Intraocular Pressure Measurement after Photorefractive Keratectomy: Does Contact Area Matter?

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Abstract

Background: Refractive laser surgery induces substantial changes in corneal structure, causing inaccurate intraocular pressure (IOP) readings. Pascal dynamic contour tonometry (PDCT) and Icare rebound tonometer (RBT) are two novel devices that do not depend on applanation to measure IOP. Purpose of this prospective study was to compare PDCT and rebound tonometry versus Goldmann tonometry (GAT) in a group of patients who underwent photorefractive keratectomy (PRK).

Methods: Central corneal thickness and IOP were measured in 54 eyes before and after PRK. All IOP measurements were taken by the same examiner, using PDCT, RBT and GAT in a randomised, masked fashion.

Results: After excimer laser surgery, PDCT measurements were higher than GAT \( (p<0.0001) \) and RBT \( (p=0.0012) \). Multiple linear regression analysis indicated that size of contact area was significant \( (b=-0.504; p=0.0001) \) while corneal thickness was not \( (b=0.003; p=0.169) \). Bland-Altman test showed that there was good agreement between RBT and PDCT \( (p=0.454) \), whereas GAT gave lower IOP values than both RBT \( (p=0.0103) \) and PDCT \( (p=0.0031) \).

Conclusion: PDCT and RBT are less dependent on iatrogenic corneal changes than GAT and this might be related to their small contact area. In order to minimise IOP underestimation after excimer laser surgery, the clinician should consider adopting non-applanation tonometers like RBT and PDCT as an alternative to GAT.

Keywords: Corneal transplant; Penetrating keratoplasty; Graft rejection; Systemic immunosuppression

Introduction

Intraocular pressure (IOP) measurement plays an important role in glaucoma diagnosis and management and the quest for a rapid, accurate, reliable method to measure IOP is still ongoing. Goldmann applanation tonometry (GAT) is currently the gold-standard but over the years a number of alternatives have been introduced on the market, each trying to address a specific GAT shortcoming (portability, infection risk, operator learning curve, etc.).

In particular, patients who underwent laser corneal refractive surgery pose a challenge for tonometers based on corneal applanation techniques. Laser refractive surgery causes significant changes in the corneal surface profile and its thickness and therefore altering corneal biomechanics and GAT accuracy [1,2]. Taking into account the number of patients who underwent laser refractive surgery since its introduction in 1983 and now should be screened for glaucoma, there is increasing demand for an accurate and reliable test in order to avoid delays in glaucoma diagnosis, with potentially serious consequences.

Icare (Tiolat Oy, Helsinki, Finland) is a hand-held, rebound tonometer (RBT) with a 1-mm-diameter tip. It contains a solenoid mechanism that launches a magnetised probe and detects its deceleration when it impacts on the cornea [3,4]. Main advantages of RBT over GAT are its hand-held format, its ease of use also for non-experienced tonometrists [5] and its tolerability without the need for topical anaesthetic, making it an attractive option also for paediatric use [6]. On the other side, to date there are no studies that tested its accuracy and reliability in post-laser refractive surgery patients.

Pascal DCT (PDCT) tonometers (Swiss Microtechnology AG, Ziemer Ophthalmics, Port, Switzerland) provide a trans-corneal IOP measurement using the principle of contour-matching. The PDCT is mounted on a slit-lamp and utilises a pressure sensor embedded within a concave disposable tonometer tip (1.2 mm diameter), shaped like a tight-fitting shell. Once the central cornea has taken up the shape of the tip, the integrated pressure sensor begins to acquire IOP measurements (at the rate of 100 per second). The main advantage of PDCT is its accuracy, as PDCT values seem not to be influenced by central corneal thickness (CCT), corneal curvature and other corneal biomechanical factors [7,8]. Intuitively, the larger the contact area with the cornea, the higher the possibility of a mismatch between the corneal surface profile and the tip of the tonometer lower. If this were true, then we wondered if smaller tonometry tips would be less influenced by changes in corneal properties. Aim of our study is firstly to compare RBT and PDCT versus GAT in post-refractive surgery patients, as it has not been reported before. Secondly, we aimed to verify whether smaller contact areas are truly less affected by variations in corneal characteristics, as reported by previous studies.

Materials and Methods

Patient selection

All new myopic patients referred for excimer laser surgery at the Eye Department, University Hospital of Bari, Italy, between January

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and June 2009 were eligible for the study. The study received approval from the University Ethics Committee. Exclusion criteria were: age below 18 years, presence of corneal abnormalities that might affect IOP measurements (e.g. severe epithelial/stromal oedema, large central scars) or might represent a risk factor for corneal abrasions following application tonometry (e.g. corneal dystrophies), active ocular infective disease, blepharospasm, previous ocular surgery, history of glaucoma or presence of either disc cupping or visual field defects, IOP measurements higher than 21 mmHg at the first visit, attempted myopic correction lower than −3 D and above −9 D, astigmatism, if present, above 3 D, patient preference for other refractive procedures, poor subject cooperation, participation to other trials, hospital inpatient status, refusal to participate. A total of 54 patients (54 eyes) met the above-mentioned criteria and entered the study. Informed consent according to the tenets of the Declaration of Helsinki was obtained from each patient.

All patients were told to stop using soft contact lenses at least 2 weeks before PRK. After obtaining informed consent, each patient was examined by one experienced investigator (MV). The examination included measurement of CCT using Pachmate DHG55 pachymeter (DGH Technology, Inc, Exton, PA, USA) and application tonometry. Only one eye was included in the study and the laterality was chosen at random, following a computer-generated list. The investigator measured the IOP three times, using the standard GAT, RBT and PDCT. GAT and RBT tonometers were used three times and an average IOP measurement was calculated from each triplet of data. This procedure was not repeated for PDCT, as the instrument displayed an averaged measurement directly, taken from six “shots”. In order to avoid errors and bias, the three devices were used according to a pre-determined, computer-generated random list and the measurements were taken at ten-minute intervals.

For GAT, the IOP was measured on the slit-lamp microscope after instillation of a drop of oxybuprocaine and fluorescein sodium 0.25% preservative free solution. One ophthalmologist (FP) sat at the slit-lamp and looked through the eyepiece, carrying out the IOP measurement without looking at the dial. Another ophthalmologist (VM) stood nearby and entered the IOP measurements in a datasheet, returning the GAT dial to zero after each measurement. All IOP measurements were performed between 10 and 12 am.

Within a fortnight from the pre-assessment visit, all patients underwent routine PRK procedure using a third-generation laser device (Laserscan 2000, Laserglight, Orlando, FL). This laser reprofiled corneal surface by means of a computer-assisted scanning delivery system (flying spot), which is able to extend optic zone diameter up to 9 mm. Other technical features included: repetition rate of 100 Hz, beam diameter of 1 mm and fluence of 160 mJ/cm². The laser ablation algorithm allowed the operator to perform corneal ablations using a singlepass multizone technique; the number of zones and ablation algorithm allowed the operator to perform corneal ablations according to a pre-determined, computer-generated random list and the measurements were taken at ten-minute intervals. Further safety devices were the active eye-tracker, that centered the ablation over the pupil automatically and the internal power stabilizer that ensured an uniform delivery of energy throughout PRK treatment. Moreover, the ablation and beam profile characteristics were tested at the beginning of each treatment day and they were checked up every 2 treatments.

Topical analgesia was achieved by instilling one drop of 0.4% oxybuprocaine hydrochloride (Novesina, Sandoz, Italy) and repeating the instillation 5 minutes later. After the insertion of a lid speculum, the patient was invited to fixate a blinking green light in axis with the laser beam and then the eye tracker was switched on. After the marking of the ablation zone, the epithelium was removed using a 20% alcoholic solution. On completion of the surgical treatment, the ablated surface was moistened with a drop of netilmicine (Nettacin, SIFI, Catania, Italy) and 0.03% flurbiprofen sodium preservative-free drops (Ocufen 40 monodose, Allergan, Rome, Italy) before a soft contact lens was applied (Acuvue, Johnson and Johnson Prod. Inc, Jacksonville, FL). Topical ketorolac and tetracycline-betamethasone-naphazoline association were prescribed 4 times a day until epithelialization. After this first postoperative phase, our protocol includes 0.1% fluorometholone eyedrops (Fluaton PVA, Allergan, Rome, Italy) 4 times a day for 4 weeks and then with decreasing frequency every 20 days [9]. The whole examination procedure, including repeating tonometry with the three methods, was reproduced at the final post-operative visit (three months after PRK). No IOP lowering agents were prescribed at any point during the study.

### Statistical analysis

Statistical analysis was performed using SAS 9.1 statistical software. P values of <0.05 were considered as statistically significant. Differences in IOP among tonometers were compared using a multilevel model (two hierarchical levels, namely patients and laterality, i.e. right/left). Tonometer type and time to surgery were considered fixed-effect covariates. Multiple comparisons were performed comparing between methods and within methods with least mean square estimation obtained from the multilevel model, with p-value adjusted for multiple comparisons. The effect of area size of tonometer on IOP was evaluated with a multiple linear regression model, assuming 3.06 mm² for GAT, 1.2 mm² for PDCT and 0.65 mm² for RBT. Agreement between two tonometers were evaluated with the Bland-Altman method, i.e. plotting the difference between two methods against their average and linear regression (mean Vs difference).

### Results

Overall, 54 patients (54 eyes, 24 females) entered the study. Mean age was 31 ± 6.7 years. Mean IOP measurements are shown in Table 1. Mean CCT measurements were 517 ± 51.3 µm (pre-operatively) and 389 ± 54.17 µm (post-operatively). Laterality had no significant effect on IOP measurements (p=0.07), while variables having a significant effect on IOP were tonometer type (F=25.54, <0.0001), time relation to surgery (i.e. being pre- or post-operative measurements, F=14.49, p=0.0002) and their interaction (F=3.11, p=0.046).

ANOVA test showed that a significant difference among tonometers existed already before (p=0.035) and after excimer laser surgery (p=0.004). Multiple comparison tests indicate that GAT measurements were significantly lower than PDCT preoperatively (p=0.005), while there was no difference between RBT/PDCT and GAT/RBT. After surgery, PDCT measurements were higher than GAT (p<0.0001) and RBT (p=0.0012). Moreover, we also compared the

<table>
<thead>
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<th></th>
<th>GAT (mmHg)</th>
<th>RBT (mmHg)</th>
<th>PDCT (mmHg)</th>
<th>p-value (ANOVA)</th>
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<tbody>
<tr>
<td>Preoperative IOP</td>
<td>14.1 ± 1.96</td>
<td>14.8 ± 1.96</td>
<td>15.0 ± 1.71</td>
<td>0.035</td>
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<tr>
<td>Postoperative IOP</td>
<td>14.6 ± 2.16</td>
<td>15.3 ± 2.7</td>
<td>16.3 ± 2.94</td>
<td>0.004</td>
</tr>
<tr>
<td><em>p-value</em> (paired <em>t</em>-test)</td>
<td>0.062</td>
<td>0.092</td>
<td>&lt;0.001</td>
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**Table 1**: Average and SD of IOP measurements before and after PRK.
pre- and postoperative values for each tonometer with paired t-test. While there was no significant difference for GAT and RBT, PDTC values were higher after excimer laser surgery (p<0.0001). On the other hand, there was no significant association between CCT and IOP (b=0.003; p=0.169). Bland-Altman test results between GAT and RBT are shown in Figure 1. There was good agreement between methods before surgery without proportional bias (b=0.01; p=0.9339; Figure 1a). After surgery, regression test showed a steep slope (b=-0.24; p=0.0103; Figure 1b), indicating that GAT values tended to be lower than RBT.

Multiple linear regression analysis indicated that the larger the size of contact area, the smaller was the IOP measurement (b=-0.504; p<0.0001). On the other hand, there was no significant association between CCT and IOP (b=0.003; p=0.169). Bland-Altman test results between GAT and RBT are shown in Figure 1. There was good agreement between methods before surgery without proportional bias (b=0.01; p=0.9339; Figure 1a). After surgery, regression test showed a steep slope (b=-0.24; p=0.0103; Figure 1b), indicating that GAT values tended to be lower than RBT.

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Figure 2 shows Bland-Altman test results between GAT and PDCT. We found a tendency for measurements taken with GAT to be lower than PDCT, although it was not significant (b=0.15; p=0.0706; Figure 2a). After surgery, we found that GAT measurements were systematically lower than PDCT (b=-0.36; p=0.0031; Figure 2b). We found good agreement between RBT and PDCT measurements preoperatively (b=0.14; p=0.102; Figure 3a) and postoperatively (b=-0.11; p=0.4541, Figure 3b), with no evidence of proportional bias.

Discussion

Variations in corneal thickness and structural rigidity of the cornea are recognized sources of error in applanation tonometry. Independently from refractive procedures, changes in CCT are reflected in either under- or over-estimation of the “true” IOP, as already reported elsewhere [10]. However, in post-laser refractive surgery patients, a general trend toward IOP reduction measured by GAT can be attributed to both iatrogenic thinning and other factors, such as subclinical oedema between the corneal lamellae, increase in proteoglycans deposition or stromal softening [11-13].

Our study showed how GAT is fairly consistently giving lower IOP measurements than RBT and PDCT and that there was no significant disagreement between RBT and PDCT. Other studies have compared GAT with RBT using a population of healthy subjects [14,15] or glaucomatous patients [4,16-18] with no data available for post-refractive laser surgery patients. Chui, et al. established that GAT measurements were significantly lower than RBT [14]. These findings have been supported by several other recent studies [4,19] and were in contrast with previous articles reporting no significant difference between GAT and RBT [15,18,20]. Chui elegantly demonstrated that RBT was significantly correlated to corneal hysteresis and corneal resistance factor rather than CCT whereas previous studies suggested a correlation between RBT and CCT [17]. While some differences might be explained by differences in sample size, it is possible that some studies have been carried out on healthy volunteers only, which could have been younger than the patients with glaucoma enrolled in other studies.

Martínez de la Casa et al have investigated the effect of corneal thickness on dynamic contour, rebound and GAT in a group of patients with ocular hypertension and glaucoma [16]. Their study showed that PDCT and RBT correlate well with GAT over a vast range of IOP values. This was not confirmed by our study, as we did not find agreement between GAT and non-applanation methods. Another point raised by Martínez de la Casa et al was that PDCT did not seem to be much affected by corneal thickness, while RBT and GAT measurements seemed to be positively correlated to central corneal thickness. In our study, on the other hand, we did not demonstrate a significant association between CCT and IOP measurements. This could be explained by the statistical methodology adopted (multilinear regression). This method included changes in central corneal thickness in the calculation instead of stratifying the sample according to it.

In our study, the variable most strongly associated with IOP measurements was size of the corneal contact area. This would suggest that a tonometer like GAT, with a larger contact area (3.06mm²), would give lower IOP measurements than PDCT or RBT. We found interesting that PDCT gave higher IOP measurements than RBT, despite PDCT having a slightly larger tip. Nevertheless, RBT and PDCT show good agreement between them and therefore it can be disputed whether there is a significant difference between RBT and PDCT and whether this matters in clinical practice.

Why smaller tips give higher IOP readings? A possible explanation could be that PDCT is not affected by elastic and viscous properties, as suggested by Pepose, et al. [21] and this could give non-applanation tonometers an advantage over GAT. As mentioned before, refractive-surgery induced changes in corneal rigidity might explain why GAT readings are consistently lower than PDCT readings after LASIK, as described by Siganos, et al. [22]. Finally, Kaufman et al recommended the use concluded that rather than use a tonometer where adjusting for correction factors can be problematic, it should be preferable to use PDCT [7].

Our study confirms that both PDCT and RBT are less dependent on iatrogenic changes and our explanation for these findings is that non-applanation tonometers have smaller contact areas and rely on dynamic corneal changes rather than static forces. Few comments should be made about study limitations: firstly, the timing of the IOP measurements was not recorded. While all IOP readings occurred between 10:00 and 12:00, ruling out circadian patterns would have provided extra information. Secondly, all patients examined post-operatively were given a steroid-antibiotic combination. At the present, we have not fully understood the complex interactions after corneal refractive surgery that determine corneal biomechanics – such as changes in hydration or a steroid-mediated IOP raise.

In conclusion, the risk of serious visual loss following IOP underestimation should not be dismissed, as reported by two separate studies [23,24] in which measurement errors led to a delay in glaucoma diagnosis. In order to minimise IOP underestimation, the clinician should consider adopting non-applanation tonometers like RBT and PDCT as an alternative to GAT for glaucoma screening in post-refractive surgery patients.

References


