Contact Based Stiffness Sensing of Human Eye

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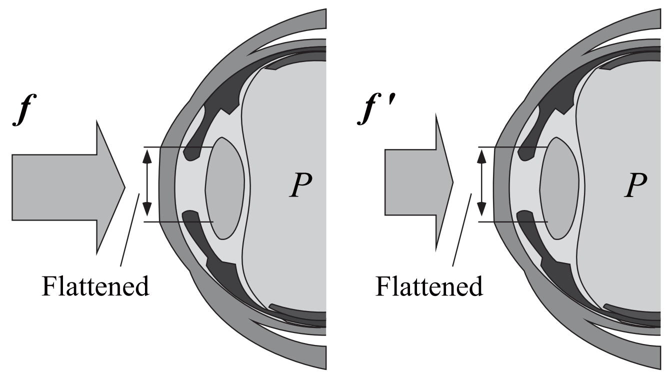
***Zusammenfassung*—Goldmann applanation tonometry is commonly used for measuring IOP (IntraOcular Pressure) to diagnose glaucoma. However, the measured IOP by conventional applanation tonometry is valid only under the assumption that all subjects have the same structural eye stiffness. This paper challenges in vivo measurement of eye stiffness with a non-invasive approach and investigates individual differences of eye stiffness. Eye stiffness is defined by the applied force and displacement of the cornea. The displacement is detected based on captured images by a high resolution camera. The experimental results show that the measured stiffness nicely matches the analytical result that is derived from a simple spherical deformation model with an internal pressure. However, some subjects have different eye stiffness even with the same IOP. IOP with abnormal stiffness may be over/underestimated by conventional applanation tonometry. The proposed eye stiffness measurement can help detect the misestimated eye and it contributes to the early detection of glaucoma.**

***Index Terms*—Stiffness Sensing, Human Eye, Contact Method, Glaucoma**



(a) Normal eye (b) Abnormal eye

Abbildung 1. Influence of the difference in structural eye stiffness under the same internal pressure (P). In this case, the abnormal eye is deformed easier than the normal eye ($f > f'$) and thus, the IOP with abnormal stiffness may be underestimated.

I. Introduction

EXTRAORDINARILY increased internal eye pressure damage the eye's nerve system. The subsequent partial death of the eye's nerve system causes gradual loss of the patient's eyesight. In the worst case, the patients completely lose their eyesight. This disease is called glaucoma. Today, there is no essential medical treatment for recovering the lost part of the nerve system. An effective treatment to avoid further progress of glaucoma is to decrease internal eye pressure using either an eye drop or a medical operation. In addition to the observation of the abnormality of eyesight, the measurement of internal eye pressure (IOP: IntraOcular Pressure) is important in judging whether the eye suffers from glaucoma or not.

Accurately measuring the IOP without penetrating the eyeball with a pressure needle is difficult. A less accurate, but also less invasive method estimates the IOP by observing the deformation of the cornea when external force is applied. In applanation tonometry[1], IOP is measured by static-based sensing where a medical doctor presses a rigid probe onto an anesthetized eye until the flattened area becomes a circle with a diameter of 3.06[mm]. However, conventional applanation tonometry is valid only under the assumption that all subjects have the same structural eye stiffness.

Let us consider the two eyes shown in Fig. 1, where the eyes in (a) and (b) have normal and abnormal structural stiffness, respectively. The deformed area in (b) becomes flat with less external force than that in (a), even if these eyes have the same internal eye pressure. This figure indicates that the applanation tonometers currently used always provides the wrong IOP values for patients with abnormal stiffness. Detecting such abnormality is useful in finding the eyes with misestimated IOP and will contribute to a more precise diagnosis of glaucoma.

A simple method to detect abnormal deformation requires capturing the deformation of the cornea by a camera. Kaneko et al. [2], [3] have captured corneal deformation when an air puff is applied to an eye, and they have measured eye stiffness based on a force-displacement relationship. The authors defined eye stiffness on the assumption that the influence on the deformation coming from viscosity and inertia is sufficiently small in comparison with the stiffness. However, deformation by the air puff is always delayed with respect to the force. This delay indicates that this eye stiffness includes the influence of the viscosity and inertia of the eye.

The aim of this paper is to measure the static force-displacement relationship and evaluate individual differences

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in eye stiffness. First, a simple spherical eye model is introduced to deriving analytical eye stiffness when a static force is applied to an eye. Next, a deformation measurement system for living human eyes composed of an applanation tonometer and a high-resolution camera is presented. The measurement system can simultaneously measure force and displacement when a rigid probe is pressed onto the eye. Static-eye stiffness is defined based on the measured force-displacement relationship. The experimental results show that the measured eye stiffness nicely matches the analytical result. However, some subjects have different eye stiffness even with the same IOP. IOP with abnormal stiffness may be over/underestimated by current applanation tonometry. The proposed eye stiffness measurement can help detecting misestimated eyes.

II. Related Works

Because applanation tonometry is based on the assumption that all subjects have the same structural eye stiffness, individual differences in corneal characteristics cause errors in IOP measurements [4], [5], [6]. It is well known that the corneal thickness influences the IOP measurements [7], [8], [9]. The same applies to the elasticity of the cornea, which was measured in vitro [10], [11]. Consequently, several papers propose statistical IOP correction methods that consider the corneal characteristics [12], [13].

Few works investigate living human eyes, but ocular rigidity might be index for distinguishing eyes with abnormal corneal characteristics. Silver et al. have measured the pressure-volume relationship for living human eyes [14]. Pallikaris et al. [14], [15] have also measured the pressure-volume relationship and they have determined an ocular rigidity coefficient. However, when measuring the pressure-volume relationship, it is necessary to penetrate an eyeball with a needle and inject liquid into the eye. An easier and a less invasive method measures the force-displacement relationship and proposed eye stiffness [2], [3].

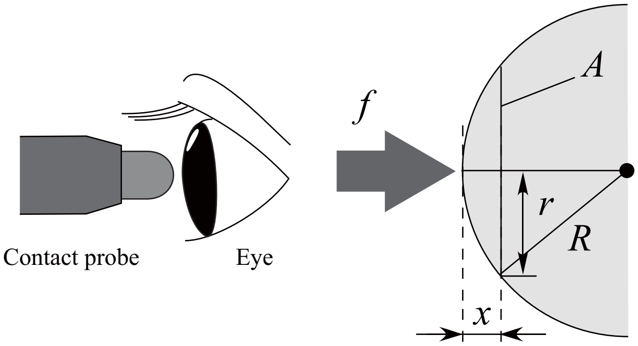
Computational models of human eyes have been constructed for more precise diagnosis of eye diseases [16], [17], [18]. Purslow et al. [19] have shown an analytical pressure-volume relationship to characterize deformability of the ocular shell. However, the analytical results have not been compared with the experimental results of a real human eye. As far as we know, this is the first work which reports static eye stiffness for living human eyes and compares the experimental results with the analytical results.

III. Analytical eye model and the stiffness

Fig. 2 shows a simple spherical eye model that has an internal pressure p where $R, f, x, A,$ and r are the radius of the sphere, the applied force, the displacement at the corneal tip, the deformed area, and the radius of the deformed area, respectively. Let us assume that the eye does not change its internal pressure during deformation and the cornea has neither bending stiffness nor flexibility.

From Fig. 2 (b), we can formulate the following geometrical relationship:

$$R^2 = (R-x)^2 + r^2. \tag{1}$$



(a) Actual (b) Spherical model

Abbildung 2. Model of a human eye

On the assumption that only the cornea is deformed, we can use the curvature radius of the cornea as the radius of sphere R. We assume that x is sufficiently smaller than R and that the following relationship among $r, R,$ and x can be derived:

$$r^2 \simeq 2Rx. \tag{2}$$

Multiplying both sides by πp and using $\pi r^2 = A$ results in

$$f = pA = 2\pi Rpx. \tag{3}$$

From Eq. (3), eye stiffness k is derived by the following equation:

$$k = \frac{f}{x} = 2\pi Rp. \tag{4}$$

Eq. (4) indicates that eye stiffness k is proportional to internal pressure p. This discussion provides us with a good hint for evaluating the validity of experimental results.

IV. Experimental system

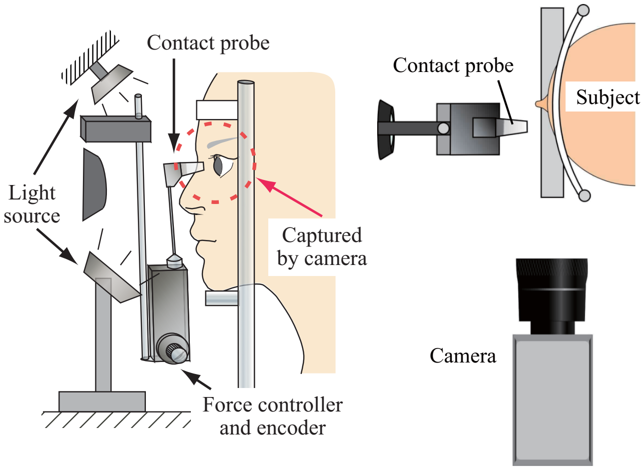
A. System configuration

The experimental system is composed of an applanation tonometer and a camera (Flovel co., Ltd.: ADP-210B). The camera has a spatial resolution of 5.6[μm/pixel], a time resolution of 5[Hz], and an image size of 1624×1234[pixels].

Fig. 3(a) and (b) show the side and the top view of the experimental system, respectively. The camera is set up perpendicular to the axial direction of subject's eyes and additional light sources are installed to ensure sufficient illumination for the measurement.

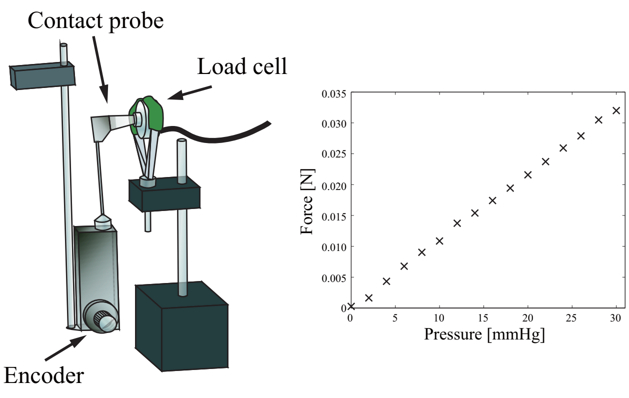
B. Force calibration

Since it is hard to measure the actual force applied on the cornea during the experiment, the force calibrated prior to the experiment is used for the calculation of eye stiffness. Fig. 4(a) shows the overview of the calibration. The force can be changed by rotating the dial connected to the probe link of the tonometer. The relationship between the pressure value of the dial and the force applied on the load cell is shown in Fig. 4(b). The tonometer used in this study is commercially available and the repeatability of the force is guaranteed. We measured the relationship three times and used the conversion equation of f [N] $= 0.0011 \times p$ [mmHg] based on the measurements.



(a) Side view (b) Top view

Abbildung 3. Experimental system



(a) Diagram (b) Measured relationship

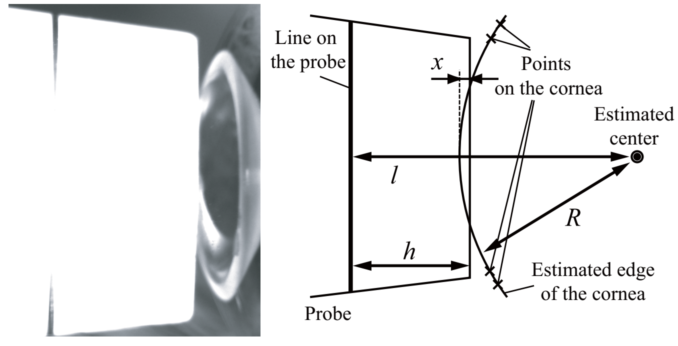
Abbildung 4. Force calibration

C. Measurement of the displacement

Fig. 5(a) shows a captured image of the deformed cornea. Because the whole eyeball moves backward while being pressed by the probe, the displacement detection method should consider the change in the position of the eyeball. In this study, the boundary of the corneal surface is estimated to detect the entire eye movement.

We assume that the corneal surface is spherical. Based on the curvature radius of the cornea and some points on the fringe of the cornea obtained from the captured images, we estimate the center of the curvature and detect the eye movement. The curvature radius of the cornea is measured by medical equipment (Carl Zeiss Co., Ltd.: IOLMaster) prior to the experiment. The overlapping area between the extracted boundary and the probe is the bending area of the cornea. We define the displacement at the tip of the bending area as the "displacement".

Fig. 5 (b) shows diagram Fig. 5 (a) where $h, R, l,$ and x are the distance between the line on the probe and the head of the probe, the curvature radius of the cornea, the distance between the line on the probe and the estimated center of the corneal curvature, and the displacement, respectively. Since



(a) Captured image (b) Diagram

Abbildung 5. Detection of the displacement

the position of the line on the probe can be clearly observed in the images, l can be calculated based on the estimated center of the corneal curvature. h is a geometrical parameter. Thus, displacement x can be derived based on the following geometrical relationship:

$$x = (h + R) - l. \quad (5)$$

V. Experiment

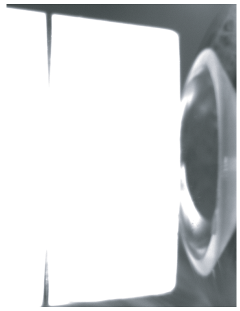
A. Subjects and procedure

35 healthy subjects and 7 glaucoma subjects aged 19∼78 years old (23 males and 19 females) participated in the experiment. The glaucoma subjects were hospital patients in Hiroshima University Hospital for observation and treatment of glaucoma. The experimental procedure is almost the same as that in normal applanation tonometry. A medical doctor pressed the probe onto the subject's cornea, which was anesthetized using an eye drop. The applied force was measured by an encoder attached on the pressure dial of the tonometer and the deformation of the cornea was captured by the camera. The applied force was gradually increased from 0.005[N] to 0.025[N] for healthy subjects, and 0.005[N] to 0.035[N] for glaucoma subjects. We obtained informed consent before beginning the experiment and made one measurement for each subject to prevent damage on the cornea from subsequent multiple measurements. The curvature radius of the cornea and the central corneal thickness (CCT) of each subject were measured prior to the experiment.

B. Experimental results

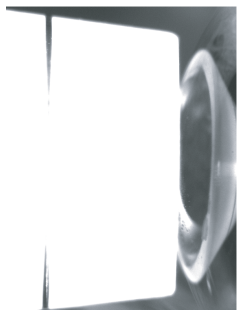
Fig. 6 shows the representative pictures of the cornea during the experiment: (a) before contact, (b) when the force of 0.005[N] is applied, (c) when the force of 0.015[N] is applied, and (d) when the force of 0.025[N] is applied, respectively. The displacement is calculated based on method described in section IV-C. Six representative examples of the relationship between the force and the displacement are shown in Fig. 7. Fig. 7(a)∼(d) and (f) show examples for healthy subjects with IOP of 12∼18[mmHg], and (e) shows an example for a glaucoma subject with IOP of 31[mmHg]. We can observe a linear relationship between the force and the displacement. This

(a) $f = 0$[N]



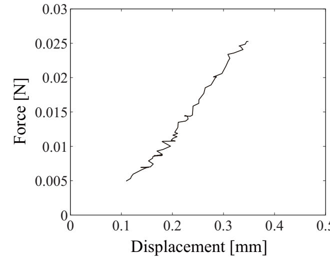
(b) $f = 0.005$[N]

(c) $f = 0.015$[N]

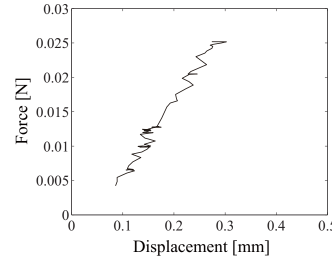


(d) $f = 0.025$[N]

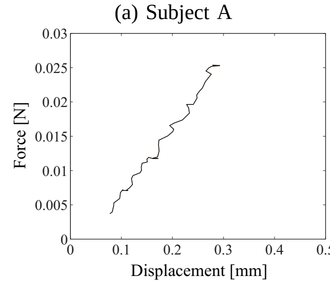
Abbildung 6. Deformation of the cornea during the probe contact



(a) Subject A



(b) Subject B



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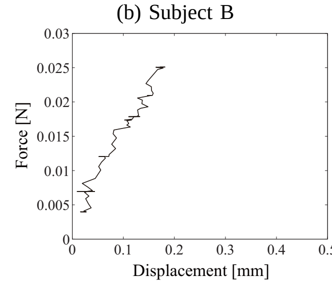
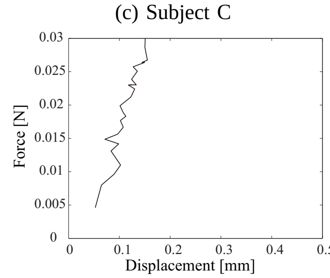
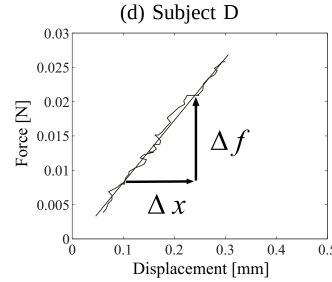


(d) Subject D



(e) Subject E



(f) Subject F

Abbildung 7. Relationship between the force and the displacement. Subjects A∼D and F are healthy subjects with IOP of 12∼18[mmHg], and Subject E is a glaucoma patient with the pressure of 31[mmHg]. Contact eye stiffness k_{cnt} is defined by $\boldsymbol{\Delta} f$ and $\boldsymbol{\Delta} x$, which are based on the slope of the regression line detected through least-square best fit.

linear relationship agrees well with the analytical relationship between f and x shown in Eq. (3).

The overlapped line in Fig. 7 (f) shows the regression line obtained through the least-square best fit of the experimental data. In this study, the contact eye stiffness k_{cnt} is defined by the increase of the force and the displacement:

$$k_{cnt} = \boldsymbol{\Delta} f / \boldsymbol{\Delta} x \tag{6}$$

where $\boldsymbol{\Delta} f$ is the increase of the force and $\boldsymbol{\Delta} x$ is the increase of the displacement based on the regression line. The mean of the standard deviation from the regression line for all the subjects is 0.0138[mm].

Fig. 8 shows the relationship between the IOP measured by the applanation tonometer and the computed contact eye stiffness for all the subjects. A statistically-significant correlation is observed between them (the correlation coefficient is 0.828, $p < 1 \times 10^{-10}$).

VI. Discussion

The analytical result of the eye stiffness described in section III depends on the curvature radius of the cornea. We normalize the stiffness by the curvature radius in order to compare the analytical values with the experimental values. The following relationship can be derived from Eq. (4):

$$k/R = 2\pi p. \tag{7}$$

Fig. 9 shows the relationship between the normalized stiffness k_{cnt}/R and the pressure related value $2\pi p$. The dashed line in the figure indicates the analytical result. The analytical relationship nicely matches the experimental result.

Our deformation model used for the calculation of the analytical eye stiffness ignores some important factors. The real cornea has a thickness, and this thickness brings out the bending stiffness and the elasticity of the cornea. The tear film makes a tension between the probe and the cornea. Moreover, when an eyeball is deformed, the tissue in the eyeball absorbs aqueous fluid and the internal eye pressure itself might change. These factors seem to influence corneal deformation and stiffness. However, the measured value of eye stiffness by the contact method ($60 \sim 140$[N/m] for healthy subjects) is close to the analytical result in comparison with the stiffness measured by the non-contact method ($500 \sim 3500$[N/m] for healthy subjects [3]). This indicates the contact method is appropriate for the evaluation of the contact stiffness.

Here we discuss the difference of the stiffness value between the contact method and the non-contact method. The main difference of these methods is how the force is applied to the cornea. The deformation of a cornea starts when an external force generates a sufficient pressure on the area of deformation. In the contact method, the force is applied directly and the threshold pressure is created in a certain area. In the non-contact method, the force of the air puff is dispersed over the cornea and generates a pressure distribution on a large area. Thus, only a fraction of the force acts

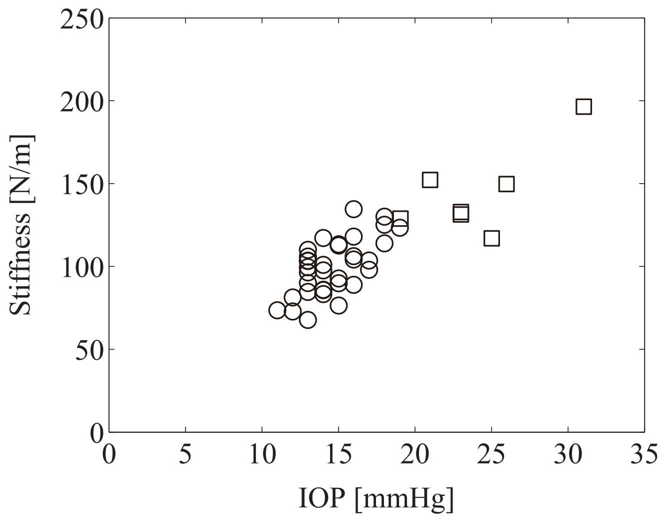


Abbildung 8. Correlation between eye stiffness and IOP. Circles are healthy subjects and squares are glaucoma patients. IOP was measured by means of an applanation tonometer manipulated by a medical doctor.

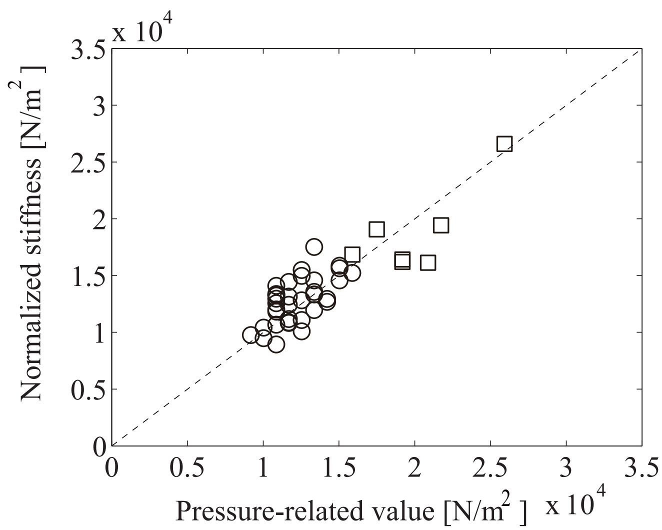


Abbildung 9. Normalized stiffness by the curvature radius. Circles are healthy subjects and squares are glaucoma patients. The vertical axis shows the normalized stiffness k_{cnt}/R, and the lateral axis shows the pressure-related value $2\pi p$ where k_{cnt}, R, and p are the eye stiffness, the curvature radius of the cornea measured by IOLMaster, and the IOP measured by the applanation tonometer, respectively. The correlation coefficient between them is 0.847, $p < 1 \times 10^{-11}$. The dashed line shows the analytical relationship $k_{cnt}/R = 2\pi p$.

on the deformed area. As a consequence, the stiffness is overestimated when we use the total force of the air puff to calculate the stiffness. In addition, note that the contact and the non-contact method have different definitions for eye stiffness. In the non-contact method, stiffness is defined based on the force and the displacement at a prescribed time because the applied force dynamically changes depending on the time. In the contact method, the stiffness is defined based on the increase of the force and the displacement. Since stiffness with different definitions has different characteristics, a direct comparison is not possible. The difference in eye stiffness depending on the measurement method will be discussed in our future work.

It is well known that the corneal thickness influences the accuracy of IOP measurement. We have measured the central cornea thickness (CCT) of all subjects and analyzed the influence of CCT on measured IOP. The experimental results show that the correlation between CCT and IOP is 0.0728 with $p > 0.6$, and the correlation between CCT and eye stiffness is 0.00789 with $p > 0.9$. We do not believe that this low correlation comes from errors in measurements. The sensing accuracy of eye stiffness is influenced by both force and displacement measurements. As for force sensing, we are simply utilizing an encoder to obtain the dial value of the applanation tonometer, where the force repeatability is guaranteed. As for displacement sensing, we are utilizing camera images. The accuracy of displacement sensing is influenced greatly by how the boundary between the cornea and the outer scene are extracted. To check the accuracy of the boundary extraction, we compared the curvature radius of the cornea obtained by two approaches; one approach is obtained by an IOLMaster and the other is estimated by least-square best fit based on the same points used in the boundary extraction. The results show that the radius estimated by the points on the camera images has good coincidence with the radius obtained by the IOLMaster (the mean difference between the two is 1.19[%]). This result indicates the appropriate accuracy of the boundary extraction. Simmyo et al. [13] have measured about 2,000 eyes and shown that the correlation between CCT and IOP is 0.238 with $p < 0.001$, but we would like to note that the correlation is originally not very high. A very large number of measurements are necessary to discuss the influence of CCT on eye stiffness.

A noteworthy point is that we can observe some subjects have different stiffness with the same IOP. The subjects with extraordinarily low or high stiffness might have abnormal structural eye stiffness and this stiffness causes the underestimation or the overestimation of the internal eye pressure. Current applanation tonometry only evaluates the force and the contact area. Therefore, it can not discriminate the deformations shown in Fig. 10 due to the abnormality of structural eye stiffness. The proposed eye stiffness measurement can detect such abnormality in vivo and non-invasively because the stiffness includes displacement information. Evaluating eye stiffness in addition to the IOP information currently used might contribute to early detection and treatment of glaucoma. Since the applanation tonometer is delicate equipment, we did not make any conversion on the tonometer in order to retain safety and repeatability of the force. A customized tonometer that can directly measure the displacement will help make more accurate measurements of eye stiffness.

VII. Conclusion

This paper has accomplished the following:

- Analytical eye stiffness was formulated based on a simple spherical eye model.
- A deformation measurement system of living human eyes composed of a contact tonometer and a high resolution camera was developed.
- Eye stiffness was measured for 42 subjects including glaucoma patients.

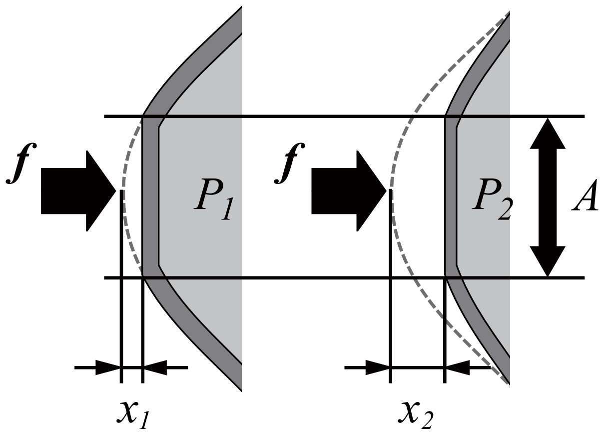


Abbildung 10. Possible corneal deformation with same contact area but different displacement. Even if the true internal eye pressures of these two eyes are different ($P_1 \neq P_2$), current applanation tonometry assumes that these eyes have same IOP because the same deformed area (A) is made by the same applied force (f).

- The experimental results nicely matched the analytical results.
- Some subjects have different eye stiffness even with same IOP detected by the applanation tonometer.

Abnormal deformation of a cornea causes the misestimation of IOP. The results presented in this paper show that information about stiffness is a good index for distinguishing abnormal corneal deformation. The proposed eye stiffness measurement is non-invasive and easy to use for living human eyes, and it can help detect misestimated eyes.

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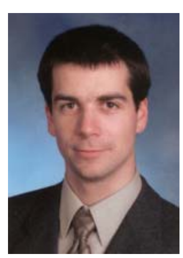

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