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Appplanation Tonometry Versus Dynamic Contour
Tonometry in Eyes Treated With Latanoprost

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Purpose: To examine the differences between Goldmann Appplanation Tonometry (GAT) and Dynamic Contour Tonometry (DCT) associated with latanoprost use.

Methods: Twenty-four eyes (of 24 patients) treated with latanoprost monotherapy (latanoprost group, LG), 11 eyes (of 11 patients) not receiving prostaglandin analogs (nonlatanoprost group, NLG), and 20 eyes of 20 nonglaucomatous patients (control group, CG) were included. GAT, DCT, measurement of central corneal thickness and axial length of the eyeball were performed. The difference between GAT and DCT intraocular pressure (dIOP) was calculated. Differences in dIOP among LG, NLG, and CG and correlations of dIOP with other clinical parameters were examined.

Results: dIOP was significantly higher in LG, compared with NLG or CG. The correlations of dIOP with central corneal thickness and axial length of the eyeball were statistically significant in the LG but not in NLG or CG. The correlations of dIOP with central corneal thickness, patients’ age, and duration of latanoprost use (LG) were statistically not significant.

Conclusions: The fact that dIOP was significantly higher in LG, compared with NLG and CG implies that latanoprost may affect the biomechanical properties of the ocular walls.

Key Words: Goldmann application tonometry, dynamic contour tonometry, latanoprost, rigidity

Goldmann Appplanation Tonometry (GAT) is considered the “gold standard” of clinical evaluation of the intraocular pressure (IOP). However, its accuracy may be affected by various corneal or ocular parameters, including central corneal thickness (CCT), corneal astigmatism, corneal curvature, and axial length of the eyeball (AL). CCT is very important for the evaluation of glaucomatous patients, as it has been connected not only to the accuracy of IOP measurement but also to an increased susceptibility for glaucoma development. Dynamic Contour Tonometry (DCT; SMT Swiss Microtechnology AG, Port, Switzerland) uses a “sensortip” to measure IOP directly and is theoretically far less affected by CCT than GAT. Earlier studies have reported general agreement between DCT with GAT, with the former providing slightly higher IOP readings than the latter. Nevertheless, an increased disparity in IOP readings between GAT and DCT has been reported for very high or very low CCT values.

By inducing connective tissue remodeling through activation of metalloproteinases (MMP), prostaglandin analogs (PGA) enhance uveoscleral (and possibly trabecular) aqueous outflow. In addition, PGA may directly induce scleral matrix MMP thus affecting scleral biomechanical properties and transcleral fluid diffusion. PGA also produce various corneal effects, including a decrease in CCT, possibly through remodeling of corneal stromal collagen. CCT changes in response to PGA imply that the accuracy of GAT readings may be affected by PGA administration. This study aims at evaluating differences between GAT and DCT readings associated with latanoprost use. Results obtained could help us in understanding the factors that are affecting the accuracy of GAT and further clarifying the ocular effects of latanoprost.

METHODS

This is a prospective nonrandomized case series. All patients included were Whites, recruited from the Department of Ophthalmology of the University Hospital of Heraklion, Crete, Greece. The latanoprost group (LG) included primary open-angle glaucoma (POAG) patients under monotherapy with latanoprost in at least 1 eye who had not used other antiglaucomatous medications in that eye in the past. In case of patients under latanoprost monotherapy in 1 eye and different or additional antiglaucomatous medications in the fellow eye, only the eyes under latanoprost monotherapy were included in the analyses. In the case of patients under latanoprost monotherapy in both eyes, only the right eye was included.

The nonlatanoprost group (NLG) included patients diagnosed with POAG in at least 1 eye who had not used latanoprost or any other PGA in the past, but were instead using other non-PGA topical antiglaucomatous medications. In the case of patients with glaucoma in both eyes under non-PGA treatment in one eye and under latanoprost or other PGA treatment in the fellow eye, only the eyes under non-PGA treatment were included in the analyses. In the case of patients under non-PGA treatment in both eyes, only the right eye was included. The control group (CG) included cataract surgery candidates in whom glaucoma had been excluded in both eyes and who received no ocular medications. Again, only the right eye was included in the analyses for the CG. Patients with previous history of ocular surgery (including cataract or refractive surgery), trauma or inflammation and patients with pseudoxefelation or pigment dispersion were excluded.
rule our possible changes in corneal or scleral biomechanical properties attributed to these factors. All patients signed a written informed consent form in accordance with the tenets of the Declaration of Helsinki.

All patients underwent a comprehensive clinical ophthalmic examination. Parameters recorded included the GAT-IOP (mm Hg), DCT-IOP (mm Hg), CCT (μm), and AL (mm). The duration of latanoprost use in the eyes examined (mo) was also recorded and the difference between DCT and GAT readings (dIOP) was calculated. Furthermore, in LG and NLG the pattern standard deviation (PSD) from the last routine visual field testing (with central 30-2 threshold test; Humphrey Field Analyzer/HFA II-I, 30-2, Carl Zeiss-Meditec Inc, Dublin, CA) was also recorded. DCT (SMT Swiss Microtechnology AG, Port, Switzerland) was performed first, immediately after the instillation of proparacaine eye drops in the examined eyes. Three readings of good quality (Q1 to Q3, as recommended by the manufacturer) were taken and the mean value recorded. GAT was then performed, at least 10 minutes later (after the application of a fluorescein strip at the lower conjunctival fornix). The examination of CCT and AL was carried out last with the Alcon OcuScan RxP Ophthalmic Ultrasound System, using a 20-Mhz probe for pachymetry, with a resolution of ± 1 μm, and an accuracy of ± 0.05 mm, according to the manufacturer’s (Alcon laboratories, Alcon, Irvine, CA) instruction. For both CCT and AL, 10 successive measurements were taken and the mean was recorded. All clinical ophthalmic examinations were carried out by the same experienced examiner (V.A.) who was masked against the classification of participants into LG, NLG, or CG.

The LG included 24 eyes of 24 patients (14 males, 58.33%), aged 67.14 ± 11.70 years (49 to 82 y) (mean ± SD, range). The NLG included 11 eyes of 11 patients (6 males, 54.54%), aged 65.19 ± 17.13 years (55 to 79 y), whereas the CG included 20 eyes of 20 patients (20 males, 50%), aged 71.32 ± 5.64 years (59 to 87 y). PSD (in dB) in the LG and NLG was 3.41 ± 0.10 (2.29 to 6.74) and 2.92 ± 1.29 (2.98 to 5.68), respectively. The number of eyes studied and respective duration of antiglaucomatous medications use in the LG and NLG are presented in Table 1.

Statistical analysis of findings was performed using SPSS 8.0 (SPSS, Chicago, IL). Statistical significance was set at 0.05. Differences in GAT, DCT, and dIOP and also in age distribution and AL among the LG, NLG, and CG were examined using I-way analysis of variance (ANOVA). Post hoc analysis of differences between groups was performed with Dunnett T3 test. Differences in sex distribution among LG, NLG, and CG were examined with Pearson χ2 test. The correlations between age and AL among LG, NLG, and CG were examined (Pearson bivariate correlation coefficient). Furthermore, in the LG, correlations between the duration of latanoprost use and GAT-IOP, DCT-IOP, or dIOP were also examined using Pearson bivariate correlation coefficient.

### RESULTS

Differences in the age and AL distribution among the 3 groups were statistically not significant (ANOVA). Differences in sex distribution between the 3 groups were also statistically not significant (Pearson χ2 test) whereas LG and NLG did not differ significantly concerning PSD (independent samples t test). GAT-IOP and DCT-IOP did not differ significantly among LG, NLG, and CG (ANOVA). On the contrary, dIOP was significantly different among LG, NLG, and CG. Post hoc analysis of differences in dIOP between the groups examined revealed that dIOP was significantly higher in LG compared with NLG (Dunnett T3 test, *P* = 0.04) and with CG (Dunnett T3 test, *P* = 0.02), whereas the respective difference between NLG and CG was statistically not significant. GAT-IOP, DCT-IOP, and dIOP in the groups examined, respective ANOVA *F* values and statistical significance of differences are presented in Table 2.

Correlations between patients’ age or CCT and GAT-IOP, DCT-IOP or dIOP and were statistically not significant in all groups examined (Pearson bivariate correlation coefficient). Correlations between AL and GAT-IOP or DCT-IOP were also statistically not significant in all groups examined (Pearson bivariate correlation coefficient). On the contrary, the correlation between AL and dIOP was statistically significant in the LG (Pearson bivariate correlation coefficient 0.52, *P* = 0.005). Respective correlations in the CG and NLG were statistically not significant, although in the case of NLG the correlation approached (but did not exceed) statistical significance (*P* = 0.05). Furthermore, in the LG, correlations between the duration of latanoprost use and GAT-IOP, DCT-IOP, or dIOP were statistically not significant (Pearson bivariate correlation coefficient). Scattergrams of the correlations between tonometric readings examined (GAT-IOP, DCT-IOP, and dIOP) and CCT in the LG with respective trend lines are presented in Figure 1 (A, B, and C, respectively). Scattergrams of the correlations between tonometric readings examined (GAT-IOP, DCT-IOP, and dIOP) and AL in the LG with respective trend lines are presented in Figure 2 (A, B, and C, respectively).

### DISCUSSION

This study examined differences between GAT and DCT in glaucomatous eyes treated with latanoprost as monotherapy, and in a group of glaucomatous eyes under...
non-PGA treatment and in a control group of nonglaucomatous eyes. Results imply that latanoprost affects differences in IOP readings between GAT and DCT, which could be attributed to induced alterations in the biomechanical properties of the ocular walls. DCT uses a contoured 10.5-mm diameter tip with a concave surface that conforms to the anterior corneal surface thus causing minimal corneal distortion.8,9,16 The tip incorporates a 1.7-mm diameter sensor that measures IOP without errors attributed to force-to-pressure translations thus rendering IOP measurements less dependent on corneal biomechanical properties, including CCT, astigmatism, curvature, and rigidity.17 As DCT is theoretically far less affected by corneal biomechanical properties than GAT, diOP may be used to evaluate the effects of such parameters on the accuracy of IOP measurements. Although both GAT and DCT involve contact with the anterior corneal surface and could theoretically induce neuropsychologic effects on the IOP, GAT is further associated with a massaging effect on the aqueous associated with application. To avoid this, DCT was systematically performed before GAT in this study. Furthermore, to allow for resolution of induced changes in the IOP, the 2 measurements were separated by a time interval of at least 10 minutes.

There are controversial reports on the effects of glaucoma per se on ocular rigidity.18,20 By evaluating the correlation between AL changes (with partial coherence laser interferometry) and IOP changes (with DCT) a previous study has reported increased ocular rigidity in patients with established glaucoma, in comparison with control subjects.20 However, other studies have reported that untreated glaucomatous eyes may be less rigid than nonglaucomatous eyes and that their rigidity may increase after the administration of topical medications such as b-blockers or pilocarpine.18,19 In this study, diOP was comparable to that reported in earlier studies.5,8 However, it was significantly higher in the LG, compared with CG and NLG, whereas respective differences for GAT and DCT were statistically not significant. Taking into account that age and sex differences in the study groups examined were statistically not significant, these findings imply that diOP differences may be attributed to latanoprost use, rather than to glaucomatous changes. Earlier studies have also reported differences in diOP between treated and untreated glaucomatous eyes and suggested that antiglaucomatous medications, especially PGA, may affect ocular rigidity and the accuracy of IOP measurements.21 The fact that LG and NLG did not differ significantly concerning PSD (implying that glaucoma was equally advanced in both groups) further supports the possibility that the difference in IOP is associated with latanoprost use rather than with potential changes on corneal biomechanics associated with glaucoma. Furthermore, earlier studies evaluating ocular effects of latanoprost have reported that chronic use has more pronounced effects on the ocular surface than short-term use.22 On the contrary, the correlation between GAT-IOP, DCT-IOP, or diOP and the duration of latanoprost use was statistically not significant in this study implying that the potential effects of PGA on ocular rigidity or IOP measurements may not be time-dependent.

A previous study on patients with ocular hypertension or pigment dispersion syndrome reported significant positive associations of the difference between GAT and DCT with CCT and with age.21 According to that study, DCT readings were higher than GAT readings in younger participants but the opposite was found for older participants, a finding possibly attributed to age-related changes in ocular rigidity.21 The fact that the correlation between age and diOP was statistically not significant in all groups

### TABLE 2. GAT-IOP, DCT-IOP, and diOP (mm Hg) in CG, LG, and NLG, One-way Analysis of Variance F Values and Respective Levels of Statistical Significance

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<th>Group</th>
<th>GAT-IOP</th>
<th>DCT-IOP</th>
<th>diOP</th>
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<td>CG</td>
<td>15.25 ± 1.91 (12 to 18)</td>
<td>15.83 ± 5.72 (10 to 30)</td>
<td>2.88 ± 2.98 (−0.02 to 8.50)</td>
<td>9.00-15.00</td>
<td>3.14 0.04</td>
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<td>LG</td>
<td>18.13 ± 3.27 (13.50 to 22.50)</td>
<td>20.58 ± 6.67 (11.20 to 38.50)</td>
<td>4.92 ± 6.42 (−9.00 to 15.00)</td>
<td>1.79 ± 2.97 (−3.90 to 8.10)</td>
<td>1.18 0.31</td>
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<tr>
<td>NLG</td>
<td>18.16 ± 3.37 (12.10-23.60)</td>
<td>18.16 ± 3.37 (12.10-23.60)</td>
<td>2.88 ± 2.98 (−0.02 to 8.50)</td>
<td>9.00-15.00</td>
<td>3.14 0.04</td>
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CG indicates control group; DCT, Dynamic Contour Tonometry; diOP, difference between GAT and DCT intraocular pressure; GAT, Goldmann Applanation Tonometry; IOP, intraocular pressure; LG, latanoprost group; NLG, nolatanoprost group.

### FIGURE 1. Scattergram of the correlation between central corneal thickness and Goldmann Applanation Tonometry (GAT) (A), Dynamic Contour Tonometry (DCT) (B), and the difference between GAT and DCT intraocular pressure (diOP) (C) in the latanoprost group, with associated trend lines and respective levels of statistical significance (Pearson bivariate correlation coefficient).

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in this study may be because of the higher mean age of participants or to the different pathologic entities (prevalence of POAG in this study, instead of ocular hypertension or pigment dispersion syndrome previously examined). The fact that the correlations between GAT and CCT or between dIOP and CCT were statistically not significant in this study may possibly be because of the less number of eyes studied and to the fact that the correlation between GAT and CCT is statistically weak (r² ranging from 0.06 to 0.17), whereas dIOP may be more pronounced in very thick or very thin corneas. Furthermore, a previous study using a corneal biomechanical model to assess the effects of corneal variables on the accuracy of measurements of IOP by applanation tonometry concluded that differences in corneal biomechanics may have greater impact on IOP measurement errors than corneal thickness or curvature and the fact that the correlation between CCT and dIOP was statistically not significant in this study may reflect this point.

Taking into account, the lack of intergroup differences in AL, the significant correlation of dIOP with AL in the LG (but not in NLG or CG) in this study implies an effect of latanoprost, independently from the glaucomatous pathologic process, on the biomechanical properties of the sclera and possibly the choroid (apart from the cornea). This hypothesis is supported by findings of several previous studies on PGA-associated genetic triggering of MMP in the sclera and resulting in enhanced uveoscleral outflow and transcleral diffusion profile. PGA also have profound uveal effects, including an increase in the production of melanin in iridal (but possibly also in ciliary and choroidal) melanocytes, induction of the expression of MMP-1 in ciliary body melanocytes, increase in the thickness of ciliary body, and association with choroidal effusions and detachment. The choroid constitutes an important element of total ocular rigidity and a correlation between AL and choroidal thickness has been previously reported.

In this study, the association between dIOP and AL in the LG may therefore reflect latanoprost-induced changes in choroidal structure or hemodynamic status. The nonrandomized design and the relatively small number of participants limit the strength of this study. In contrast, the fact that all measurements were performed by the same experienced examiner who was masked against the identity of the participant enhances the validity of results. The best design to answer the questions concerning the role of PGA in modifying ocular biomechanical properties would be a truly prospective trial with randomized assignment of treatment-naive eyes to PGAs versus non-PGAs, baseline determination of the various measures and follow-up measures. As measurable changes in CCT have been reported to occur after about 6 weeks of treatment, changes in dIOP could be determined at that interval. Future research in this area may also aim at evaluating the effects of other PGA, such as bimatoprost or travoprost, on ocular rigidity and may include direct manometric in vivo observations in the analyses, as suggested earlier. Taking into account the widespread use of PGA in glaucoma treatment, their potential effects on the accuracy of IOP measurements imply that findings may play a role in the follow-up and decision making for glaucomatous patients.

REFERENCES


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