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Original Article

Intraoperative Measurement of Crystalline Lens Diameter in Living Humans

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ABSTRACT

Background There are no reports on accurate measurement of lens equatorial diameter of the living human eye. This study aimed to measure lens equatorial diameter with a special measurement device during cataract surgery and examine the relationships with preoperative parameters.

Methods From April 7 to December 1, 2019, the equatorial diameters of 24 eyes from 24 patients who underwent cataract surgery at Kushimoto Arita Hospital were measured with a loop shaped measurement device during cataract surgery. Correlations between the value of the diameters and various preoperative parameters measured by CASIA2® were evaluated.

Results The average value of the measured equatorial diameter using the device was 10.5 ± 0.4 mm and the value estimated by circular approximation using the CASIA2® was 10.1 ± 0.7 mm. A significant difference was observed between these two groups (P = 0.016), and only a weak correlation was observed (γ = 0.31). A positive correlation was observed between equatorial diameter and anterior chamber depth (ACD) or anterior chamber width (ACW) (γ = 0.57 and 0.47, respectively). No significant correlation was found between other parameters and the value measured by the device.

Conclusion Our method is a completely new approach to measuring the living human lens equatorial region of the eye. No complications were observed in any of the cases. One new finding was the values of the lens equatorial diameters are actually longer than those reported previously. The results suggest that the values of the equatorial diameter measured by the loop device and those estimated by CASIA2® measurement were closer than those reported previously by other methods, although both were slightly different. We conclude that it is still difficult to estimate the equatorial diameter of the living human lens using preoperative examination parameters. This research will greatly contribute to the development of accommodative intraocular lenses in the future.

Key words anterior segment; crystalline lens; optical coherence tomography

By introducing phacoemulsification and intraocular lenses, the current style of cataract surgery was established, where the capsular bag is preserved, the cortex and nucleus are removed, and an intraocular lens is inserted into the capsule bag. Currently, more than 1.5 million cataract surgeries are performed annually in Japan,[1] generally regarded as highly safe surgeries sufficient for providing good visual acuity. In natural crystalline lenses, accommodation is possible by changing lens thickness. However, conventional intraocular lenses have a single focal point with no accommodation ability. Therefore, reading glasses are required for near vision if the patient has an intraocular lens inserted with distant focus. In recent years, in order to solve this problem, multifocal intraocular lenses with two or three focal points have been developed by utilizing the diffraction phenomenon.[2] However, multifocal intraocular lenses are not empowered with real accommodative power. Therefore, it is difficult to obtain a sharp image with them, unlike the single focus lens, and some patients complain of poor focus at any distance. Moreover, complications of scattering light such as halo and glare impair good visual acuity in multifocal intraocular lenses,[3] leading to surgical exchange to a single focus intraocular lens in some cases.[4] On the other hand, attempts have been made to develop an intraocular lens with real accommodative power,[5] resulting in no success so far. Under such circumstances, we have been developing an accommodative intraocular lens through our own original idea and design, being able to move forward and backward while changing thickness in the capsular bag. For that purpose, it has become an important issue to measure the equatorial diameter of the capsular bag.

According to previous reports, the human crystalline lens has a diameter of approximately 8.54–9.70 mm,[6] but these were all measured in the extracted eye.

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Abbreviations: ACD, anterior chamber depth; ACW, anterior chamber width; CCT, central corneal thickness; CT, computed tomography; LT, lens thickness; MRI, magnetic resonance imaging; OCT, optical coherence tomography; UBM, ultrasonic biomicroscopy

The configuration of the biological capsular bag changes according to the tension of the lens equator brought about by the ciliary muscle through the supporting tissue of the crystalline lens known as the Zinn zonule. Since tension is lost in extracted eyes, it is highly possible that the measured values of the capsular equator diameter are different from those of eyes in the living human body.

There have been many reports of studies on human eye morphology, including the crystalline lens of living organisms. Most of the reports have been made using imaging such as computed tomography (CT), magnetic resonance imaging (MRI),[7] and ultrasonic biomicroscopy (UBM) specialized for ophthalmology.[8] However, equatorial diameter measurement is difficult due to low resolution of CT and MRI, the possibility of cataract induction by CT,[9] and artifacts caused by measurement from eye movement during MRI.[10] UBM can visualize the structure of the posterior surface of the iris; however, it is difficult to accurately depict the equatorial region of the crystalline lens even with the new UBM (VuMAX II®: sonomed, Optimetrics, Hialea, FL).

In recent years, with the advent of optical coherence tomography (OCT) using a near-infrared low-interference beam, it has become possible to more easily and non-invasively examine the morphology of the anterior segment of the eye, including the crystalline lens of the human body. As a result, reports of new findings have been increasing.[11–15] However, at present, there are no reports on the accurate measurement of the human lens equatorial diameter of the living body. The main reason for the difficulty in accurately measuring the equatorial diameter of the human crystalline lens is that the equatorial part of the lens is located under the iris, and it is difficult to directly observe it even with mydriatic condition by OCT. The second-generation anterior ocular segment OCT (CASIA2®: TOMEY, Nagoya, Japan) has a lens morphology analysis program that can calculate the diameter of the equatorial region of the capsular bag, which is a circular approximation from the radius of curvature of the anterior-posterior surface of the crystalline lens that can be imaged under the non-iris region. However, there is at least one report which explains that the position of the lens equator was different between the UBM image and the CASIA2® image actually taken from the same subject.[16]

Therefore, to accurately measure the equatorial diameter of the crystalline lens in living human body, it is considered that conventional equipment is insufficient, and another approach must be considered. So, we devised a method to directly measure the crystalline lens diameter of the equatorial region using a special scale during cataract surgery. After developing the measurement device, we performed a measurement simulation using a pig eye, which is relatively similar in size and structure to the human eyeball, and confirmed its safety and effectiveness. Then, at the time of cataract surgery in cataract patients, we tried to directly measure the diameter of the equatorial region of the human capsular lens. In this paper, we report the results of measured data and their relationships with other parameters, such as crystalline lens-related measurements.

SUBJECTS AND METHODS

Subjects

This study included 24 eyes from 24 patients who underwent cataract surgery at Kushimoto Arita Hospital from April 7 to December 1, 2019, after obtaining informed consent from the patients and their families. The exclusion criteria were as follows: (1) poor mydriasis, (2) exfoliation syndrome, (3) nuclear hardness exceeding grade III in Emery-Little classification,[17] (4) corneal opacity, (5) phacodonesis (Zinn zonule fragile eye), (6) shallow anterior chamber, and (7) history of surgery in other areas of ophthalmology.

This study was approved by the Ethics Committee of Kushimoto Arita Hospital (approval number 2019E01). Based on the Declaration of Helsinki, only patients who provided informed consent were included in the study.

Methods

First, we developed an injector-type measurement device. There is a loop with a measuring gauge at the tip of the inner cylinder of the injector, which was housed inside the outer cylinder (Fig. 1A). By pushing the plunger, the measuring gauge stored in the outer cylinder is pushed out from the tip of the outer cylinder and spreads out in a loop (Figs. 1B and C). The measurement gauge has a shape in which three memories were connected, and one memory had a diameter of 1 mm, and so it was possible to measure in units of 0.1 mm under a microscope (Fig. 1D).

Second, we conducted a simulation using the measuring device with a pig eye to confirm the safety and effectiveness of the device. Specifically, after removing the cornea and iris of the pig's eye and making a circular incision in the capsular bag, we made sure the equatorial region was visible, then the lens nucleus and cortex were removed and the capsular bag was emptied. After that, the capsular bag was dilated with a viscoelastic substance. It was confirmed that the position of the equatorial region of the capsular bag was not changed after filling the empty capsular bag with

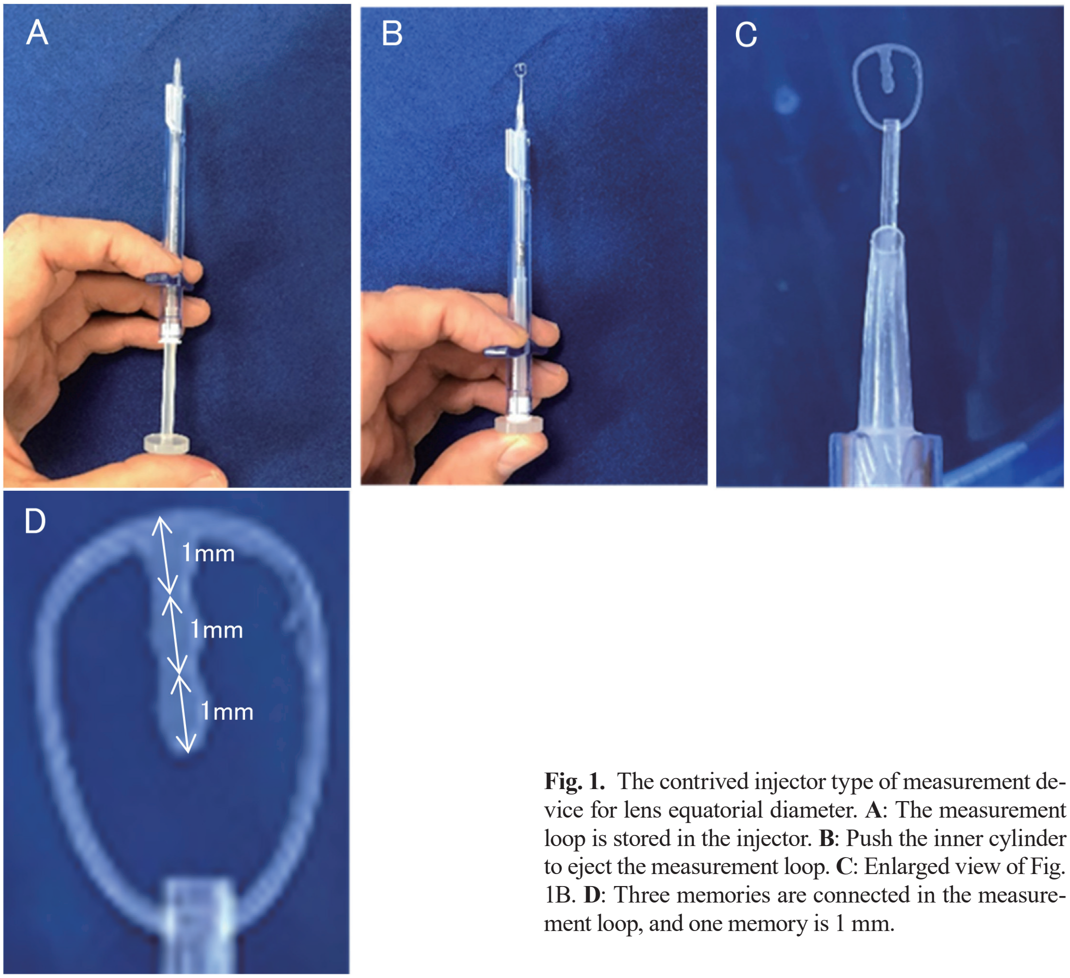

Fig. 1. The contrived injector type of measurement device for lens equatorial diameter. **A**: The measurement loop is stored in the injector. **B**: Push the inner cylinder to eject the measurement loop. **C**: Enlarged view of Fig. 1B. **D**: Three memories are connected in the measurement loop, and one memory is 1 mm.

the viscoelastic substance compared with pre-operation condition. Then, we confirmed that there was no deformation of the equatorial part of the capsular bag after maximal deformation of the loop by pressing it into the equator (Fig. 2B) compared with the situation before pressing the tip of the loop from the injector against the equator (Fig. 2A). At the same time, we confirmed that the capsule was not damaged after the measurement. The above simulations were performed with three pig's eyes and the results were all the same. Afterwards, at the time of cataract surgery of the target patient, the equatorial diameter of the crystalline lens was actually measured using the above-mentioned measuring device.

Cataract surgery was performed by general phacoemulsification under mydriasis. After suction removal of the lens nucleus and cortex, the empty capsular bag and anterior chamber were filled with viscoelastic material. Then, after inserting the tip of the injector into the anterior chamber from the main wound, the inner cylinder was pushed to slowly eject the measurement loop (Fig. 3), and the tip of the loop was placed on the equator of the capsular bag. The length of the capsular bag under the iris was measured when the loop was maximally deformed (Fig. 4). The reason for measuring at that moment was that we confirmed the loop fit snugly in the lens equator and the equator of the lens bag was not deformed by maximal deformation of the loop, exactly the result we had in the pig eye experiment. The crystalline lens equatorial diameter was calculated by applying the measured value to the formula [equatorial diameter of the capsular bag = sub-iris capsular bag length × 2 + pupil diameter]. All the operations were video-recorded, and after cataract surgery the images at the time of measurement were carefully analyzed on a monitor screen. The sub-iris capsular bag length and the pupil diameter were calculated based on the length of the scale. In this study, the sub-iris capsular bag length was considered to be the same at any angle because of mydriatic condition, so we measured only one angle point in order to protect the subject from injury.

In all cases, during the preoperative examination of the cataract, the axial length of the eyeball was measured using an optical interference-type axial length measuring device (IOL master), and central corneal

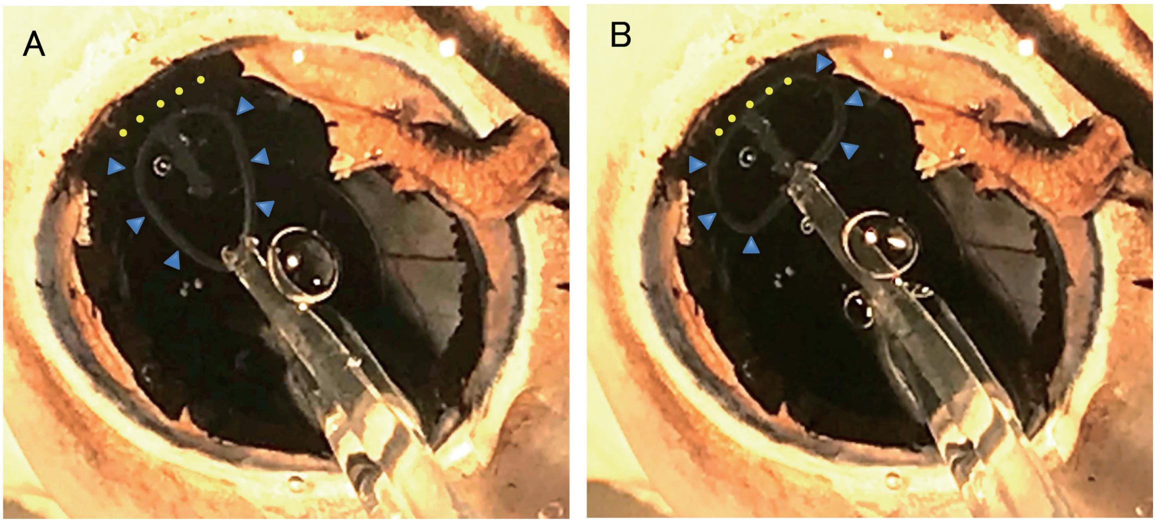

Fig. 2. The simulation using the measuring device with a pig's eye. The blue triangle indicates the outline of the measurement loop, and the yellow circle point indicates the outline of lens equatorial part. There was no change in the position of the equator between **A** and **B**. **A**: before pressing the tip of the loop from the injector against the equator of the capsular bag. **B**: The loop was maximally deformed by pressing to the equator of the capsular bag.

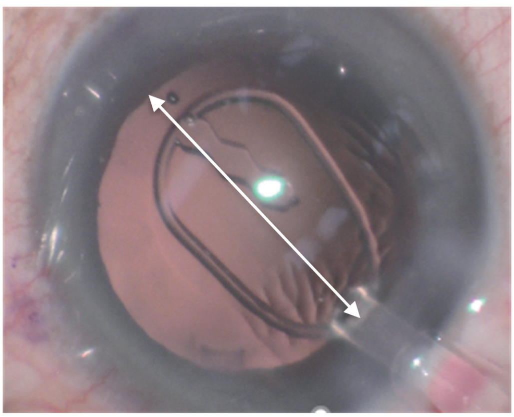

Fig. 3. After inserting the injector tip from the main wound of the cornea, push the inner cylinder to slowly eject the measurement loop. Arrow shows the pupil diameter.

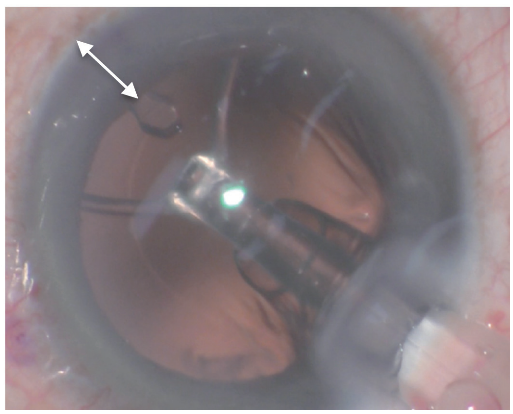

Fig. 4. As the measurement loop is pushed forward, the length of the capsular bag under the iris is measured when the leading part contacts with the lens equatorial part and then undergoes maximum deformation. Arrow shows the capsular length under the iris.

thickness (CCT), anterior chamber depth (ACD: the distance from the corneal endothelium to the anterior surface of the lens), anterior chamber width (ACW: horizontal distance between the scleral spurs), and lens thickness (LT) were measured using CASIA2®. In addition, the presumed diameter of the lens' equatorial diameter was calculated by approximating a circle from the radius of curvature of the anterior-posterior surface of the crystalline lens that can be imaged under non-iris by CASIA2® (Fig. 5). The correlation between each preoperative parameter and the actual measured capsular equatorial diameter was examined.

Statistical analysis

Student's *t*-test was used for statistical analysis between men and women. The significance level was set at $P < 0.05$. Pearson correlation coefficient was used to analyze the correlation between the measured value with the device and various preoperative measured values or age. In addition, the Wilcoxon signed-rank test was used to determine whether or not there was a significant difference between the equatorial diameter calculated by the CASIA2® crystalline lens morphological analysis program and the equatorial diameter directly measured

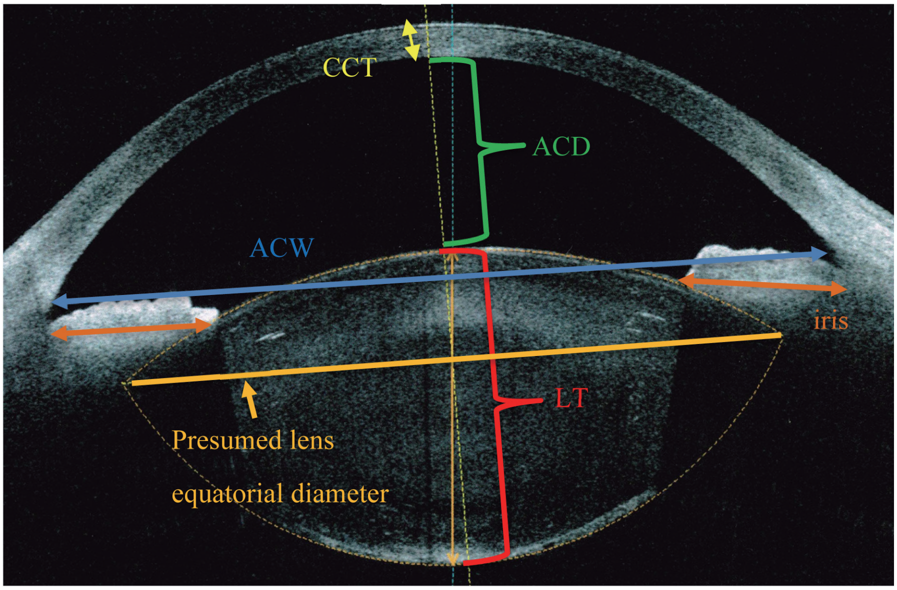

Fig. 5. Measurement image of CASIA2®. ACD, anterior chamber depth; ACW, anterior chamber width; CCT, central corneal thickness; LT, lens thickness.

by the measuring device.

RESULTS

The subjects were 11 males providing 11 eyes aged 58–86 years (mean ± standard deviation: 74.7 ± 7.1 years), and 13 females providing 13 eyes aged 62–90 years (mean 73.3 ± 8.0 years). The nuclear hardness of the crystalline lens was equivalent to degree II in 22 cases and degree III in 2 cases, respectively, according to Emery-Little classification.

At the time of surgery in all cases, no complications related to device insertion and measurement were observed, and the intraocular lens was inserted and fixed into the lens capsule as scheduled after the measurement of the equatorial diameter.

The average value ± standard deviation of the measured lens equatorial diameter using the device was 10.5 ± 0.4 mm, which was 10.6 ± 0.4 mm for men and 10.3 ± 0.4 mm for women. No significant differences were found between men and women (P = 0.090). Lens equatorial diameter measured by the device was longer than that of the extracted eye and that measured by UBM, as previously reported. The average value ± standard deviation of the lens equatorial diameter group calculated by circular approximation using the CASIA2® lens morphology analysis program was 10.1 ± 0.7 mm (10.2 ± 0.6 mm for men and 10.0 ± 0.8 mm for women), and no significant difference was observed between men and women (P = 0.46). In addition, a significant difference was observed between the lens equatorial diameter group measured by the device and by CASIA2® (P = 0.016), and only a weak correlation was observed (γ = 0.31) (Fig. 6). These results suggest that the value of the equatorial diameter measured by CASIA2® and by the device were different.

Examining the comparison of age, axial length of the eye, CCT, ACD, ACW, and LT measured by CASIA2® and the lens equatorial diameter measured by the device, a positive correlation was observed between equatorial diameter and ACD or ACW (correlation coefficient γ = 0.57 and 0.47, respectively) (Figs. 7A and B). In addition, a weak positive correlation with the axial length of the eye (γ = 0.32) (Fig. 7C) and a weak negative correlation with LT (γ = –0.20) were observed (Fig. 7D). No significant correlation was found between CCT and equatorial diameter (γ = –0.15) (Fig. 7E). In addition, there was no difference between age and equatorial diameter (γ = 0.009) (Fig. 7F). These results are summarized in Table 1.

In the relation with age and measurement of anterior segment of the eye, The CASIA2® measurement showed no relation between age and ACW (Fig. 8A), ACD (Fig. 8B), or CCT (Fig. 8C), and a weak positive correlation (γ = 0.38) between age and LT (Fig. 8D). However, no significant correlation was found between age and equatorial diameter of the human lens (γ = 0.012) (Fig. 8E), similar to the results measured by the device. These results are summarized in Table 2.

DISCUSSION

Many studies have been conducted on the human crystalline lens of a living body other than anatomical

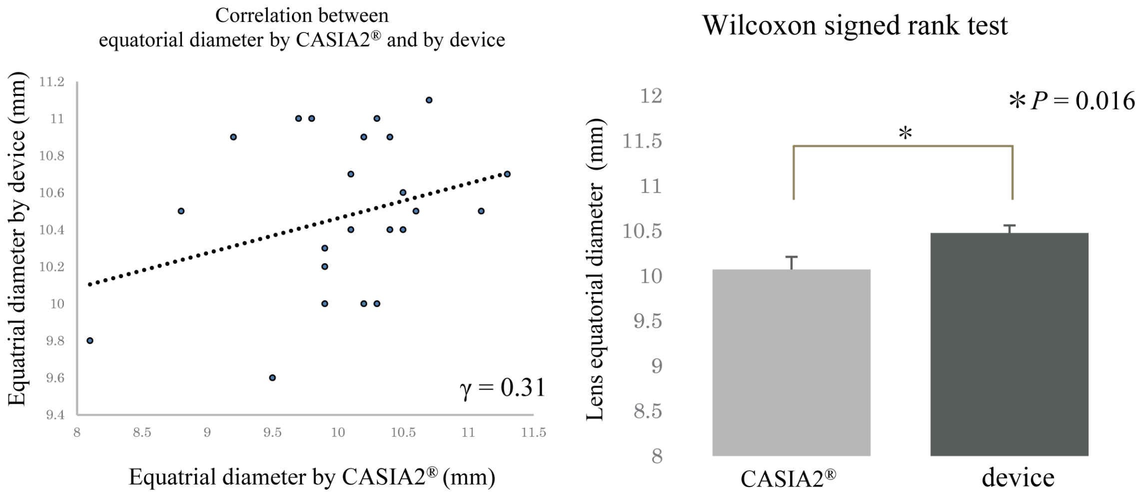

Fig. 6. Comparison of the lens equatorial diameter values estimated by CASIA2® and that measured by the scale device.

samples. However, there are few reports on the equatorial diameter of the crystalline lens. Since the equatorial diameter of the crystalline lens is difficult to measure using conventional ophthalmic examinations or an imaging apparatus, and considered to have no clinical significance in daily ophthalmology, it has not been studied seriously.

To the best of our knowledge, direct measurement of the equatorial diameter of the lens in a living body has never been reported, and our method is a completely new approach to the living human lens equatorial region. We have repeatedly improved the measuring device by performing simulations on pig eyes, resulting in improved safety and efficacy. At the time of actual measurement, no complications occurred in any case; the measurement time was about 15 seconds on average and which is considered very short. Therefore, the operation could be completed without any harm on the subjects.

Anatomically, the human crystalline lens continues to form new crystalline lens fibers throughout its life. The new crystalline lens fibers are piled up one after another on the old fibers, and the crystalline lens continues to increase in thickness. Many clinical tests have reported that the lens thickness increases with aging, but there is also a report that it does not become thicker after it reaches a certain thickness.[18] The CASIA2® measurement in this study also showed a weak positive correlation between age and lens thickness (Fig. 8D). However, there are no reports on age-related changes in the equatorial diameter of the human crystalline lens. From the results of this study, no significant correlation was found between age and equatorial diameter of the human lens, at least with the age of onset of cataract in the 50s to 90s (Figs. 7F and 8E). In addition, the results show that there is no correlation between lens thickness and the equatorial diameter. Considering these results, it was suggested that lens volume tends to increase with age, but mainly only in a vertical direction, and there is little change in horizontal direction or equatorial direction.

Furthermore, the value of the lens equatorial diameter obtained by this measurement is in the 10-mm range, which is longer than the previously reported measurement value (8–9 mm range) of the crystalline lens equatorial diameter of the living eye using UBM or by measurement of extracted eyes. On the other hand, the values of the equatorial diameter estimated by the circle approximation mode of CASIA2® in a previous report[19] and our current study were close (Table 3).

As for our method of direct measurement, there is a possibility the measured diameter was larger than the actual value due to the risk of excessive filling of the viscoelastic substance in the lens bag or the excessive push and displacement of the lens equatorial part by the measurement device, although we tried to carefully avoid this as much as possible. However, considering the actual measurement value is close to the value estimated in the human living eyes using the CASIA2® crystalline lens morphological analysis program, it can be described as a new finding that the human crystalline lens equatorial diameters are actually longer than those reported previously.

It was reported to estimate the distance of the ciliary groove, which is located under the iris, with high accuracy using the anterior segment parameter value,

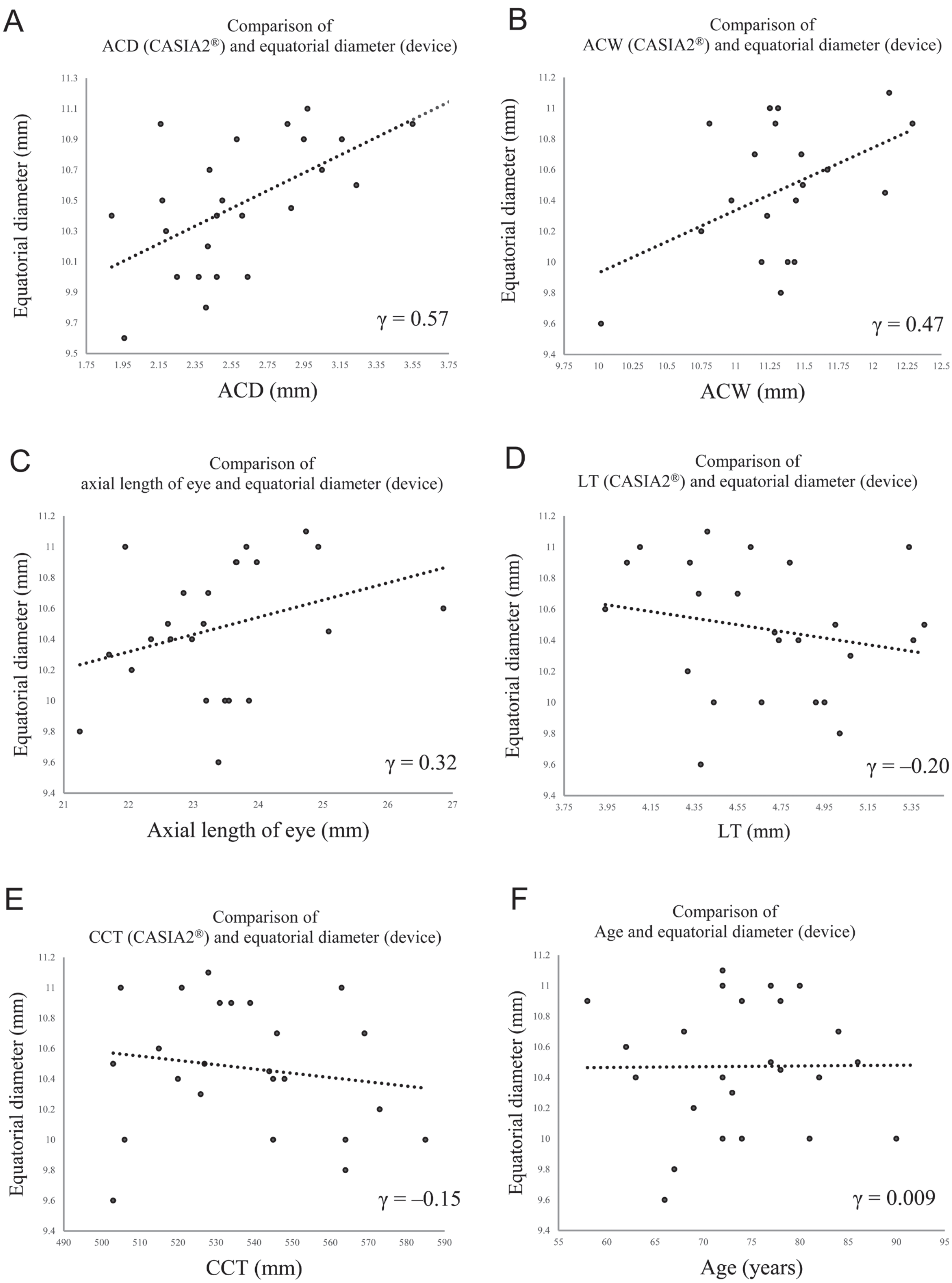

Fig. 7. Correlation between axial length of the eye, CASIA2® measurements, age, and equatorial diameter value measured using the scale device.

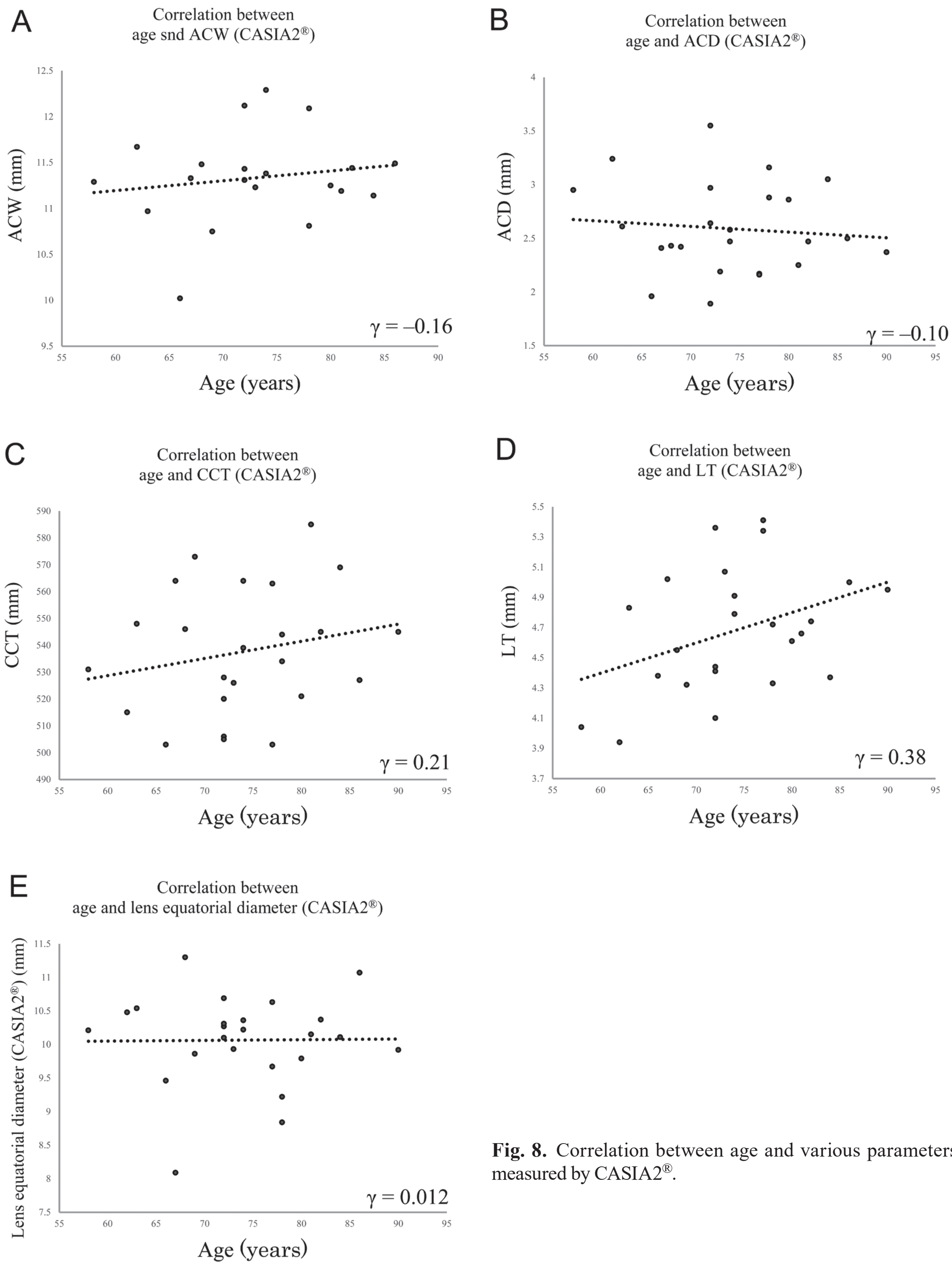

Fig. 8. Correlation between age and various parameters measured by CASIA2®.

such as ACW, of the anterior segment OCT.[21] Thus, it is desirable that the actual equatorial diameter value of the lens can be predicted from the test parameters in non-invasive CASIA2®. In our current study, statistical analysis showed a significant difference between the value by CASIA2® and direct measurement ($P = 0.016$), however the correlation coefficient was $\gamma = 0.31$, which means that there was no strong correlation. Also, the

Table 1. Correlation with lens equatorial diameter (device)

	γ	P value
ACD (CASIA2®)	0.57	0.052
ACW (CASIA2®)	0.47	0.123
Axial length of eye	0.32	0.301
Age	0.009	0.978
CCT (CASIA2®)	–0.15	0.625
LT (CASIA2®)	–0.20	0.521

Table 2. Correlation with age

	γ	P value
LT (CASIA2®)	0.38	0.216
CCT (CASIA2®)	0.21	0.508
lens equatorial diameter (CASIA2®)	0.012	0.971
ACD (CASIA2®)	–0.10	0.759
ACW (CASIA2®)	–0.16	0.616

Table 3. Comparison of the equatorial diameter of the human lens by various methods

Report	Human lens equatorial diameter (Mean ± SD mm)	Method
Sakabe et al.[20]	9.70 ± 0.32	Direct measurement of extracted eyes (eye bank)
Majima et al.[6]	8.47 ± 0.11~8.92 ± 0.10	UBM
Zheng X et al.[19]	10.49 ± 0.69	CASIA2®
This study	10.1 ± 0.7	CASIA2®
	10.5 ± 0.4	Direct measurement with the scale device

difference between the measured value of both groups is –0.21 ± 0.7 mm (mean ± standard deviation), and the number of difference within ± 0.5 mm was limited to 13 of 24 cases, which was approximately half, and the largest one had a difference of 1.7 mm (data not shown). From the results of this study, no parameter was found that showed a strong correlation between the CASIA2® parameters and the equatorial diameter value measured by the device. We conclude that it is still difficult to estimate the equatorial diameter of a living human lens using the existing preoperative examination parameters. From the experience of this study, the circle approximation in the CASIA2® lens morphological analysis program was often slightly unnatural, therefore it may cause poor accuracy and reproducibility.

There are some limitations to our research model. The first limitation is that it can be measured only under the conditions of cataract surgery with mydriasis. In the lens of a living human, the tension of Zinn zonules occurs with mydriasis, which may change the shape of the lens. However, in our current study, it is not possible to examine the effect of mydriasis on the lens equatorial diameter, because our measurement is possible only under mydriasis, but not under non-mydriasis. Similarly, in our study, it is difficult to examine how accommodation affects lens shape, which is possible by anterior segment OCT.[22]

The second limitation was derived from the viewpoint of safety. This study intentionally selected only cases with low difficulty of cataract surgery, therefore variations in the case were biased. In order to ensure safety, we only chose cases with poor mydriasis, such as exfoliation syndrome eyes. Cases with fragile Zinn zonules, and cases with hard lens nucleus were excluded from the study. In addition, cataracts may occur in young people due to atopic dermatitis and trauma, and should be examined in cataract patients from their teens up to their 40s. These various cases should eventually be investigated.

In the future, the insertion of an accommodative intraocular lens may develop as an operation to cure presbyopia, impaired accommodation with aging, without cataracts as well as with cataracts. Therefore, it is necessary to develop a completely new approach from that used in this study to investigate the lens equator diameter of non-cataract patients.

As mentioned in the introduction, the development of intraocular lenses with accommodative functions is underway, especially in Europe and the United States, but products with effective function have not yet been developed. We are working on the development of a unique accommodative intraocular lens, the concept of which is to have the accommodative function obtained by combining a capsule-type device that expands the capsular bag of the lens from the inside and an intraocular lens with movable support parts.

In the development of a capsule-type device, which is crucial in the accomplishment of an adjustable intraocular lens, it is important to know the accurate lens equatorial diameter of the human eye in order to determine its size and deformability. We believe that this research will greatly contribute to the development of accommodative intraocular lenses in the future by measuring the lens equatorial diameter of the human body, which has been difficult to measure up until now.

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The authors declare no conflict of interest.

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