Central and peripheral intraocular pressure measured by a rebound tonometer

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Purpose: We investigated at which corneal region the intraocular pressure as measured by the Icare® rebound tonometer (Finland Oy, Espoo, Finland) (hereinafter referred to as IC) was closest to the intraocular pressure as measured by the Goldmann applanation tonometer (hereinafter referred to as GT). We also investigated which parameters would be best for preparing the most suitable model for predicting GT.

Methods: A total of 102 normal eyes in 102 subjects were enrolled. IC measurements were carried out at the central, superior, inferior, temporal, and nasal regions of the cornea (ICC, ICS, ICI, ICT, and ICN, respectively), followed by GT calculations. Differences between GT and IC were analyzed using the Bland–Altman method. Stepwise multiple regression analysis was performed using GT as the objective variable, and age, laterality of eye, spherical equivalent refractive error, corneal radius, axial length, central corneal thickness, GT, ICC, ICS, ICI, ICT, and ICN as the explanatory variables.

Results: IC was higher than GT at all of the corneal regions, but the region with the least bias was ICC, followed by ICT. In the multiple regression analysis, the following prediction formula was calculated: GT = (0.445 × ICC) + (0.198 × ICN) + 3.022. When ICC was excluded from the explanatory variables, ICT had the highest partial correlation coefficient with GT.

Conclusion: ICC was closest to GT, but GT could be explained better by adding ICN to the prediction model. Moreover, in instances where ICC cannot be calculated or where reliability is clearly poor due to abnormal ocular rigidity, ICT was the closest to GT measured in the central corneal region.

Keywords: IOP, Icare, Goldmann applanation tonometer, ocular rigidity

Introduction

Glaucoma is a disorder that causes serious visual impairment that leads to blindness if not treated appropriately. 1 The greatest risk factor associated with the onset and progression of glaucoma is elevation in intraocular pressure (IOP). 1 Therefore, the accurate measurement of IOP is extremely important for glaucoma management in patients.

The current gold standard for tonometers in ophthalmological practice is the Goldmann applanation tonometer (GAT). 2 However, “IOP as measured by a GAT” (hereinafter referred to as GT) is affected by ocular rigidity. 3 Ocular rigidity is defined as the distensibility or resistance to deformation in the ocular coat. 3 If the ocular rigidity is abnormal due to abnormal corneal thickness, corneal disease, or ocular surgery, GT measurements will be inaccurate. 3 For example, in cases where abnormal ocular rigidity occurs in association with disease or surgery, it is known that GT in the affected...
area is higher than that in other corneal regions, following
corneal calcareous degeneration such as band keratopathy.\(^5\)
On the other hand, GT in the affected area is lower than that
in other corneal regions in the case of keratoconus\(^4\) and laser
in situ keratomileusis.\(^7\)

Obtaining accurate GT measurements in eyes with
abnormal ocular rigidity is not an easy task. In cases where
abnormal ocular rigidity of the central corneal region is
encountered, IOP must sometimes be measured in the
peripheral corneal regions. However, since the area that
aplanates cornea is large, 3.06 mm in the case of using
a GAT, the measurement might be affected by the ocular
rigidity in the central corneal region in no small way when
measuring IOP in the peripheral corneal regions. Moreover,
obtaining a measurement may be impossible in cases where
the measured region contains corneal scarring or sclera.

Icare\(^9\) (Finland Oy, Espoo, Finland), a recently developed
rebound tonometer, makes it possible to measure IOP with-
out anesthesia, and it is portable due to its small size and
light weight.\(^8\)–\(^10\) In addition, the diameter of the probe tip
that comes into contact with the cornea is extremely small
at 1.4 mm,\(^10\) making it easy to measure IOP in peripheral
corneal regions.

In the present study, we investigated at which corneal
regions “IOP measurements using the Icare rebound tonom-
eter” (hereinafter referred to as IC) were closest to GT at the
central corneal region. We also investigated which param-
eters would be best for preparing the most suitable model
for predicting GT.

**Subjects and methods**

A total of 102 eyes in 102 subjects (male/female = 52/50)
without any abnormality on ophthalmologic examination,
other than refractive error, were studied. Informed consent
was obtained from all subjects prior to the study. Niigata
University Institutional Review Board approved all
methodology. Study methods adhered to the provisions of
the Declaration of Helsinki guidelines for research involving
human participants.

Spherical equivalent refractive error (D) and corneal
radius (mm) were calculated using the KR-8100P autore-
fractometer (Topcon Corporation, Tokyo, Japan).

IC was measured in the central corneal region (ICC) and
four other regions (superior [ICS], inferior [ICI], temporal
[ICT], and nasal [ICN]) located about 2 mm from the limbus.
Subjects were instructed to look head-on (primary position)
for measurement of ICC. For measurement of IC in the
peripheral corneal regions on the other hand, subjects were
instructed to look contralateral (secondary position) to the
measured region. For example, subjects were instructed to
look downward when measuring ICS. The peripheral corneal
measurements were achieved by having the subjects fixate
at the target on the wall. The order of the measurements
was random. To investigate the reproducibility of Icare
tonometry, an averaged IC (ICC) calculated from six
consecutive measurements was obtained three times (from
18 measurements) in the central corneal region. In this study,
median ICC was used for all analyses other than calculation
of coefficients of variation and intraclass correlation
coefficients. In the case of the superior, inferior, temporal
and nasal corneal regions, IC was measured only once (from
six consecutive measurements) to calculate ICS, ICI, ICT,
and ICN, respectively.

GT was then measured in the central corneal region using
a GAT (Haag-Streit, Koeniz, Switzerland). Finally, the central
corneal thickness and axial length of each study eye were
measured using an SP-2000 ultrasound pachymeter (Tomey,
Nagoya, Japan) and a UD-6000 ultrasonic A/B scanner
biometer (Tomey), respectively.

Coefficients of variation and intraclass correlation coeffi-
cients were calculated for the three consecutive measure-
ments of ICC. ICC, ICS, ICI, ICT, and ICN were compared
using a mixed model with IC as a fixed factor, and subjects
and laterality of eye (right/left = 51/51) as random factors.
The Bonferroni method was used for multiple comparison
adjustments.

Pearson correlation coefficients were calculated, and a
correlation matrix was prepared for the following parameters:
age, spherical equivalent refractive error, corneal radius, axial
length, central corneal thickness, GT, ICC, ICS, ICI, ICT,
and ICN. Differences between GT and IC were analyzed
using the Bland–Altman method.

To generate a model for predicting GT, multiple regres-
sion analysis was performed by the stepwise procedure, using
GT as the objective variable, and age, laterality of eye, spheri-
cal equivalent refractive error, corneal radius, axial length,
central corneal thickness, GT, ICC, ICS, ICI, ICT, and ICN
as explanatory variables. In addition, assuming there will be
instances where ICC cannot be calculated or where reliabil-
ity is clearly poor due to abnormal ocular rigidity, multiple
regression analysis was also performed without ICC as an
explanatory variable. When an explanatory variable with a
variance inflation factor exceeding 10 was present, another
model was generated without the explanatory variable.

All statistical analyses were performed using SPSS
17.0 J (SPSS Japan Inc, Tokyo, Japan) and MedCalc version
10.1 (MedCalc Software bvba, Mariakerke, Belgium). A significance level below 5% was considered to be statistically significant.

**Results**

A summary of the 102 eyes in 102 subjects in the present study is shown in Table 1. The average coefficient of variation of ICC was 8.8%. The intraclass correlation coefficient was 0.879.

ICS and ICN were significantly higher than ICC ($P < 0.001$ and $P = 0.003$, respectively), but there was no difference between any of the other regions. In terms of the correlation matrix of each parameter (Table 2), there was a strong positive correlation between GT and each IC. In addition, there was a significant correlation between the corneal radius and the central corneal thickness, and many ICs.

Differences of GT and IC using the Bland–Altman method are shown in Table 3. ICs were higher than GT in all of the corneal regions, but the IC with the least bias relative to GT was ICC (Figure 1), followed by ICT.

In multiple regression analysis using the stepwise procedure, GT was explained by the following formula:

$$GT = (0.445 \times ICC) + (0.198 \times ICN) + 3.022 \times (\text{coefficient of determination} = 0.636) \quad (1)$$

When approximated using only ICC, which had the highest coefficient of determination, GT was explained by the following formula:

$$GT = (0.530 \times ICC) + 5.196 \times (\text{coefficient of determination} = 0.599) \quad (2)$$

### Discussion

In the present study, the average of the coefficients of variation of ICC was 8.8%, and the intraclass correlation coefficient was 0.879. These are comparable to the findings (coefficient of variation: 8.9%, intraclass correlation coefficient: 0.73–0.87) reported from a study by Martinez-de-la-Casa et al11 carried out in subjects with glaucoma or ocular hypertension. Therefore, the IC measurements in this investigation have good reproducibility.

In the present study, ICS and ICN were significantly higher than ICC, but there were no differences between any of the other regions. There have been several reports in the past of IOP comparisons in the central and peripheral corneal regions. In a study using a GAT,12 there was no difference in GT between the central corneal region and the peripheral corneal regions. In studies using the Tono-Pen tonometer, no difference in IOP was reported between the central corneal region and peripheral corneal regions in one study,13 while IOP was slightly higher in the temporal corneal region as compared with the central corneal region in another study.14 A past study using Icare reported no difference in IOP between the central

### Table 1

| Summary of subjects (n = 102, male/female = 52/50, right eye/left eye = 51/51) |
|-----------------------------|-----------------|---------------------------------|-----------------|-----------------|
| Age (years) | 36.2 | 8.1 | 21 | 56 |
| Spherical equivalent refractive error (D) | −3.4 | 2.7 | −9.5 | 1.1 |
| Corneal radius (mm) | 7.9 | 0.3 | 7.2 | 8.6 |
| Axial length (mm) | 25.1 | 1.3 | 22.3 | 28.0 |
| Central corneal thickness (μm) | 554.4 | 39.8 | 456.0 | 651.0 |
| GT (mmHg) | 13.3 | 3.0 | 7 | 21 |
| ICC (mmHg) | 15.3 | 4.4 | 7 | 32 |
| ICS (mmHg) | 18.4 | 5.0 | 9 | 40 |
| ICI (mmHg) | 17.0 | 4.6 | 9 | 38 |
| ICT (mmHg) | 16.9 | 4.1 | 9 | 29 |
| ICN (mmHg) | 17.6 | 3.6 | 11 | 28 |

**Abbreviations:** GT, intraocular pressure measured by a Goldmann applanation tonometer; ICC, intraocular pressure in the central corneal region measured by Icare®; ICS, intraocular pressure in the superior corneal region measured by Icare®; ICI, intraocular pressure in the inferior corneal region measured by Icare®; ICT, intraocular pressure in the temporal corneal region measured by Icare®; ICN, intraocular pressure in the nasal corneal region measured by Icare®.

When ICC was excluded from the explanatory variables, GT was explained by the following formula:

$$GT = (0.203 \times ICT) + (0.159 \times ICS) + (0.215 \times ICN) + 3.166 \times (\text{coefficient of determination} = 0.447) \quad (3)$$

When approximated using only ICT, which had the highest coefficient of determination, GT was explained by the following formula:

$$GT = (0.451 \times ICT) + 5.695 \times (\text{coefficient of determination} = 0.360) \quad (4)$$
Table 2 Correlation matrix for each parameter

| Age, years | Spherical equivalent refractive error, D | Corneal radius, mm | Axial length, mm | Central corneal thickness, μm | GAT, mmHg | ICC, mmHg | ICS, mmHg | ICI, mmHg | ICT, mmHg | ICN, mmHg |
|------------|----------------------------------------|-------------------|-----------------|-------------------------------|---------|---------|---------|---------|---------|---------|
| 0.126 (0.209) | -0.147 (0.139) | 0.163 (0.101) | -0.177 (0.075) | -0.823 (0.000) | 0.232 (0.019) | 0.126 (0.209) | 0.163 (0.101) | -0.177 (0.075) | -0.823 (0.000) | 0.232 (0.019) |

Notes: *P < 0.01; †P < 0.05. Numbers in parentheses represent P values for each correlation coefficient.

Abbreviations: GAT, intraocular pressure measured by a Goldmann applanation tonometer; ICC, intraocular pressure in the central corneal region measured by icare®; ICS, intraocular pressure in the superior corneal region measured by icare® rebound tonometer according to Bland–Altman method; ICT, intraocular pressure in the temporal corneal region measured by icare®; ICN, intraocular pressure in the nasal corneal region measured by icare®.

Figure 1 Scatter diagram of means and differences between gT and iCC according to the Bland–Altman method. gT, intraocular pressure measured by a Goldmann applanation tonometer; iCC, intraocular pressure in the central corneal region measured using icare®. SD, standard deviation.

Table 3 Differences in intraocular pressure measured by the Goldmann applanation tonometer and intraocular pressure measured by the icare® rebound tonometer according to the Bland–Altman method.

| gT – ICC | Bias | Precision | Lower limits | Higher limits |
|---------|------|-----------|--------------|--------------|
| -2.0    | -1.31| 0.63      | -3.5         | 0.5          |
| -1.9    | -1.26| 0.57      | -3.1         | 0.3          |
| -1.8    | -1.21| 0.52      | -2.8         | 0.2          |
| -1.7    | -1.16| 0.48      | -2.5         | 0.4          |
| -1.6    | -1.11| 0.44      | -2.3         | 0.5          |

Notes: 100% confidence limits for the limits of agreement.
using subjects’ right and left eyes as random effects, thereby taking into account the effects of the differences between the right and left eyes on IC for comparison of IOP levels between corneal regions in the same cornea.

In the present study, there was a strong positive correlation between GT and IC, with the correlation between GT and ICC being the highest ($r = 0.777$). In a past report involving healthy subjects, the correlation coefficient between GT and ICC was 0.82. In a report involving patients with glaucoma or ocular hypertension, the correlation coefficient between GT and ICC was 0.865. The results of the present study are comparable to the results in these reports. In the present study, differences between GT and IC were investigated using the Bland–Altman method, which showed that the bias between GT and ICC was $-2.0$ mmHg, while that between GT and IC in the other corneal regions was $-3.6$ to $-5.1$ mmHg. Overall, these data indicate that IC was higher than GT at all corneal regions. These results are also comparable to a past report of healthy persons (bias (GT – ICC) = $-1.94$) and the results of a study involving patients with glaucoma or ocular hypertension (bias (GT – ICC) = $-1.8$). Based on these results, we concluded that IC correlates well with GT. However, since some differences were seen, some correction was needed to predict GT based on IC.

In the present study, generation of a model for predicting GT using the stepwise procedure, with each IC as well as age, laterality of eye, spherical equivalent refractive error, corneal radius, axial length, and central corneal thickness as explanatory variables, yielded Equation (1) above. ICC had the highest coefficient of determination with GT ($r^2 = 0.599$) and was selected as a significant explanatory variable. Moreover, the coefficient of determination did not decrease much, even when a model was generated with only ICC as an explanatory variable. Therefore, it is likely inferior to ICC measurements when trying to obtain consistency with GT measurements.

Parameters thought to be related to ocular rigidity such as corneal curvature radius and central corneal thickness were not selected as significant explanatory variables in these prediction models. According to past reports, corneal curvature radius and central corneal thickness were found to have a significant correlation with GT and ICC, and corneal curvature radius and central corneal thickness were found to have a significant correlation with GT and many ICs in the present study, as well. When generating a multiple regression model using the stepwise procedure, therefore, corneal curvature radius and central corneal thickness were believed to have acted as confounding factors with respect to the objective variable GT and the explanatory variable IC and been removed from the prediction model. Moreover, this revealed that corneal curvature radius and central corneal thickness data are not necessarily required when predicting GT with IC.

IOP decreases when it is measured consecutively with various tonometers, as in the case of IOP measurements by GAT, a phenomenon that was first pointed out during the development of the tonometer. Significant IOP-lowering effects as a result of consecutive measurements are not seen with Icare, or are less than those associated with consecutive measurements using a GAT. In the present study, IOP was measured with Icare before measurement with GAT, in order to partially prevent the IOP-lowering effects associated with consecutive measurements. However, it was reported that an IOP-lowering effect was seen with consecutive measurement of IOP with a rebound tonometer at the animal experiment level. In the present study, IOP was measured randomly in each of the corneal regions using Icare, but we cannot rule out the effects of changes in IOP that may have been caused by consecutive measurements.

In conclusion, of the ICs measured in the central or peripheral corneal regions, ICC was the closest to GT. In addition to ICC, GT could be explained better by generating
a prediction model using ICN. Moreover, in instances where ICC cannot be calculated or where reliability is clearly poor due to abnormal ocular rigidity, ICT was the closest to GT measured in the central corneal region.

Disclosure
The authors report no conflicts of interest in this work.

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