the corneal deformation. The average of five values was used for the statistical analyses.

We studied a second group of 12 eyes from 12 subjects (3 men and 9 women) with a mean age of 31.5 ± 6.4 years (range 26–48 years) who all agreed to undergo multiple examinations to test the repeatability of the results. They were recruited separately from the main examination group. The IOPs were measured twice within 90 min. Each session consisted of five consecutive measurements.

Statistical analyses

To determine the relationships among the amount of corneal displacement and other factors, owing to the skewed distribution of the displacements, the corneal displacement was log-transformed. Relationships among the amount of corneal displacement and age, IOP, CCT, corneal curvature radius, axial length, and anterior chamber depth were evaluated by Pearson correlation coefficients. Next, the subjects were divided by age into two groups: those aged 50 years and younger (66 eyes, 23.9 ± 4.6 years) and those aged older than 50 years (45 eyes, 70.0 ± 7.8 years)

Fig. 3 Experimental system. The lines of the camera and tonometer were placed at right angles. The camera shutter and tonometer switch were also synchronized



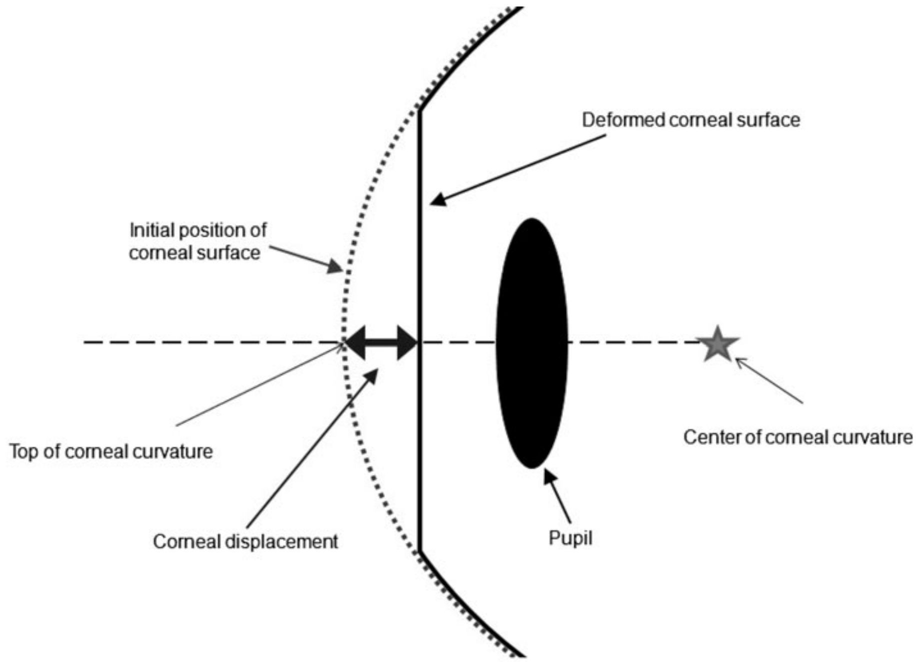


Fig. 4 Corneal displacement was considered to be the distance between the initial corneal position and the displaced corneal surface on the line over the surface of the cornea at 13.2 ms after application of the air puff

because the distribution of the subject age showed peaks in the 20s and 60s. The amounts of corneal displacement between the age groups and male or female sex were compared by the Mann-Whitney test. The relationships among the amount of corneal displacement and age, sex, IOP, CCT, axial length, corneal curvature, and anterior chamber depth were analyzed by stepwise multiple linear regression analysis. The data were analyzed with the JMP software program (version 8.0; SAS Institute, Cary, NC, USA). Probability values of less than 0.05 were considered statistically significant.

Results

Scatterplots of the degree of corneal displacement as a function of age, IOP, CCT, anterior chamber depth, axial length, and corneal curvature radius analyzed by Pearson correlation coefficients are shown in Fig. 5. The amounts of corneal displacement as compared between the age groups and male or female sex were compared using the Mann-Whitney test because these data were not continuous valuables. Among these variables, age ($P < 0.001$), IOP ($P < 0.001$), CCT ($P = 0.007$), axial length ($P = 0.005$), and the radius of curvature of the cornea ($P = 0.014$) were found to be significantly correlated with the amount of corneal displacement. The corneal displacement was greater in older than in younger subjects ($P < 0.001$). On the other hand, the corneal displacement in the male subjects was not significantly different from that in the female subjects ($P = 0.172$).

The subjects' age, sex, IOP, CCT, anterior chamber depth, and axial length were selected by the stepwise method. The results of multiple linear regression analysis for these selected variables are shown in Table 3. The coefficient of determination, R^2, was 0.49, and the goodness of fit to the model was significant ($P < 0.001$). Among these factors, multiple linear regression analysis showed that age ($P < 0.001$), sex ($P = 0.021$), and IOP ($P < 0.001$) were significantly associated with the amount of corneal displacement. More specifically, a lower IOP was significantly associated with a greater displacement of the cornea, i.e., a 1-mmHg increase in the IOP was associated with a mean decrease of 0.07 μm in the corneal displacement ($P < 0.001$). In addition, both the age group ($P < 0.001$) and sex ($P = 0.0212$) of the subjects were significantly correlated with the amount of central corneal displacement. The average amount of corneal displacement in the older group was 0.38 μm higher than that in the younger group. The average amount of corneal displacement in female subjects was 0.15 μm less than that in male subjects.

The first set of measurements was significantly correlated with the second set ($P = 0.0065$). The Pearson correlation coefficient (R^2) of the first measurement with the second measurement was 0.518. The interclass correlation coefficient obtained from the test-retest examinations was 0.54. The coefficient of variation of the measurements was 7.4 %.

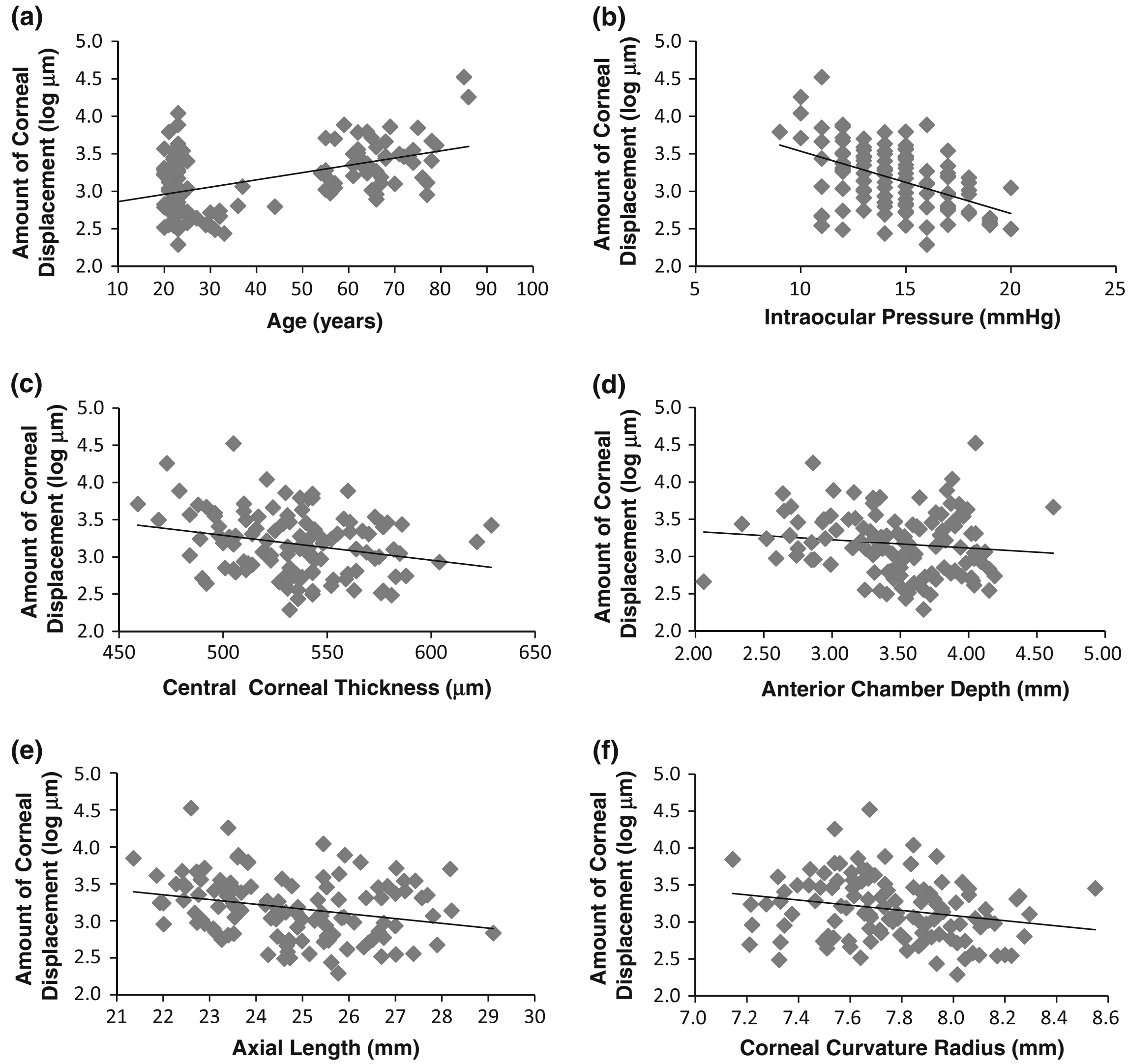


Fig. 5 Scatterplots with a regression line between the amounts of log-converted corneal displacement and **a** age ($r = 0.5053$, $P < 0.001$); **b** intraocular pressure ($r = -0.4662$, $P < 0.001$); **c** central corneal thickness ($r = -0.2505$, $P = 0.007$); **d** anterior chamber depth ($r = -0.1223$, $P = 0.1929$); **e** axial length ($r = -0.2611$, $P = 0.005$); and **f** corneal radius of the curvature ($r = -0.2283$, $P = 0.0141$)

Table 3 Results of stepwise multiple linear regression analysis in which the log-scaled amount of corneal displacement was the outcome variable

Variable	Estimator	(95 % CI)	*P* value
Sex (baseline = female)	0.1460	(0.0223, 0.2698)	0.0212
Age Group (baseline = younger)	0.3864	(0.2324, 0.5404)	<0.0001
IOP	−0.0740	(−0.0989, −0.0491)	<0.0001
CCT	−0.0015	(−0.0034, 0.0004)	0.1241
ACD	0.1494	(−0.0200, 0.3187)	0.0832
AL	−0.0349	(−0.0847, 0.0149)	0.1681
Intercept	5.1312	(3.5487, 6.7136)	<0.0001

Six variables were selected from the seven variables by the stepwise method: $R^2 = 0.49$, $P < 0.001$

Log (amount of corneal displacement) = 5.1312 + 0.1460 × Sex + 0.3864 × Age group − 0.0740 × IOP − 0.0015 × CCT + 0.1494 × ACD − 0.0349 × AL

IOP intraocular pressure, *CCT* central corneal thickness, *ACD* anterior chamber depth, *AL* axial length

Discussion

To evaluate the biophysical properties of the cornea noninvasively, we measured the degree of displacement of the central cornea after applying an air puff generated by a noncontact tonometer. To do this, we photographed the cornea with a camera capable of a frame rate of 5000 frames/s. The central cornea starts to move abruptly when the applied puff exceeds a critical level [13]. This is why we could not use the corneal displacement divided by the applied force (μm/N) as an indicator of the corneal bioproperty and therefore elected to use the amount of corneal displacement at a designated time as an indicator of ocular bioproperty in living human eyes.

We analyzed the data from the center of the cornea in the early phase by stepwise multiple regression analysis in 115 subjects. Our results showed that the IOP, age, and sex of the subjects were significantly correlated with central corneal displacement (Table 3). Based on previous studies [4, 5], our expectation was that the IOP would be significantly correlated with the extent of the corneal displacement; that is, higher IOPs were expected to be associated with lower corneal displacements. Thus, the cornea becomes more difficult to deform by use of an external force as the internal force of the eye increases. This is the basic concept by which the applanation tonometer works.

We had assumed that younger subjects would have more pliable tissues than older subjects and that this would be manifested by larger displacements in younger than in older subjects. Contrary to our expectation, the younger subjects had less corneal displacement than did the older subjects. Pallikaris et al. [8] reported that the coefficient of rigidity increases with age. They evaluated the degree of corneal extension by adding force from the inside of the eye by slowly injecting balanced salt solution into the anterior chamber. In contrast, in the present study, we evaluated the amount of corneal displacement by adding force to the cornea from the outside. We hypothesize that the corneas of older individuals have a high resistance to stretching but are weakly resistant to bending forces. The difference in the corneal deformation in younger and older subjects was probably caused by changes in the corneal biophysical properties associated with increasing age [13, 14]. The age-related changes in the composition of the cornea are also likely responsible for some of the effects of aging on the biophysical properties of the cornea.

The multiple regression analysis showed that corneal displacement in female subjects was significantly lower than that in male subjects. Differences in the biophysical properties of the cornea in men and women have been reported. For example, it has been demonstrated that women have a steeper corneal curvature than men [15] and that the progression of corneal astigmatism with increasing age is different between men and women [16]. The female subjects tended to have a steeper cornea than did the male subjects (Table 2), which is in line with the findings of a previous report [15]. In addition, the corneal thickness in women changes during pregnancy [17]. Corneal homeostasis is controlled by various hormones, and it is known that receptors exist in the corneal stroma for androgens, estrogens, and progesterone [18]. These differences between the sexes are therefore considered to be caused by the influence of the sex hormones.

The ocular response analyzer (ORA) is a new noncontact tonometer that can measure the IOP and the corneal biomechanical responses to the indentation caused by an air puff [19, 20]. The differences in the applanation pressures between the rising and falling phases to the air puff provide two measures of the corneal biomechanical properties: the corneal hysteresis and the corneal response factor [21]. This system is also good for obtaining information about the corneal biomechanical parameters using noninvasive methods. Thus far, the relationship between the amount of corneal displacement obtained by our method and the biomechanical parameters of the ORA is unknown.

We were concerned that relatively large variations in the measurements would be obtained by the noncontact tonometer. Therefore, we followed the recommendation of taking several readings and using the average as the IOP [21]. This is why measurements of the extent of the corneal displacement were performed five times, and we used the averaged data. The coefficient of variation obtained from five consecutive measurements was 7.4 %. The observed small coefficient of variation means that consecutive single sessions of five measurements provide us with stable data. The Pearson correlation coefficient (R^2) of the first measurement with the second measurement was 0.518 ($P = 0.0065$). Although a significant correlation was observed between the first and second measurements, the ICC reproducibility during the test and retest measurement was 0.54. The moderate level of ICC showed that the difference between the average data obtained from the first and second sessions was not small. The difference in the alignment at the first and second sessions might have influenced the magnitude of the average data and the level of ICC. We made very certain to have the same alignment at all the measurements. The small difference in the alignment on the measurements may have had some effect on our findings. In this study, we were able to quantitatively confirm the results reported by Kempf et al. [11, 12] that there is a difference in corneal deformation between older and younger subjects. We therefore believe that our data are sufficiently reliable for analysis of the extent of corneal deformation.

Another limitation of our method is that it does not allow analysis of the corneal movement when the top of the cornea has a concave shape. We therefore focused on the early phase of corneal displacement after the air puff generated by the noncontact tonometer was applied. Kempf et al. [11, 12] pointed out that the characteristic effect of aging on corneal movement appears more during the late recovery phase, i.e, the return to the initial position and shape of the cornea from the compressed shape. A detailed analysis of corneal movement during the late phase of tonometry will be necessary to fully understand the factors that affect corneal displacement and IOP readings.

In conclusion, we examined corneal movement with a high-speed camera during tonometry using a noncontact tonometer. We measured the extent of the corneal displacement in the early phase of the displacement, and the subjects' IOP, age, and sex were determined to be factors that were significantly associated with the amount of corneal displacement. Our method can contribute to a better understanding of corneal movement during tonometry, and the amount of corneal displacement at a designated time may be used as an indicator of the biophysical properties of the eye.

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