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Central and paracentral corneal pachymetry in patients with normal tension glaucoma and ocular hypertension

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Abstract *Purpose:* The difference in central corneal thickness among subgroups of glaucoma patients, as well as its influence on Goldmann applanation tonometry, has been well documented in several clinical trials. In the present study, possible similarities and differences between central corneal thickness and corneal thickness of paracentral quadrants in patients with normal tension glaucoma (NTG) and ocular hypertension (OHT) were investigated. *Methods:* Central and paracentral corneal thickness was measured by optical slit scan pachymetry (Orbscan II). Fourteen patients (28 eyes) with NTG and 11 patients (22 eyes) with OHT were included in this study. *t*-Test was performed for statistical analysis. To evaluate overall corneal topography, the mean and SD values of the differences between the central corneal thickness and each peripheral quadrant were analysed. *Results:* The following data was obtained (μm): (central, upper, temporal, nasal, inferior paracentral quadrant): OHT group 617–695–663–687–660. NTG group 568–629–593–612–616. Corneal thickness of all four paracentral quadrants differed significantly between the OHT and NTG groups. There was a more heterogeneous intraindividual pattern of overall corneal topography in the OHT group, and a more heterogeneous pattern of corneal topography among the individuals of the NTG group (interindividual heterogeneity). *Conclusions:* A comparison of central corneal thickness and paracentral corneal thickness revealed clinically relevant differences between the OHT and NTG groups. The presented data underlines the importance of correlating the site of applanation with the corresponding corneal thickness, especially in OHT patients. It further substantiates the necessity to obtain individual pachymetric data for each NTG patient.

Keywords Normal tension glaucoma · Orbscan · Pachymetric topography · Ocular hypertension

Introduction

Applanation tonometry, as developed by Goldmann in the 1950s [11], is based on an assumed "standard" central corneal thickness (CCT) of 520 μm. Following physical calculations, he designed the known tonometer head as a truncated cone with an applanation area of 3.06 mm in diameter, to obtain valid intraocular pressure (IOP) measurements.

We know from current literature that CCT may vary significantly. For people classified as healthy, average CCT is around 555 μm. In patients with primary open angle glaucoma (POAG) it is around 545 μm, and therefore does not differ significantly from normal subjects. However,

patients with normal tension glaucoma (NTG) or ocular hypertension (OHT) are reported to have significantly thinner (510 μm), or thicker (595 μm) CCTs, respectively (averaged measurements taken from previous studies [1, 2, 6, 9, 13, 14, 19, 21, 23–25]). Due to this fact, several formulae have been published correcting the value of applanated IOP: making lower adjustments for a thinner and higher adjustments for a thicker than average CCT.

In this paper, we address the question of whether there are differences or similarities between CCT and corneal thickness of paracentral quadrants in patients with NTG and OHT. Further, using slit scan pachymetry, we have investigated the overall corneal pachymetric topography of patients classified as NTG or OHT.

Patients and methods

Patients

Fourteen consecutive patients with normal tension glaucoma (NTG, 28 eyes) and 11 consecutive patients with ocular hypertension (OHT, 22 eyes) were included in this study. By our definition, NTG patients had a history of progressive glaucomatous optic disc cupping and visual field defects despite an untreated maximum IOP of 21 mmHg. The maximum IOP of the included NTG eyes ranged from 12 to 21 mmHg with a mean of 17.9 mmHg. In all of these patients, a 24 h IOP curve had been performed. OHT patients had an untreated IOP of 24 mmHg or higher without showing optic disc cupping or visual field defects. The maximum IOP of the included OHT eyes ranged from 24 to 30 mmHg with a mean of 26.1 mmHg. Mean age of the NTG patients was 63.1 years, and 44.3 years for the OHT patients, respectively.

Exclusion criteria were refractive errors above ±5 dioptres, any surgical history, any corneal diseases, dystrophies or scarring. No patients wearing contact lenses were included.

Slit scan pachymetry

Slit scan pachymetry of the cornea was performed using Orbscan II (Bausch & Lomb Surgical, Munich, Germany). The Orbscan corneal topography system measures anterior and posterior corneal elevation as well as anterior and posterior surface curvature. Based on the principle of light reflection and scattering, as well as ray trace triangulation, it calculates the corneal thickness as a difference between sets of obtained data.

The optical acquisition head scans the cornea using two slit beams, projecting from an angle of 45 degrees. The cornea is scanned by sequentially projecting 20 slits from right and from left. The software analyses 240 data points from each single slit scan, obtaining a total of 9600 data points per cornea. The mean pachymetric value for the CCT and each paracentral quadrant is the calculated average of data points taken from a circle based around the corneal center (visual axis) and four points located 3 mm paracentral from this center. Each circle measures 2 mm in diameter. Five averaged values are obtained: mean CCT and mean corneal thickness of the superior, temporal, nasal and inferior paracentral quadrant.

Orbscan II is known to create a thicker than actual pachymetric map of the cornea. The application of an acoustic equivalent correction factor of 0.92 is recommended by the manufacturer [12]. In this paper, the originally obtained data is given. The correction factor has not been applied, as it only describes a linear transformation.

Three scans of each eye had been performed after each other on one day. Patients had been informed in detail about the purpose of the slit scan pachymetry and this study in advance. As the Orbscan is a non-contact diag-

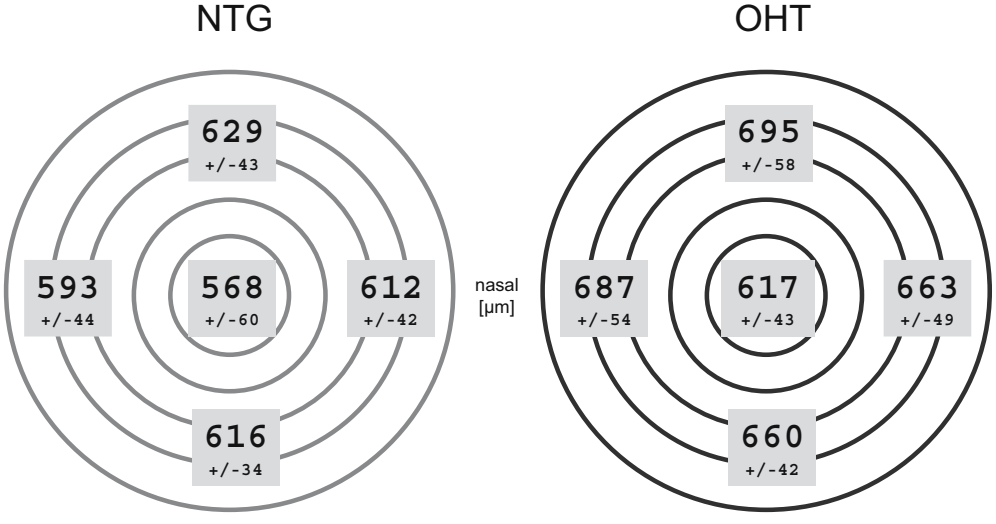

Fig. 1 Pachymetric data obtained by Orbscan slit scan pachymetry. The pachymetric data (μm) are given as mean± SD for CCT and paracentral quadrants. As recommended in the current literature, a correction factor of x 0.92 should be applied to compare the obtained Orbscan data with ultrasound pachymetric data

nostic device in general clinical use, no additional written informed consent had been requested from the patients.

Statistics

Statistical analysis was performed by applying the Student's *t*-test to the obtained data. Statistical significance was assumed for $P<0.05$. No correction for multiplicity was performed.

To investigate inter- and intraindividual differences between the OHT and the NTG group, the mean and standard deviation (SD) values of the differences between pachymetric data of the central cornea and each peripheral quadrant were analysed. Larger mean values represent larger intraindividual differences, larger SD values represent larger interindividual differences.

Results

Using Orbscan slit scan pachymetry as described in detail above, we obtained the following data (Fig. 1): For NTG patients, we measured a mean CCT of 568±60 μm, and for patients with OHT a mean CCT of 617±43 μm. The mean pachymetric data for the paracentral quadrants are as follows. For the NTG group: in the superior quadrant 629±43 μm, temporal quadrant 593±44 μm, nasal quadrant 612±42 μm, inferior quadrant 616±34 μm. For the OHT group: in the superior quadrant 695±58 μm, tempo-

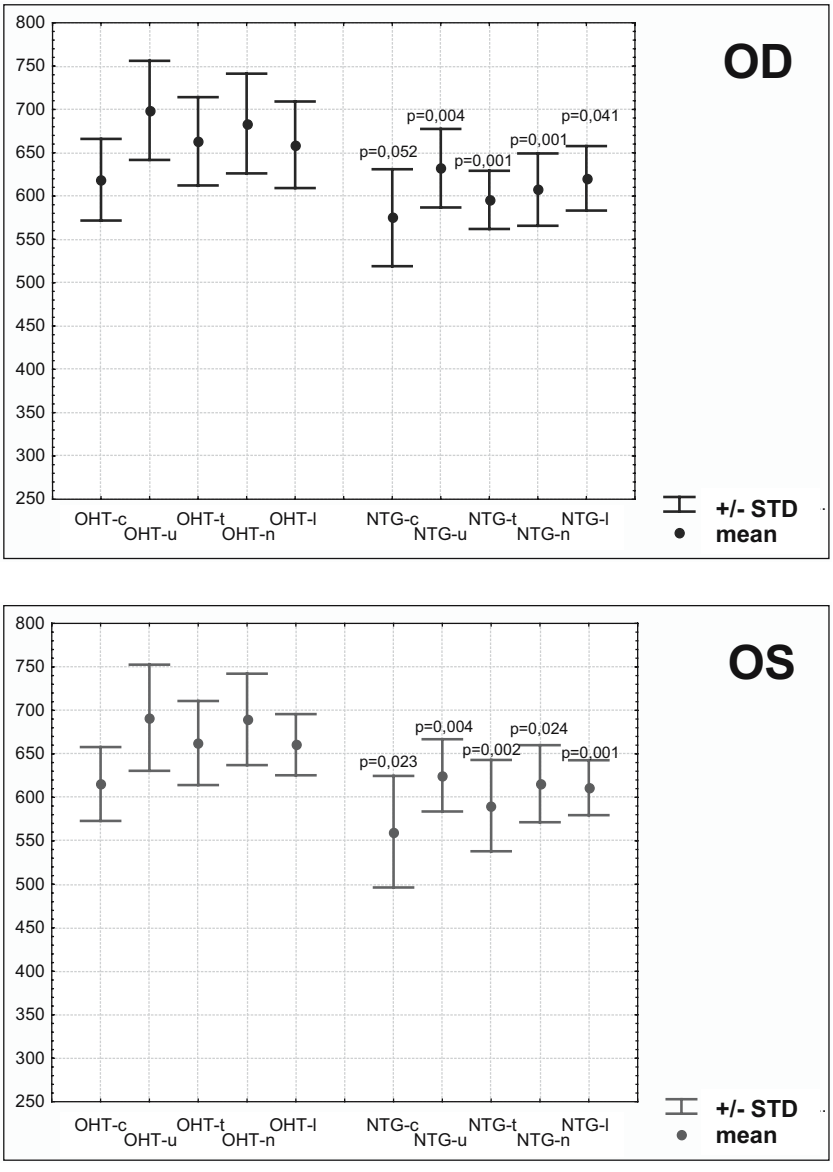

Fig. 2 Statistical analysis of pachymetric data. Mean corneal thickness of CCT and each paracentral quadrant±standard deviation (STD) are displayed for the right and the left eye. *P*-values derive from an independent Student's *t*-test comparing data from CCT or each corresponding peripheral quadrant of the OHT and the NTG group, respectively. Data are given in μm. Values from right and left eyes did not differ significantly within either group (data not shown). Please note that values for each paracentral quadrant differed significantly between the two groups (significance assumed for $P<0.05$)

Table 1 Analysis of the data obtained from Orbscan central and peripheral optic pachymetry to further analyse intraindividual and interindividual differences between the OHT and the NTG groups

Group		Difference right eye central-upper	c-temp	c-nasal	c-lower	Difference left eye central-upper	c-temp	c-nasal	c-lower
OHT	Mean	80.09	44.36	64.91	40.36	76.18	47.09	74.27	45.18
	STD	22.96	16.19	25.86	21.98	28.33	13.43	22.12	12.81
NTG	Mean	53.57	18.79	27.64	44.14	59.67	26.53	50.79	48.73
	STD	54.68	30.01	46.66	26.23	57.79	51.17	52.39	38.95

Mean and standard deviations (SD) of the differences between central (c) corneal thickness and each peripheral quadrant are given. Larger mean values represent larger intraindividual differences, larger SD values represent larger interindividual differences

ral quadrant 663±49 μm, nasal quadrant 687±54 μm, inferior quadrant 660±42 μm.

The statistical analysis of the comparison of CCT and the paracentral quadrants between the two groups showed significant differences in central corneal thickness and for each single, corresponding quadrant. There were no significant differences between the right and the left eye (data not shown). Please see Fig. 2 for the statistical analysis.

To analyse intraindividual and interindividual differences between the two groups of patients, the mean (for intraindividual analysis) and standard deviations (for interindividual analysis) of the differences between the peripheral and central pachymetric values were analysed (Table 1). In patients with OHT, a more heterogeneous (intraindividual) difference between central and mid-peripheral corneal thickness was observed. In the NTG group, among the patients, a more heterogeneous interindividual difference of central and mid-peripheral corneal thickness was observed.

Discussion

Knowledge of individual corneal thickness in individual eyes is proving more and more crucial for correcting Goldmann applanation tonometry It has become an important factor in determining appropriate glaucoma therapy. With regard to CCT, values from patients with NTG or OHT differ significantly from those reported for normal subjects in the literature. Pachymetry and the evaluation of real IOP in these patients is of particular importance for effective clinical management.

Although many clinical studies have revealed significant differences in CCT between subgroups of glaucoma patients [1, 2, 6, 9, 13, 14, 19, 21, 23, 25], the relation of intraocular pressure to corneal thickness is still a matter of debate. Based on manometric cannulation experiments, Ehlers et al. in 1975 originally reported from experiments in rabbits and humans a correlation between the "error" in applanation tonometry and corneal thickness, based on measurements describing the coincidence of the differences between intracameral hydrostatic pressure and applanation readings [8]. From his experiments, Ehlers suggested a correction factor of 0.7 mmHg for each 10 μm of pachymetric difference from the mean CCT of 520 μm. These results were questioned by Feltgen et al. [10] who performed further cannulation experiments, with increasing and decreasing CCT, but could not find any discrepancy between applanation tonometry and intracameral IOP readings that was of statistical relevance to clinical practice. Stodtmeister et al., though, shed doubt on the validity of these latter results by pointing to methodological deficiencies in Feltgen's experimental settings [22]. In a population based study on applanation tonometry, CCT-pachymetry and linear regression analysis of the obtained data, Wolfs et al. confirmed a positive relation between CCT and IOP. Their mean reported CCT was 537 μm. The relation they found was 0.19 mmHg of IOP rise (as measured by applanation) with each 10 μm increasing CCT (as measured by pachymetry), independent from adjusting for age or gender (including 352 control subjects, 30 POAG, 13 OHT patients; The Rotterdam Eye Study [25]).

The importance of corneal thickness, and its predictive value for glaucoma progression has recently been underlined in several clinical studies ([15, 16, 18], see Brandt for a review [3]). The Ocular Hypertension Treatment Study (OHTS), in particular, has identified CCT as a strong predictive factor for the risk of glaucoma conversion [4, 20]. This large clinical trial involved 1636 patients with IOPs of between 24 mmHg and 32 mmHg, with normal white/white visual fields and normal discs. Glaucoma conversion rate was investigated under medical antiglaucomatous treatment or without treatment over a follow-up period of 5 years, and the results are indeed interesting. Mean CCT of all participants was 573±39 μm. With respect to baseline IOP and baseline glaucomatous optic disc cupping, the possible predictive value of corneal thickness was analysed. The risk of damage at 5 years with a baseline IOP >26 mmHg was 36% for patients with a thin cornea versus 13% (i.e. about one-third of the risk) for those with a thicker than average cornea. For patients with a cup to disc ratio of >0.3, the risk was 24% for those

with thin corneas, versus 16% (i.e. about half the risk) for patients with a thick cornea.

Our study corroborates the known data showing differences in corneal thickness in patients with NTG and OHT. We measured a CCT of 568 μm for NTG patients and a CCT of 617 μm for the OHT patients (applying the manufacturers' suggested correction factor, this is 522 μm and 568 μm, respectively). Using Orbscan slit scan pachymetry, we furthermore showed that the corresponding paracentral quadrants differ significantly between the two groups. There was no significant difference between the right and left eyes. Our data confirm that patients with NTG have an overall thinner, and those with OHT an overall thicker cornea.

According to recent studies, there is no significant correlation between the central corneal thickness and age or gender [7, 23, 25]. Therefore, the difference in mean age between the NTG (63.1 years) and OHT (44.3 years) group seems not to be of significance for the obtained results.

In the literature, Orbscan is reported to be a reliable pachymetric device, even for repeated corneal thickness measurements [17]. Good repeatability of Orbscan measurements for CCT values is well documented. Repeatability for the peripheral measurements has been doubted in a study by Cho et al., though also these authors could not find a significance in the variability of repeated measurements taken for peripheral corneal locations [5]. We did repeat the slit scan pachymetry 3 times for each eye, all measurements taken on one day. There were no outlined measurements. The overall variability of the repeated measurements was 2.1% in our series, with 1.1% for the CCT measurements, 2.2% for the upper, 2.4% for the nasal, 2.3% for the inferior and 2.7% for the temporal paracentral quadrant. This, for each area, is below our reported standard deviation. Hence, repeatability and variability of peripheral Orbscan measurements do not interfere with our results.

This is the first study to analyse the overall pachymetric topography in NTG and OHT patients and to note topographical differences between the two groups. According to our analysis of differences between the CCT and each single peripheral quadrant, OHT patients have a more heterogeneous overall corneal topography with larger mean values. Therefore, in these patients, the site of applanation should be carefully correlated to the site of pachymetric measurements. This is of particular importance for the most widely used pachymetric system, the ultrasound contact pachymetric device. Though quite easy to handle and renowned for producing reliable results, the reliability of pachymetry strongly depends on the site of cone end contact, which is only a rather small area. If not correlated carefully with the site of applanation, this could easily lead to false correction of the applanated IOP.

The larger STD values of this analysis in the NTG group express the heterogeneity of the NTG patients in respect to the corneal thickness. It underlines the diagnostic necessity to obtain pachymetric data for each single NTG patient in order to be able to initiate appropriate individual treatment.

As reported from other studies both, corneas of patients with NTG and PEX are reported to be thinner than normal [2, 24]. Further studies will be needed to establish possible similarities or differences in pachymetric topography between different forms of glaucoma.

Before being classified as NTG or OHT, many of these patients are first regarded as borderline cases. Finding the correct diagnosis is seldom easy. Especially in these cases, knowledge of valid pachymetric data can be crucial for making decisions on further clinical management. Our study underlines the importance of corneal pachymetry in NTG and OHT patients. Heterogeneity in the NTG population makes it crucial to obtain pachymetric data for each individual. It also emphasizes the need to adjust pachymetric measurements according to the site of applanation (intraindividual heterogeneity of especially OHT corneas). New and fixation based non-contact pachymetric devices (e.g. laser interferometry-based pachymetry) will possibly help to facilitate the clinical handling of this problem.

However, whether corneal thickness is the only physical variable warranting correction of IOP measurements remains to be elucidated.

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