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ORIGINAL ARTICLE

Underestimation of intraocular pressure after photorefractive keratectomy: a biomechanical analysis

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Abstract Excimer laser surgery, to correct corneal refraction, induces changes in corneal thickness and curvature. Both factors can cause measurement errors when determining intraocular pressure (IOP). This study evaluates effects of photorefractive keratectomy (PRK) on IOP measurements, using Goldmann applanation tonometry (GAT) and Applanation resonance tonometry (ART), in an in vitro model. Six porcine eyes was enucleated and pressurised to a constant IOP = 30 mmHg. After removal of the epithelium, the eyes were PRK-treated for a total of 25 dioptres. The measured IOP decreased 13.2 mmHg for GAT and 9.0 mmHg for ART. The total underestimation by GAT was larger than for ART, and a part of the ART underestimation (3.5 mmHg) was assigned to sensitivity to the change in corneal surface structure resulting from the removal of epithelium. The flat contact probe of GAT, as compared with the convex tip of ART, provided explanation for the difference in IOP measurement error after PRK.

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Keywords Refractive correction · Laser · Applanation resonance tonometry · Goldmann applanation tonometry · Glaucoma · Measurement error · Eye

Abbreviations

GAT	Goldmann applanation tonometry
ART	Applanation resonance tonometry
PTK	Photo therapeutic keratectomy
PRK	Photo refractive keratectomy
PZT	Lead zirconate titanate
IOP	Intraocular pressure (mmHg)
IOP_{GAT}	IOP measured with GAT (mmHg)
IOP_{ART}	IOP measured with ART (mmHg)
IOP_{VC}	IOP in the vitreous chamber set by a saline column (mmHg)
CCT	Central corneal thickness (μm)
$CCT_{Pach\text{-}Pen}$	CCT measured with Pach-pen (μm)
ΔCCT	The difference between $CCT_{Pach\text{-}Pen}$ and CCT estimated from the expected ablanation (μm)
A	Contact area between cornea and sensor tip (mm^2)
D	Dioptres (m^{-1})
Q	Refractive power (D)
R	Corneal curvature (mm)
F_C	Contact force (mN)
$F_{Rigidity}$	Force related to corneal rigidity
$F_{Surface\ tension}$	Capillary forces related to the surface tension
f	Frequency (Hz)
β	Coefficients in the ART model
L	Applanation depth (mm)
L_f	Applanation depth related to ‘‘flowing’’ (mm)

dF_C	Change in contact force (mN)
df	Change in resonance frequency (Hz)
dL	Change in applanation depth (mm)
dA	Change in contact area (mm^2)
ρ	Radius of sensor tip curvature (mm)
λ	Proportionality constant between df/dL and dA/dL

1 Introduction

Measurement of the intraocular pressure (IOP) is part of the regular medical examination at an eye clinic. The estimate of the IOP is usually done with an indirect method that indentates or applanates a part of the cornea. The force needed to sustain the applanation of the cornea is related to the pressure inside the eye and is usually calibrated in mmHg. Goldmann applanation tonometry (GAT) is regarded as the golden standard. It is based on Imbert Fick's law which states that the force (F_C) required to applanate an area (A) of a sphere is equal to the pressure inside the sphere, i.e. the IOP, Eq. 1 [13]:

$$F_C = \mathrm{IOP} \times A. \tag{1}$$

Imbert Fick's law is valid under ideal conditions, which include an infinitely thin cornea with a dry surface and perfect elasticity. The human cornea does not meet these conditions. The cornea is a complex biomechanical system that introduces several errors into the measurement process. Goldmann recognised the rigidity of the cornea and the influence of the tear fluid [13]. Since those two parameters counteract each other, Goldmann used a predefined contact area of 7.35 mm^2, where the rigidity and tear surface tension force were balanced, Eq. 2:

$$F_C + F_{\mathrm{Surfacetension}} = \mathrm{IOP} \times A + F_{\mathrm{Rigidity}}. \tag{2}$$

Two prerequisites for correct GAT in an eye are normal central corneal thickness (CCT) and normal corneal curvature. If these factors are changed, several studies have shown that significant measurement errors will occur during the estimation of IOP with GAT [28].

Excimer laser surgery has become a common technique to correct refractive errors. Photo refractive keratectomy (PRK), Laser subepithelial keratectomy (LASEK), and Laser in situ keratomileusis (LASIK) are three methods that are frequently used. The laser induces a reduction of the corneal thickness and changes the corneal curvature. Both factors can cause measurement errors when determining IOP [19, 21, 28, 29], but their individual influences have not been clarified. Many studies have focused on the relationship between CCT and IOP [3, 4, 29]. In general, a thick cornea implies an increased contact force from the corneal rigidity and results in an overestimation of the IOP, Eq. 2. However, a thick cornea does not necessarily mean an overestimation. An oedematous cornea will give an increased CCT but an underestimation of the IOP because the spongy cornea has an increased compressibility [28]. In addition to thickness, curvature, and compressibility, the changes in elasticity have been shown in theoretical models to significantly affect the IOP reading [18, 24].

A well-known consequence of laser refractive surgery for myopia is an underestimation of the IOP measured with GAT [17, 25, 27]. However, the causes are not fully understood. For development of new tonometry methods that will give valid results for the growing population that has undergone laser surgery for correction of ametropia, it is important to understand the biomechanical system involved in the applanation process for determining IOP.

A new tonometry technique, applanation resonance tonometry (ART), has been developed [6]. ART uses Imbert-Fick's law to calculate the IOP and measures contact area with a resonator sensor device and the contact force with a force transducer, both mounted together in one probe [9, 15]. Measurement of IOP with ART has been evaluated in an in vitro (bench-based) pig eye set-up with high precision (SD = 0.9 mmHg) [9], in parity with results from in vitro evaluations of the Goldmann method [26]. The ART measures contact force (F_C) and contact area (A) continuously. In the in vitro model, the actual applanation depth during applanation can also be measured. The continuous recording of these physical parameters offers new possibilities to analyse the biomechanics during the applanation procedure. In this study, we utilised these possibilities to investigate the causes of underestimation of the IOP after PRK surgery.

The aim of this study was to evaluate biomechanical effects of PRK treatment and the resulting estimation errors on IOP measurements in an in vitro pig eye set-up. In doing so, we compared IOP measurement performed using GAT and ART.

2 Materials and methods

2.1 Animal

Six cadaver eyes from approximately 6-month-old Landrace pigs were enucleated immediately after the pigs were put to death at the abattoir (Swedish Meat, Ullånger, Sweden). The eyes were kept in saline and measurements were performed within 16 h after enucleation. The initial corneal curvature was measured with Orbscan II® (Bausch & Lomb Surgical Inc., San Dimas, CA, USA).

2.2 Goldmann applanation tonometry set-up

A fixture for a Petri dish was attached to the biomicroscope (Haag-Streit slitlamp, Bern, Switzerland) to place the eye in a similar position as a human eye in a sitting-patient position. Due to differences in corneal curvature and corneal rigidity between species, the tonometer was calibrated to match porcine eyes [2, 14, 20]. The calibration function for GAT was IOP = $1.14x+12.5$ [16], where x was the GAT reading of the IOP in the in vitro porcine eye set-up. The constant term showed that GAT can only be used if IOP exceeds 12.5 mmHg in this model [16].

2.3 Applanation resonance tonometry set-up

The ART probe was mounted on a servomotor-controlled lever and applied to the cornea of the eye with controlled velocity of 7 mm/s. Measurement of the contact area was based on a piezoelectric resonator sensor element that was made of lead zirconate titanate (PZT) (Morgan Electroceramics, Southampton, UK). A feedback circuit processed the signal from the element and powered the PZT in order to sustain the oscillations in the resonance frequency. At the back of the PZT element, a force transducer (PS-05KD, Kyowa, Tokyo, Japan) was mounted to receive the contact force, and at the opposite end of the PZT, a bakelite piece was applied for contact against the cornea. The contact surface of the piece was convex with a radius of curvature, ρ = 7 mm and diameter = 4 mm. When the contact piece touches the cornea of the eye, the resonance frequency changes. The amount of change depends on the contact area between the sensor and the cornea [7–10]. The sensor system output signals are the contact force and the shift of the oscillation frequency from the unloaded to the loaded condition, and they are sampled continuously during the applanation. The IOP was determined from the slope between contact force and frequency shift, Eq. 3:

$$\mathrm{IOP} = \beta_1 \frac{\mathrm{d}F_\mathrm{C}}{\mathrm{d}f} + \beta_0, \qquad (3)$$

where $\mathrm{d}F_\mathrm{C}$ was the change in contact force and df was the change in the resonance frequency, corresponding to a change in the contact area [9]. The beta-coefficients have been determined to β_1 = –312 mmHg Hz/mN (–41.5 Hz/mm^2) and β_0 = 2.5 mmHg (332.5 Pa). ART analyses an area interval determined throughout a frequency shift between –150 and –470 Hz (corresponding to an area of approximately 3.5–11 mm^2). The applanation depth (L) of the sensor was measured with an inductive position transducer [23] placed at the lever. Frequency, force, and position data were sampled with a data acquisition card, DAQCard-AI-16XE-50 (National Instrument Inc., Austin, TX, USA). The sampling rate was 1,000 Hz.

2.4 Photorefractive keratectomy

The porcine eyes were treated using two different ablation patterns. The procedures were performed using a Schwind Multiscan excimer laser (Schwind, Kleinostheim, Germany) with energy setting, 220 mJ/cm^2, and frequency, 13 Hz. First, the epithelium was ablated using photo therapeutic keratectomy (PTK) with an 8.0 mm ablation zone. The PTK laser treatment was finished when the characteristic change in the light reflex was seen. Subsequent PRK treatments were performed using a 7.0 mm ablation zone.

2.5 Method

To be able to keep the eye in a fixed position during measurements, the eye was fixed in the centre of a Petri dish with agar gel (15 g/dm^3). A winged, thin walled cannula (0.8 × 19.0 mm) was introduced through the side of the eyeball into approximately the middle of the vitreous chamber, and the cannula was connected to a saline column for pressurisation [7]. The interface between the cannula and the tissue was sealed with cyanoacrylate adhesive True Bond (Pro-Gruppen AB, Stockholm, Sweden) to avoid leakage [5]. The height of the saline column determined the intraocular pressure in the vitreous chamber ($\mathrm{IOP_{VC}}$). The CCT was measured with an ultrasound pachymeter ($\mathrm{CCT_{Pach\text{-}Pen}}$) (Pach-Pen XL, Mentor, Norwell, MA, USA).

On human eyes, mean CCT is about 534 μm [3], and usually, laser correction is less than 15 dioptres (D). Porcine eyes from a previous study had a mean of $\mathrm{CCT_{Pach\text{-}Pen}}$ of 842 μm [16], and we choose to use a corresponding correction of a total of 25 D.

The measurement sequence was: $\mathrm{CCT_{Pach\text{-}Pen}}$, $\mathrm{IOP_{GAT}}$, $\mathrm{IOP_{ART}}$, and then PRK laser treatment (Fig. 1). Ten measurements were performed using each procedure. The first sequence, *Treatment 0*, was measured on the unaffected cornea; the second sequence, *Treatment 1*, after the epithelium had been removed by the ex-

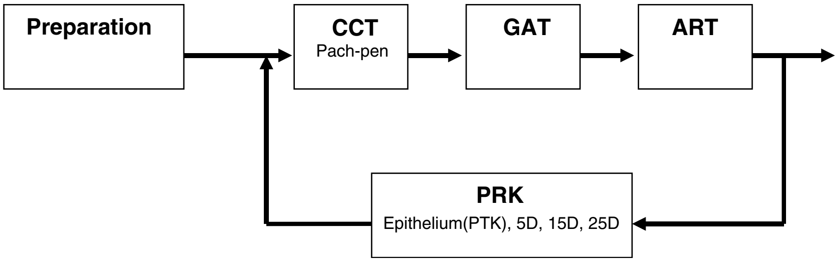

Fig. 1 After initial preparation, which including fixing the eye in a Petri dish and applying of the pressurisation device, there were a measurement- and treatment-loop. Central corneal thickness (*CCT*) was measured with a Pach-Pen pachymeter. The IOP was measured with Goldmann applanation tonometry (*GAT*) and Applanation resonance tonometry (*ART*). The eyes underwent photo-therapeutic treatment (*PTK*) followed by repeated photo refractive keratectomy (*PRK*) in three steps for a total correction of 25 *D*

cimer laser. The following sequences, *Treatments 2–4*, were measured after laser ablation in steps of 5, 10, and 10 *D*, respectively, a total of 25 *D* (Fig. 1).

Moistness of the cornea was maintained with saline, applied between applanations with a sweep of a soft goat-hair brush, Kreatima 922 (Schormdanner Pinsel, Nürnberg, Germany). The difference between $\mathrm{CCT}_{\text{Pach-Pen}}$ and CCT estimated from the expected ablanation of the excimer laser was defined as ΔCCT. Due to the GAT-limitation of only measuring IOP exceeding 12.5 mmHg in this model, together with an expected underestimation after laser correction [3, 17, 25, 29], all measurements were done at $\mathrm{IOP}_{\mathrm{VC}}$ = 30 mmHg.

2.6 Biomechanical model

A theoretic model where the cornea was assumed to be a perfect sphere (Fig. 2) was used to calculate the theoretical value of the differential relationship between the contact area, *A* and applanation depth, *L*, d*A*/d*L*. The contact area (*A*) of the ART was proportionally given as a frequency shift [7]:

$$f - f_0 = \lambda A + b, \tag{4}$$

where f_0 was the resonance frequency prior to contact, f was frequency at contact, λ the proportionality constant, and b an offset constant. A change in A corresponded to a proportional change in the frequency shift. Differentiation of Eq. 4 can be written:

$$\frac{\mathrm{d}f}{\mathrm{d}A} = \lambda. \tag{5}$$

With Eq. 3 and 5, λ can be identified from:

$$\mathrm{IOP} = \frac{\mathrm{d}F}{\mathrm{d}f}\frac{\mathrm{d}f}{\mathrm{d}A} + \beta_0, \tag{6}$$

which imply that:

$$\frac{\mathrm{d}f}{\mathrm{d}A} = \lambda = -41.5 \tag{7}$$

or,

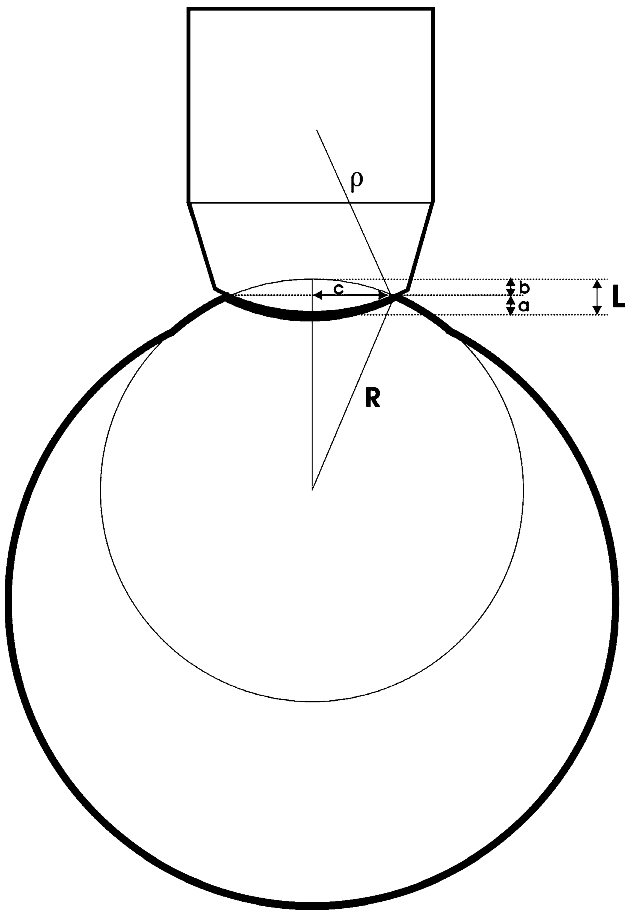

Fig. 2 The geometric relationships for the contact between the sensor tip and the cornea. The *large circle* represents the eyeball and the *small circle* represents the curvature of the cornea with radius *R*. The *upper part* of the drawing symbolises the sensor tip with a radius of curvature *ρ*. The sensor tip applanates the cornea with an applanation depth *L*

$$\frac{\mathrm{d}f}{\mathrm{d}L} = -41.5\frac{\mathrm{d}A}{\mathrm{d}L}. \tag{8}$$

The contact area (A) between the spherical sensor tip and the cornea can be described by:

$$A = 2\pi\rho a. \tag{9}$$

where ρ is the radius of sensor tip and a is the penetration as shown in Fig. 2. Given that a is separated from zero, the contact area of the sensor tip can be expressed as a function of the applanation depth, L, as:

$$A = \pi\rho L\frac{2R - L}{R + \rho - L}, \tag{10}$$

where R is the radius of corneal curvature [9]. The ablation of the cornea implies a change in R and therefore also a change in $\mathrm{d}A/\mathrm{d}L$. Differentiation of Eq. 10, with respect to L gives:

$$\frac{\mathrm{d}A}{\mathrm{d}L} = \pi\rho\frac{2R(R + \rho - L) + L(L - 2\rho)}{(R + \rho - L)^2}, \tag{11}$$

where R and ρ were the radius of the curvature from the cornea and the sensor tip, respectively (Fig. 2) [9]. The excimer laser corrects the vision by change of refractive power (Q). Refractive power can be related to corneal curvature [22] as:

$$Q = \frac{n_e - 1}{R}, \tag{12}$$

where n_e is the refractive index of the cornea. The refractive index was estimated with mean value (n = 6) of corneal curvature (R) and refractive power (Q) from the initial Orbscan analysis to $n_e = 1.34$. Using Eqs. 11 and 12, $\mathrm{d}A/\mathrm{d}L$ can be expressed as a function of Q after laser treatments:

$$\frac{\mathrm{d}A}{\mathrm{d}L} = \pi\rho\frac{2\frac{n_e-1}{Q_i}\left(\frac{n_e-1}{Q_i} + \rho - L\right) + L(L - 2\rho)}{\left(\frac{n_e-1}{Q_i} + \rho - L\right)^2}. \tag{13}$$

Q_i was calculated as initial refraction power Q_0 minus the correction (0, 5, 15, 25 D).

The contact area of the GAT probe, based on Fig. 2, can on a similar way be expressed as a function of applanation depth, L:

$$A_{\mathrm{GAT}} = \pi\left(2RL - L^2\right). \tag{14}$$

Differentiation of Eq. 14 with respect to L gives:

$$\frac{\mathrm{d}A_{\mathrm{GAT}}}{\mathrm{d}L} = 2\pi(R - L). \tag{15}$$

Using Eq. 12 to express R, and assuming that L was small compared with R, Eq. 15 can be written:

$$\frac{\mathrm{d}A_{\mathrm{GAT}}}{\mathrm{d}L} = 2\pi\frac{n_e - 1}{Q_i} \tag{16}$$

In addition, for the ART, both F_{C} and L were continuously sampled. Thus, the differential between contact force and applanation depth, $\mathrm{d}F_{\mathrm{C}}/\mathrm{d}L$, can be analysed and provide information of the biomechanics used for corneal applanation.

2.7 Statistics

Values were expressed as mean ± standard deviation (SD). Kolmogorov–Smirnoff test was used for normality analysis. One way ANOVA procedure with Bonferroni post hoc test was used to test for differences between groups and $p < 0.05$ was considered as statistically significant.

3 Results

Intraocular pressure was measured with GAT and ART on untreated porcine eyes, after PTK treatment and after each of the three consecutive PRK treatments, producing a total of five measurements. Mean of ten repeated measurement after each treatment was considered as one reading.

The measurements with GAT on eye no. 1 after *Treatments 3* and *4*, and eye no. 2 after *Treatment 4* produced no readings due to zero force needed to applanate full contact area and were therefore omitted.

Table 1 shows $\mathrm{CCT_{Pach\text{-}Pen}}$, ΔCCT, and measured IOP with both ART and GAT for each treatment level. Mean corneal curvature (R) and mean refractive power (Q) of untreated eyes were 8.88 ± 0.36 mm (n = 6) and 38.1 ± 1.5 D (n = 6), respectively (Orbscan analysis).

At measurements on unaffected eyes, *Treatment 0*, $\mathrm{IOP_{ART}}$ showed a mean non-significant difference as compared to $\mathrm{IOP_{VC}}$ of 0.7 mmHg (p = 0.30). $\mathrm{IOP_{GAT}}$ overestimated the $\mathrm{IOP_{VC}}$ by 2.2 mmHg ($p < 0.01$), Table 1.

Treatment level 1, removal of the 88 μm epithelium, was done without any change to the corneal curvature. Epithelial removal resulted in an underestimation of $\mathrm{IOP_{ART}}$ by 3.5 mmHg (p = 0.04), whereas the GAT

Table 1 Mean value and SD of six eyes (ten repetitions at each treatment level)

Treatment level	Dioptres	CCT (SD) μm	Ablation μm	ART(SD) mmHg	*n*	GAT (SD) mmHg	*n*
0	0	871 (18)	0	29.3 (1.5)	6	32.0 (07)	6
1	0 (epith)	751 (13)	88	25.8 (1.8)	6	32.2 (0.8)	6
2	5	744 (32)	165	25.7 (1.3)	6	32.0 (1.6)	6
3	15	685 (50)	311	21.3 (1.4)	6	25.0 (2.9)	5
4	25	625 (84)	457	20.3 (3.1)	6	19.0 (3.7)	4

Note that the measured CCT do not correspond to the ablation

reading was unaffected ($p = 1.00$) as compared with measurements at *Treatment 0*, Table 1 (Fig. 3).

The 5-*D* correction, *Treatment 2*, corresponded to an additional ablation of 77 μm. However, as compared to the previous measurements after *Treatment 1*, there were no significant changes in IOP_{ART} and IOP_{GAT} ($p = 1.00$ for both).

After a further correction of 10 *D*, *Treatment 3*, corresponded to a further ablation of 146 μm. IOP_{ART} was 21.3 mmHg and $IOP_{GAT} = 25.0$ mmHg, i.e. *Treatment 3* caused significant decrease in the measured IOP by 4.3 ($p = 0.01$) and 7.0 ($p < 0.01$) mmHg, respectively.

The last correction, *Treatment 4*, of 10 *D*, was done with an ablation of 146 μm. IOP_{ART} showed no significant difference as compared with *Treatment 3* ($p = 1.00$). The additional underestimation of IOP_{GAT} as compared with *Treatment 3* was 6.0 mmHg ($p < 0.01$).

3.1 Biomechanical considerations

Figures 4 and 5 both show measured and calculated values of $\mathrm{d}A/\mathrm{d}L$ and $\mathrm{d}F_C/\mathrm{d}L$, for each treatment level, i.e. how changes in contact area and contact force were related to changes in applanation depth. The $\mathrm{d}A/\mathrm{d}L$, for ART (Fig. 4, filled squares) was significantly affected by treatment (ANOVA, $p < 0.05$). The estimated $\mathrm{d}A/\mathrm{d}L$ based on the model, Eq. 13, is shown in Fig. 4 as open squares.

The $\mathrm{d}F_C/\mathrm{d}L$ from ART, showed no significant dependency on the different treatments (ANOVA, $p = 0.86$). Theoretical calculations of $\mathrm{d}F_C/\mathrm{d}L$ was based on Eq. 3 and the model for $\mathrm{d}A/\mathrm{d}L$ (Eq. 13) that is:

$$\frac{\mathrm{d}F}{\mathrm{d}L} = (IOP_{VC} - \beta_0)\frac{\mathrm{d}A}{\mathrm{d}L} \tag{17}$$

with a constant $IOP_{VC} = 3{,}990$ Pa (30 mmHg) and $\beta_0 = 332.5$ Pa, shown as open squares in Fig. 5.

4 Discussion

To our knowledge, this is the first study that investigates the relationship between repeated PRK and errors in IOP measurement with applanation tonometers. We found that accuracy with both ART and GAT was affected by PRK treatment, but to a different extent.

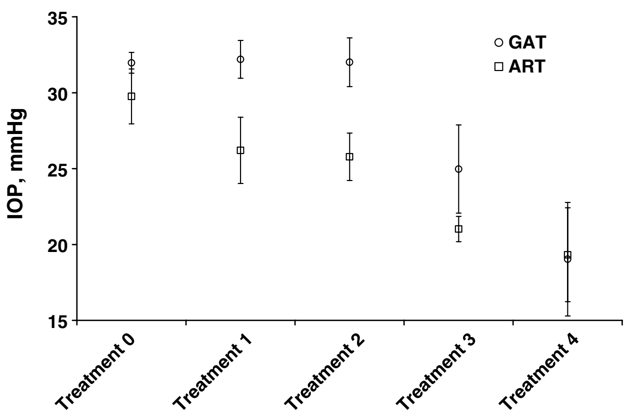

Fig. 3 Intraocular pressure measured with GAT and IOP_{ART} versus treatment for six eyes (mean ± SD). *Treatment 0* represents unchanged eye, *Treatment 1* represents epithelium removal from the cornea. *Treatment 2, 3*, and *4* were laser corrections for a total of 5, 15, and 25 *D*, respectively

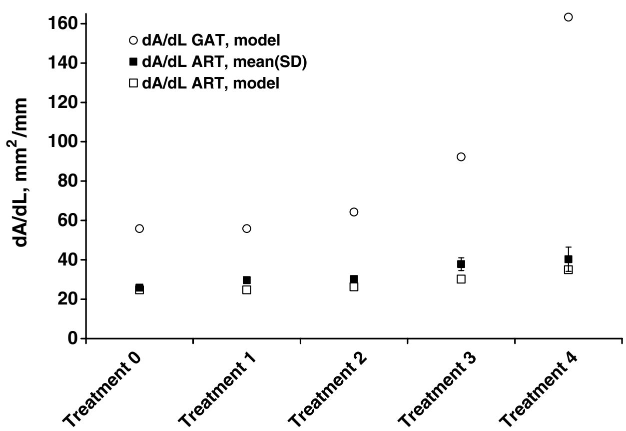

Fig. 4 Ratio between contact area (*A*) and applanation depth (*L*) as a function of treatment. Measured values from ART are shown as open squares. Calculated values for GAT (*open circles*) and ART (*open squares*) are based on a model

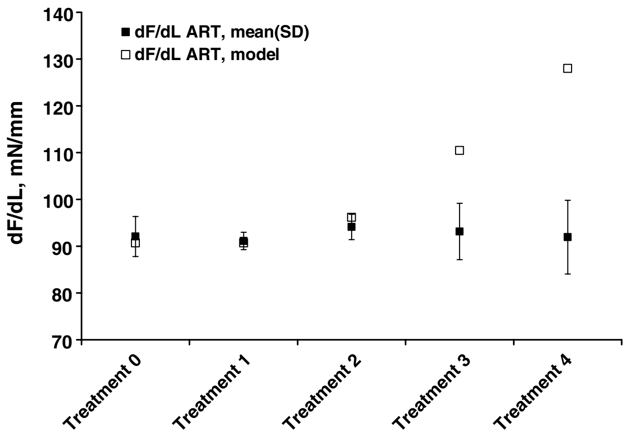

Fig. 5 Ratio between change in contact force (F_C) and applanation depth (L) for ART. Measured (*filled symbols*) and calculated (*open symbols*) values are plotted against treatment. The calculated values were based on Eq. 16

It has been shown that a thin cornea might cause an underestimation of the IOP and that photorefractive laser correction of myopia also might cause an underestimation by more than 10 mmHg when using GAT [4, 25]. Feltgen et al. [11] performed a clinical study on CCT and errors in applanation tonometry with Perkins tonometer and Tonopen on 73 human eyes with intracameral IOP as reference, but found no correlation. This ambiguousness emphasises the importance of understanding the underlying biomechanics when estimating the IOP with applanation tonometry. A number of recently presented studies regarding IOP measurement on laser treated eyes have compared GAT with Pascal tonometry, Pneumatonometry, or Tonopen [1, 12, 17]. These studies show a similar pattern as our finding and confirm that GAT is sensitive to changes in the biomechanics. Thus, different applanation tonometry methods are affected in different ways by the biomechanical change induced by photorefractive laser correction.

The total underestimation by GAT was larger than for ART, but ART was more sensitive to changes in corneal surface structure than GAT. GAT was almost unaffected after a correction of 5 D and an obvious oedema effect, Table 1, two factors that should entail an underestimation [28]. A possible explanation for the lack of an underestimation after epithelium removal is that after the hydrophobic epithelium had been removed, it might have increased the moistness of the surface. Additional fluid between the cornea and the sensor tip decrease the attractive capillary forces, resulting in a compensating overestimation of the IOP (Eq. 2). In clinical use, the semicircles used to determinate applanated area with GAT are quite distinct, and the IOP is estimated when the semicircles inner edges touch each other. The optical semicircles, in the porcine model, were indistinct and were almost filled, which supports the suggestion of increased fluid on the cornea. Thus, we have to expect a poorer precision for the GAT readings under these experimental conditions.

In this study, we were able to analyse contact force, contact area, and applanation depth during the measurements of IOP. This unique option was used to investigate their relationship to changes in corneal curvature and thickness accomplished under controlled conditions by repeated PRK treatments. How contact force and contact area relates to a change in sensor position on the cornea gives insight into the biomechanics of the applanation.

When the epithelium was removed, it did not influence the IOP_{GAT} readings, but the IOP_{ART} dropped from 29.3 to 25.8 mmHg (Fig. 3). In comparison with differential applanation depth, we conclude that from the same treatment, df/dL increased by 15% (from 1,070 to 1,226 Hz/mm; Fig. 4). *Treatment 1* did not imply any change in corneal curvature (only uniform removal of the epithelium); thus, the same contact area produced a 15% higher frequency shift due to a change in corneal surface structure and a minor reduction of the CCT. This change in the area-frequency relationship corresponds to a decrease of the estimated IOP 3.8 mmHg, i.e. very close to the measured underestimation of 3.5 mmHg (Table 1). We believe that the increased df/dL relates to a more effective acoustic contact between the sensor tip and the underlying tissue as compared with contact against the epithelium. However, in a clinical situation, there will always be an epithelium. Hence, for the biomechanical analysis, it is justifiable to use IOP measurements after *Treatment 1* as a baseline.

After epithelium removal, a total correction of 25 D caused the IOP_{ART} readings to decrease from 25.8 to 20.3 mmHg, Table 1. The corresponding value for GAT was a decrease from 32.2 to 19.0 mmHg, i.e. more than twice as much as the ART.

We have identified two major factors which could explain the difference in response to PRK between the methods: (1) GAT uses a flat contact surface and ART a convex surface, and (2) GAT uses a one-point reading of contact force and contact area while ART uses a multipoint approach. This could affect the readings, e.g. GAT always assumes that the corneal rigidity and the capillary forces from the tear fluid-surface tension cancel out each other, Eq. 2, and that IOP_{GAT} can be determined as proportional to F_C/A, according to Imbert Fick's law (Eq. 1). The pre-defined contact area is reached with an applanation force, set by the operator. It is a one-point reading marked with X on a line through the origin, dashed line in Fig. 6. ART uses continuous sampling of contact force and contact area. During a pre-defined area interval (frequency shift interval between –150 and –470 Hz), filled dots in Fig. 6, the slope between force- and frequency-shift was interpreted as proportional to the IOP_{ART}. The IOP_{ART} is only dependent on the force and area relationship within the analysis interval, i.e. constant forces that imply a parallel move of the slope do not affect the estimation of IOP_{ART}.

The measured dA/dL increased with 15% after the epithelium was removed. In exception of the 15%, the measured value showed almost no difference as compared with the expected dA/dL from the model (Fig. 4), i.e. the biomechanical model agreed well with the measured values. This supports the biomechanical model as well as the explanation of a more effective acoustic contact after the removal of the epithelium.

In addition to IOP_{VC}, dF_C/dL reflects the rigidity of the cornea depending of the tissue stiffness, and also, the capillary forces from the tear fluid. The IOP_{VC} was constant during the study. Change in corneal curvature made the dA/dL increase (Fig. 4). If the rigidity and capillary forces were constant, and no corneal oedema occurred, dF_C/dL should have increased at the same rate as dA/dL to measure constant IOP. However, dF_C/dL of ART did not change with *Treatments* in this study (Fig. 5). Both an increasing oedema and a decrease of the corneal rigidity as a consequence of the PRK, imply a, as expected, decrease of dF_C/dL. However, in a clinical situation, the epithelium would be re-grown over the cornea and the oedema effect would be negligible. Therefore, the underestimation of the IOP should be reduced.

The flat contact probe of GAT, as compared with the convex tip of ART, might provide distinction in measurements of IOP with respect to a change in corneal curvature. Both Goldmann and Moses found that a continuous contact with the cornea implies a decline of the IOP reading due to a corneal change they describe as ''flowing'' [13, 20]. Flowing assumes a small displacement of extra cellular fluid inside the cornea during applanation. It would imply a contraction of the CCT, i.e. an applanation not related to the IOP. For the purpose of estimating the effect of ''flowing'', let us assume a contraction of 2%. Since CCT in our study was 0.87 mm, a 2% contraction will be equivalent to an applanation depth due to contraction of $L_f = 0.017$ mm. For GAT at *Treatment 0*, this corresponded to a contact area of 0.98 mm^2 (calculated as $L_f \cdot dA/dL$, Eq. 13, Fig. 4), which was 13% of the total contact area. After *Treatment 4*, with a much higher dA/dL, due to the change in corneal curvature, the same contraction corresponded to a contact area of 2.86 mm^2. This means that 39% of the total applanated area was due to a contraction and not directly related to the IOP. ART is less affected by contraction of the cornea since the analysis method is independent of the initial phase of the force and frequency slope (Fig. 6). A contraction of the cornea mainly implies that the analysis interval is moved, i.e. the contact areas from ''flowing'' cause a parallel move of the curve but the IOP result is the same. Furthermore, the convex tip makes the change in dA/dL much less for the ART (Fig. 4), which makes the corresponding area from contraction, $L_f \cdot dA/dL$, only increased from 0.42 to 0.60 mm^2 with respect to treatment 0 and 4, respectively. Therefore the changes in corneal curvature have much smaller effect when using ART as compared with

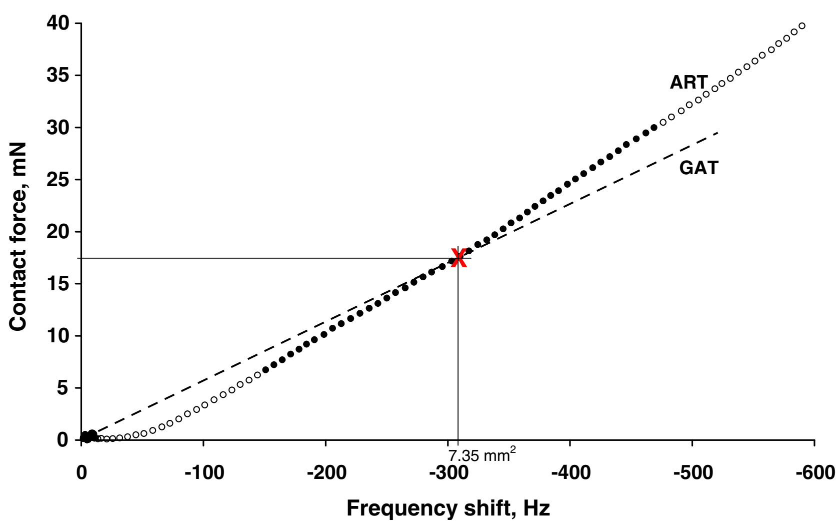

Fig. 6 Typical measurement of IOP_{ART} after Treatment 1, dotted line, with continuous sampling of contact force and contact area (throughout the frequency shift). Analysis interval was a frequency shift between –150 and –470 Hz (filled dots) and corresponds to a contact area of approximately 4–11 mm^2. The slope in that interval was considered as proportional to IOP. Goldmann uses a pre-defined contact area of 7.35 mm^2 and adjusts the force needed to reach that area, marked with X

GAT. Although the numerical assumption of a 2% flowing contraction is not verified, and we have not compensated for the change in CCT from treatment, the analyses clearly point out a difference between the methods and a possible explanation for the IOP results.

The increasing variation of corneal thickness in the later treatment sessions, Table 1, indicated corneal oedema due to the removal of the hydrophobic epithelium. The two first eyes required more total time (approximately 1.8 h) as compared with the remaining eyes (1.1–1.3 h) to accomplish the measurement sequence, which could also help explain the increase of SD in $CCT_{Pach\text{-}Pen}$. Another clear sign of oedema was the measurement of $CCT_{Pach\text{-}Pen}$, which showed at 25 *D* that the reduction on CCT was only 50% of the expected reduction from the ablation, Table 1. A dehydrating solution would probably have reduced the oedema effect, but may have damaged the cornea and caused changes in the corneal tissue.

This study had its limitations: it was performed in vitro by using an animal model, and pressure was measured after removal of the epithelium. However, the results reflect the importance of corneal curvature on the biomechanics related to IOP measurement with applanation technique, and should be confirmed in clinical studies.

5 Conclusions

This study showed that the accuracy with both ART and GAT was affected by PRK treatment, but to a different extent. The total underestimation by GAT was larger than for ART, but ART was more sensitive to changes in corneal surface structure than GAT. The flat contact probe of GAT, as compared with the convex tip of ART, and single point versus multipoint approach, might provide explanation for the difference in measurement error of IOP after PRK. Furthermore, how contact force and contact area relate to a change in applanation depth on the cornea gives insight into the biomechanics of the applanation and can be useful in modelling of the applanation.

References

1. Bhan A, Browning AC, Shah S, Hamilton R, Dave D, Dua HS (2002) Effect of corneal thickness on intraocular pressure measurements with the pneumotonometer, Goldmann applanation tonometer, and tono-pen. Invest Ophthalmol Vis Sci 43:1389–1392
2. Cohan BE, Bohr DF (2001) Goldmann applanation tonometry in the conscious rat. Invest Ophthalmol Vis Sci 42:340–342
3. Doughty MJ, Zaman ML (2000) Human corneal thickness and its impact on intraocular pressure measures: a review and meta-analysis approach. Surv Ophthalmol 44:367–408
4. Ehlers N, Brahmsen T, Sperling S (1975) Applanation tonometry and central corneal thickness. Acta Ophthalmol 53:34–43
5. Eisenberg DL, Sherman BG, Mckeown CA, Schuman JS (1998) Tonometry in adults and children. A manometric evaluation of pneumatonometry, applanation, and TonoPen in vitro and in vivo. Ophthalmology 105:1173–1181
6. Eklund A (2002) Resonator sensor technique for medical use—an intraocular pressure measurement system. Umeå University, Umeå
7. Eklund A, Backlund T, Lindahl OA (2000) A resonator sensor for measurement of intraocular pressure—evaluation in an in vitro pig-eye model. Physiol Meas 21:355–367
8. Eklund A, Bergh A, Lindahl OA (1999) A catheter tactile sensor for measuring hardness of soft tissue: measurement in a silicone model and in an in vitro human prostate model. Med Biol Eng Comput 37:618–624
9. Eklund A, Hallberg P, Lindén C, Lindahl OA (2003) Applanation resonance sensor for measuring intraocular pressure—a continuos force and area measurement method. Invest Ophthalmol Vis Sci 44:3017–3024
10. Eklund A, Lindén C, Backlund T, Andersson B, Lindahl OA (2003) Evaluation of applanation resonator sensors for intraocular pressure measurement, results from clinical and in vitro studies. Med Biol Eng Comput 41:190–197
11. Feltgen N, Leifert D, Funk J (2001) Correlation between central corneal thickness, applanation tonometry, and direct intracameral IOP readings. Br J Ophthalmol 85:85–87
12. Garzozi H, Chung H, Lang Y, Kagemann L, Harris A (2001) Intraocular pressure and photorefractive keratectomy: a comparison of three different tonometers. Cornea 20:33–36
13. Goldmann H (1957) Applanation tonometry. In: Newell FW (eds) Glaucoma, transactions of the second conference. Josiah Macy Jr. Foundation, New York, pp 167–220
14. Green K (1990) Techniques of intraocular pressure determination. Lens Eye Toxic Res 7:485–489
15. Hallberg P, Lindén C, Lindahl OA, Bäcklund T, Eklund A (2004) Applanation resonance tonometry for intraocular pressure in humans. Physiol Meas 25:1053–1065
16. Hallberg P, Lindén C, Lindahl OA, Bäcklund T, Eklund A (2006) Comparison of Goldmann applanation- and applanation resonance tonometry in a vertical in vitro porcine-eye model. J Med Eng Technol (in press)
17. Kaufmann C, Bachmann LM, Thiel MA (2003) Intraocular pressure measurements using dynamic contour tonometry after laser in situ keratomileusis. Invest Ophthalmol Vis Sci 44:3790–3794
18. Liu J, Roberts CJ (2005) Influence of corneal biomechanical properties on intraocular pressure measurement: quantitative analysis. J Cataract Refract Surg 31:146–155
19. Mark H (1973) Corneal curvature in applanation tonometry. Am J Ophthalmol 76:223–224
20. Moses RA (1958) The Goldmann applanation tonometer. Am J Ophthalmol 46:865–869
21. Munger R, Dohadwala AA, Hodge WG, Jackson WB, Mintsioulis G, Damji KF (2001) Changes in measured intraocular pressure after hyperopic photorefractive keratectomy. J Cataract Refract Surg 27:1254–1262
22. Olsen T (1986) On the calculation of power from curvature of the cornea. Br J Ophthalmol 70:152–154
23. Omata S, Terunuma Y (1992) New tactile sensor like the human hand and its applications. Sens Actuators 35:9–15

24. Orssengo GJ, Pye DC (1999) Determination of the true intraocular pressure and modulus of elasticity of the human cornea in vivo. Bull Math Biol 61:551–572
25. Rosa N, Cennamo G, Breve MA, La Rana A (1998) Goldmann applanation tonometry after myopic photorefractive keratectomy. Acta Ophthalmol Scand 76:550–554
26. Schmidt T (1957) Zur applanationtonometri an der spaltlampe. Ophthalmologica 133:337–342
27. Siganos DS, Papastergiou GI, Moedas C (2004) Assessment of the Pascal dynamic contour tonometer in monitoring intraocular pressure in unoperated eyes and eyes after LASIK. J Cataract Refract Surg 30:746–751
28. Whitacre MM, Stein R (1993) Sources of error with use of Goldmann-type tonometers. Surv Ophthalmol 38:1–30
29. Whitacre MM, Stein RA, Hassanein K (1993) The effect of corneal thickness on applanation tonometry. Am J Ophthalmol 115:592–596