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Central corneal thickness and intraocular pressure relationship in eyes with and without previous LASIK: Comparison of Goldmann applanation tonometer with pneumatonometer

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PURPOSE. *To investigate central corneal thickness (CCT) and intraocular pressure (IOP) relationship in eyes with and without previous corneal laser refractive surgery and to compare the estimates of two different tonometers–Goldmann applanation and pneumatonometer.*

METHODS. *The study population included 234 glaucoma suspects who were referred to the glaucoma clinic with cup/disc ratios greater than 0.4, asymmetric cupping, and/or IOP greater than 22 mmHg during routine eye examination. Of those, 84 had previous myopic laser-assisted in situ keratomileusis (LASIK) (Group 1) while 150 of them did not (Group 2). CCT was measured by using optical coherence tomography (OCT) and IOP with both Goldmann applanation tonometer (GAT) and pneumatonometer (PT). In both groups, the difference between IOP estimates of two different tonometers and the relationship between CCT and IOP were analyzed.*

RESULTS. *In eyes with previous LASIK, GAT measured IOP significantly lower than PT (mean difference of 3.8±1.9 mmHg, p<0.0001). In eyes with virgin corneas, IOP estimates of GAT or PT were not different from each other (19.9±2.8 versus 19.9±2.2 mmHg, respectively, p=0.81). In both groups, there was a significant positive correlation between CCT and IOP estimates of GAT (R=0.29, p=0.007 in eyes with LASIK and R=0.38, p<0.0001 in those without), while no similar relationship was present between CCT with those of PT (R=0.03, p=0.76 in eyes with LASIK and R=0.03, p=0.69 in those without).*

CONCLUSIONS. *In eyes with previous LASIK, GAT measured IOP significantly lower than PT. Because IOP estimates of PT were found to be independent from CCT in all of the study eyes, this device was considered to be a more reliable method of IOP estimation than GAT in eyes with and without previous LASIK. (Eur J Ophthalmol 2005; 15: 81-8)*

KEY WORDS. *Central corneal thickness, Intraocular pressure, Goldmann applanation tonometer, Pneumatonometer, Optical coherence tomography, LASIK*

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INTRODUCTION

In routine glaucoma practice, Goldmann applanation tonometer (GAT) is generally the universally accepted tonometry method. However, the major assumption of that device – that resistance of the cornea to indentation is compensated by the surface tension of the tear film – is true for only a central corneal thickness (CCT) of about 520 µm (1, 2). The distribution of CCT in patients seen in routine clinical glaucoma practice scatters along a wide scale and there can be 100 µm or greater difference from that ideal value for some particular eyes.

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A considerable amount of evidence has been accumulated on that subject, and it has been generally accepted by many investigators and clinicians that IOP measurements obtained with GAT are in fact influenced by CCT (2-5). CCT of ocular hypertensive patients were usually reported to be thicker than normal controls while it was much thinner in eyes with normal tension glaucoma (6-11). In a recent large controlled trial, it was demonstrated that eyes with thinner corneas carry an increased risk for conversion from ocular hypertension to glaucoma (12). Also, IOP is usually measured artificially lower following laser corneal refractive surgery (13-18).

An IOP measurement device that is not affected by CCT will be a clinically useful alternative for estimating true IOP.

In this study, we investigated the relationship between IOP estimates of GAT and PT with CCT in glaucoma suspects with or without laser-assisted in situ keratomileusis (LASIK). Our patient population included those with cup/disc ratios greater than 0.4, asymmetric cupping, and/or IOP greater than 22 mmHg during routine eye examination. We elected to conduct the study only on glaucoma suspects and were not able to include patients with established glaucoma for two reasons. First, we were trying to discover the influence of LASIK on IOP-CCT relationship, but LASIK has been only occasionally performed on patients with established glaucoma. Second, when we tried to explore the relationship between CCT and IOP and made a comparison of two different tonometers for this aspect, we found that if we included established glaucoma patients with high IOP that caused some difficulty, because IOP-CCT relationship became more complex due to large scatter of IOP.

We preferred to measure CCT by optical coherence tomography (OCT) in order to avoid any potential errors that might be due to the use of an ultrasonic pachymeter, as OCT was previously shown to be a reliable method of assessing corneal thickness (19-22). Our study also included eyes with previous LASIK as a separate group in order to draw clinically useful conclusions which could then be applied to the whole patient population of a routine glaucoma referral practice.

METHODS

A total of 234 subjects were enrolled into the study. There were 108 men and 126 women. Mean age was 55.6±28.7 years (range between 17 and 82 years). The study population included all consecutive new patients referred to our glaucoma unit with suspected glaucoma during 2002. The diagnosis was made when at least one of the following was present:

- IOP equal to or higher than 22 mmHg with GAT.
- Suspicious optic disc changes suggestive of glaucoma (cup/disk ratio equal to or greater than 0.4 and/or asymmetric cup/disk ratios between fellow eyes greater than 0.2).

None of the subjects had been using any glaucoma medications at the time of the study. Patients with known glaucoma or those who were diagnosed with glaucoma after visual field testing and retinal nerve fiber thickness analysis with OCT were excluded from the study. Eyes with IOP higher than 26 mmHg (either tonometer) were also excluded in order to avoid large scatter of IOP data.

Eighty-four patients of our study population had previous LASIK for the correction of myopia and/or myopic astigmatism elsewhere (Group 1). The remaining 150 patients did not have any type of corneal laser refractive surgery (Group 2). None of the patients in the study had any corneal disease (scar due to keratitis, corneal dystrophia, or trauma), which might have some adverse influence on the CCT measurements.

One eye of each patient was selected to prevent selection bias (selection was made by using computer oriented randomized numbers). For each of the study eyes, a routine ophthalmologic examination including refraction, visual acuity testing, and routine biomicroscopic examination was performed.

The study was carried out in two hospitals. Examination of patients, CCT, and IOP measurements were performed in Istanbul Surgery Hospital's Glaucoma Department. Data collection and statistical analysis were done in BeyoÆlu Eye Education and Research Hospital.

Central corneal thickness measurements

CCT measurements were performed with a commercially available OCT instrument (OCT-1, Humphrey Instruments, San Leandro, CA). This instrument, which uses the principle of low coherence interferometry, has been reported to give high resolution cross sectional images of various ocular tissues, such as the retina, the lens, and the cornea (23, 24). It uses a low coherent diode light at 810 nm wavelength as a light source for scanning. Because OCT device has several clinical applications such as retinal diseases, glaucoma, and anterior segment, sev-

eral scanning modes for different purposes are integrated in its software. In this study, the linear scanning mode with a scan length of 2.38 mm was used. By checking the position of the light beam with respect to the cornea on the real time monitor, the linear scan beam was carefully placed on the center of the cornea bisecting the pupil horizontally (Fig. 1A) and pseudo-color images of the cornea were generated (Fig. 1B). At least three consecutive scans were performed in each eye. After recording those images, the process of determination of CCT was performed by using the scan profile display of the instruments' software. That display shows the amount of light (OCT beam) reflected by the corneal tissue at any selected point in a topographic fashion. The anterior and the posterior corneal surface were identified as two spikes (highest reflectivity) (Fig. 1C). All of the images taken from each eye were analyzed by the scan profile display and the image with the best quality was selected. Then on that image, software-controlled cursors were placed manually at the peak of those two spikes corresponding the anterior and the posterior corneal surfaces. CCT was calculated as the distance between the two highest peaks

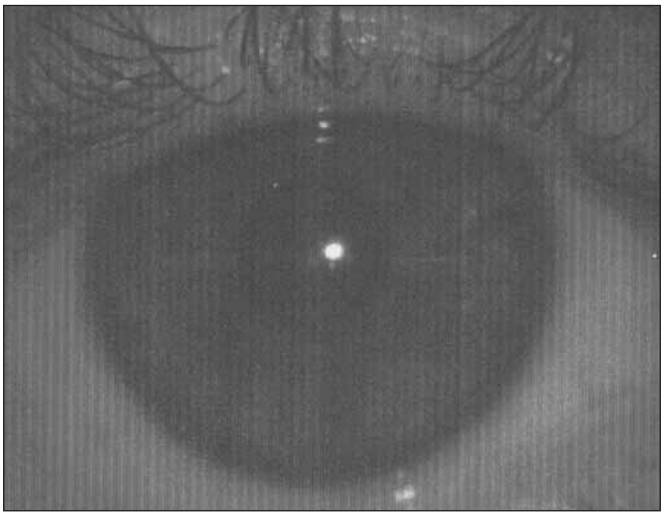

Fig. 1A - *The position of the light beam centered on the cornea on the real time monitor, the linear scan beam bisecting the pupil horizontally.*

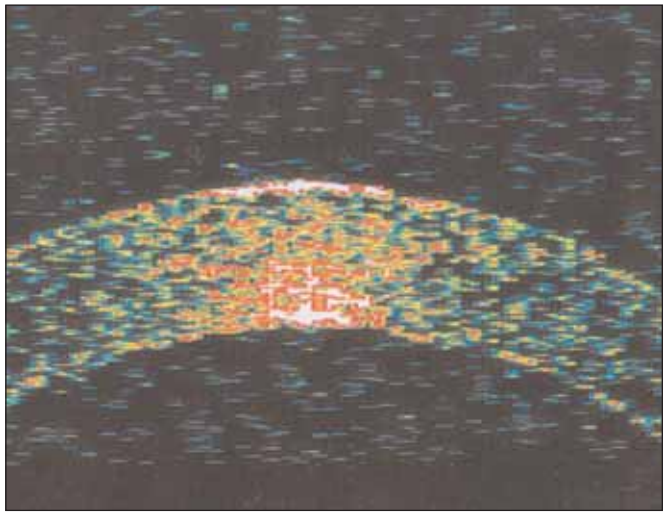

Fig. 1B - *Pseudo-color image of the cornea.*

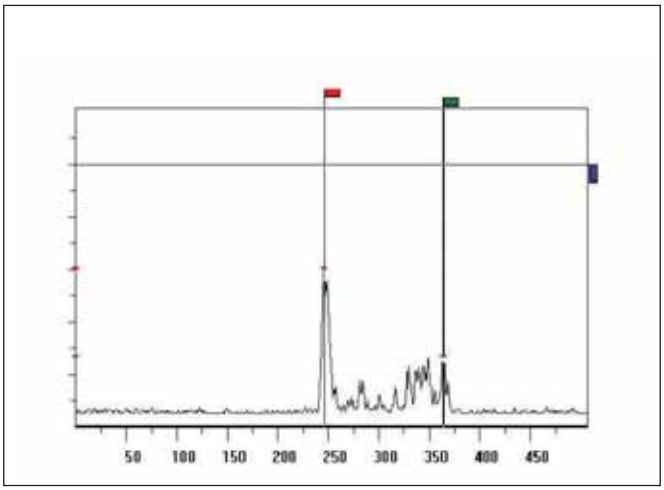

Fig. 1C - *The anterior and the posterior corneal surfaces identified as two spikes (highest reflectivity) in the Scan profile display of optical coherence tomography instrument.*

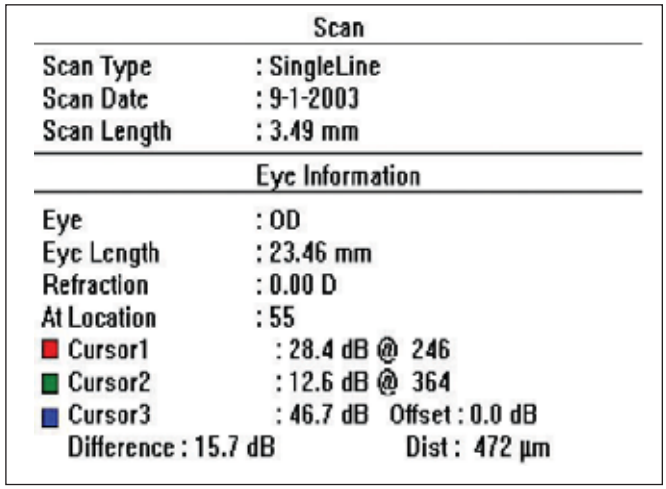

Fig.1D - *The central corneal thickness was calculated as the distance between these two highest spikes.*

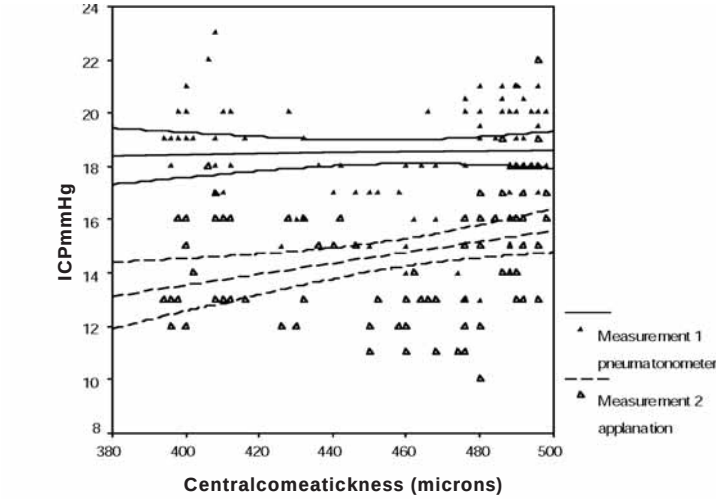

Fig. 2 - *Relationship between central corneal thickness measurements with intraocular pressure estimates of pneumatonometer and those of Goldmann applanation tonometer in eyes with previous laser-assited in situ keratomileusis (linear regression prediction lines and 95% confidence intervals).*

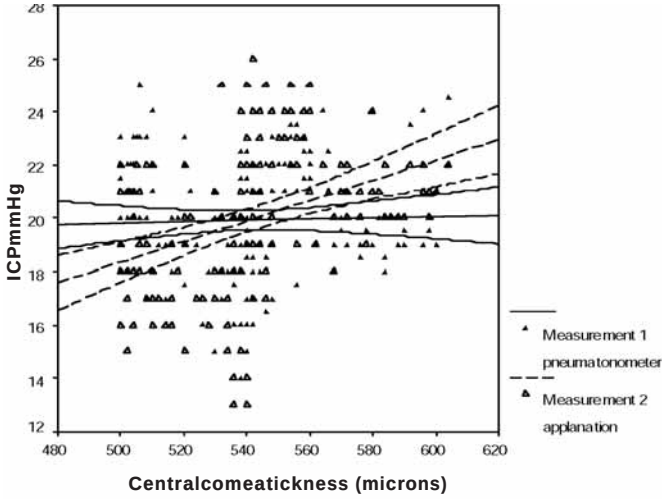

Fig. 3 - *Relationship between central corneal thickness measurements with intraocular pressure estimates of pneumatonometer and those of Goldmann applanation tonometer in eyes without previous laser-assited in situ keratomileusis (linear regression prediction lines and 95% confidence intervals).*

(Fig. 1D). CCT measurements were performed prior to IOP measurements in order to avoid the degradation of OCT images because of possible epithelial injury commonly occurring during IOP testing.

Intraocular pressure measurements

IOP measurements were performed by using two different tonometers. The sequence of IOP measurements by the two different devices was randomly determined in each eye in order to avoid any systematic measurement error.

Applanation tonometry readings were obtained with a GAT device (AT 020, Carl Zeiss Jena GmbH, Zeiss Group, Jena) mounted on a Zeiss biomicroscope (Carl Zeiss Jena GmbH, Zeiss Group, Jena). Measurements were taken by using cobalt blue filter after instillation of a topical anesthetic eye drop (Benoxinate hydrochloride 0.4%) and application of fluorescein paper.

PT measurements were performed by using a commercially available device (Model 30 Classic PT, Mentor O and O Inc., Norwell, MD) with the patients in the seated position. Manual tonometry function was selected from the main menu of the instrument. As soon as the tonometer's probe was touched to the central cornea, the instrument began to display the average IOP and its standard deviation. The actual IOP for the particular eye was recorded when the standard deviation of the measurements was below 1 mmHg for at least 3 seconds.

Data analysis

In both groups; average of the $IOP_{differences}$ ($IOP_{difference}$= $IOP_{pneumatonometer}$ – $IOP_{applanation}$) obtained from each of the study eyes with two different tonometers was calculated and the statistical significance of the difference was investigated by the paired samples t-test.

Then, for each of the tonometer types, the correlation of the CCT with the IOP estimates was investigated by separate univariate regression analysis.

Statistical analysis was performed by using the computer program SPSS for Windows, release 7.0. For the current study, p values smaller than 0.05 were considered as statistically significant.

RESULTS

Mean CCT in our whole study population was 511.4±50.6 µm. The distribution of the corneal thickness data is shown in Table I.

Patients with previous LASIK (Group 1)

GAT estimated IOP statistically lower than PT in eyes with previous LASIK. There was 3.8±1.8 mmHg difference between the estimates of those two tonometers ($p<0.0001$, Tab. II).

In those patients, a statistically significant positive correlation was found between CCT and the IOP estimates of GAT (correlation coefficient, R=0.29, R^2=0.08, p=0.007).

$IOP_{applanation}$=0.02 * CCT+5.41 (*Regression equation 1*)

IOP estimates of PT, on the other hand, did not show any correlation with CCT (correlation coefficient, R=0.03, R^2=0.001, p=0.76).

$IOP_{pneumatonometer}$=0.002 * CCT+17.67 (*Regression equation 2*)

In those eyes with previous LASIK, linear regression lines of equations 1 and 2 did not intersect each other and GAT estimated IOP systematically lower than PT in all of the study eyes (Fig. 2).

Patients without any corneal refractive surgery (Group 2)

In these eyes, it was found that IOP estimates of two different tonometers were not different from each other (p=0.81, Tab. II). Mean IOP estimated with GAT was 19.9±2.8 and 19.9 ± 2.2 mmHg with PT.

TABLE I - DISTRIBUTION OF CCT IN THE STUDY POPULATION

	Number of patients (%)	Mean ± SD corneal thickness µm
Group 1 (patients with LASIK)	84 (35.9)	457.5 ± 35.2
Group 2 (patients without LASIK)	150 (64.1)	541.6 ± 27.6
All patients	234 (100)	511.4 ± 50.6

CCT = Central corneal thickness;
LASIK = Laser-assisted in situ keratomileusis

GAT estimates were found to be strongly correlated with CCT (correlation coefficient, R=0.38, R^2=0.14, p<0.0001).

$IOP_{applanation}$=0.038 * CCT – 0.705 (*Regression equation 3*)

However, there was not any statistically significant correlation found between CCT and IOP measurements obtained by PT in these patients (correlation coefficient, R=0.03, R^2=0.001, p=0.69).

$IOP_{pneumatonometer}$=0.0026 * CCT + 18.52 (*Regression equation 4*)

The linear regression lines of equations 3 and 4 intersected each other at around a CCT of 543 µm in that group of eyes with virgin corneas; i.e., in eyes with a CCT of 543 µm both tonometers would yield the same IOP. GAT estimated IOP higher than PT in eyes with thicker corneas (CCT above 543 µm) and lower in those with thinner ones (Fig. III).

DISCUSSION

In glaucoma practice, precise and correct measurement of IOP is of utmost importance – not only for making a correct diagnosis, but also for establishing a target IOP level and monitoring the patient. In recent years, the pitfalls of the GAT, which has been previously accepted as the gold standard of clinical IOP measurement procedure, have begun to appear in the medical literature. Most of the debate has been centered around the dependence of GAT readings on corneal thickness (6-12). This issue was not only described for ordinary patients in routine glaucoma practice, but also following excimer laser corneal refractive surgery (13-18).

By comparing the true IOP in the anterior chamber with

TABLE II - IOP MEASUREMENTS OBTAINED BY USING TWO DIFFERENT TYPES OF TONOMETERS

	IOP (mmHg) applanationtonometer Mean ± SD	IOP (mmHg) Pneumatonometer Mean ± SD	IOP (mmHg) Difference Mean ± SD	p value
Group 1 (eyes with LASIK)	14.7 ± 2.5	18.5 ± 2.0	-3.8 ± 1.9	<0.0001*
Group 2 (eyes without LASIK)	19.9 ± 2.8	19.9 ± 2.2	0.04 ± 2.2	0.81
All eyes	18.1 ± 3.7	19.4 ± 2.2	–1.3 ± 2.8	<0.0001*

* Means statistically significant; IOP=Intraocular pressure; LASIK = Laser-assisted in situ keratomileusis

the GAT measurements, Ehlers and associates showed that there was 0.70 mmHg error per 10 µm change of CCT from the ideal value of 520 µm (2). Other studies on the same subject also confirmed the relationship between CCT and GAT-derived IOP measurements. The measurement errors were considerably smaller than the Ehlers et al study and reported to be between 0.18 and 0.32 mmHg for 10 µm change in CCT (3, 4, 18).

Because there is common agreement that GAT-derived IOP measurements are indeed influenced by CCT, especially in patients with previous corneal laser refractive surgery, other methods or devices that will be less affected by corneal thickness must be developed. In our study, we primarily aimed to investigate whether PT could be useful for that purpose. This device uses air pressure as a sensor for measuring the force required in order to bend the cornea (i.e., the IOP) and is reported to be a more reliable method of IOP assessment in patients with scarred, edematous, and irregular corneas (25). In previous studies, IOP measurements obtained with PT were reported to be well correlated with Goldmann applanation tonometer but it was shown to yield higher-pressure estimates (26-28). In a manometric study comparing PT with Perkins applanation tonometer and with TonoPen, Eisenberg et al concluded that the PT provided the best representation of the true IOP especially within the range of 15 and 25 mmHg, and its estimates were not affected by patient age (29). They also demonstrated that both Perkins applanation tonometer and TonoPen underestimated the manometric true IOP. In another study, Abrams and coauthors have found that the use of both TonoPen and PT yielded superior accuracy and lower variability than the use of handheld applanation tonometer in rabbits (30). Three manometric studies found that excimer laser photoablation of up to 20% of CCT did not significantly reduce the accuracy of the IOP measurements obtained by PT (31-33). Also, a clinical study found that PT was more reliable than GAT after LASIK surgery (34).

In the current study, we observed approximately 4 mmHg mean difference between the estimates of GAT and PT (i.e., GAT estimates were lower than PT) in the group of eyes with previous LASIK. GAT estimates showed statistically significant correlation with CCT in that group of eyes. However, IOP estimates of PT did not have a similar relationship with CCT.

In the subgroup of eyes without previous LASIK, on the other hand, average of the IOP measurements obtained by using two different tonometers was not different. However, in this group of eyes, IOP measurements obtained by GAT showed a good correlation with CCT, while no relationship was found between the IOP estimates of PT with CCT. In eyes with thick corneas, IOP estimates of GAT were statistically higher than those of PT, while the reverse was true for eyes with thin corneas (PT estimates were higher than GAT).

Our results are somewhat contradictory with a recent published study; Bhan et al found that PT measurements were more dependent on CCT as compared with GAT in a group of normal eyes free from glaucoma (35). There were some differences between their study and ours. First, their patient population included only normal eyes, but our study purposefully included eyes with previous LASIK and patients with glaucoma suspicion. Secondly, in their study they used a different type of PT device: OBF pneumatonometry. We believe that the device they used probably measured something different than we measured in our study and it would be inappropriate to compare our results, which were obtained with a classical PT (Mentor model 30), with their data.

We preferred to measure CCT with the OCT device instead of an ultrasonic pachymeter. The use of OCT for determining CCT is relatively new. In a recent study, CCT was measured by OCT in various types of glaucoma patients, ocular hypertensives, and normal controls and it was found that CCT was higher in OHT when compared with other groups (19). By using OCT, it is possible to obtain noninvasive, noncontact measurements of corneal thickness exactly at the central cornea, because the probe beam can be traced on a real time monitor throughout the procedure (23, 24). In the ultrasonic pachymeter, the precise positioning of the probe is difficult, the exact points of sound reflection are ill defined, and applanation force may disturb the anterior reflecting surface. But we believe that the most superior characteristic of the OCT procedure is its high resolution and reproducibility (20, 21, 23, 24). OCT uses diode light source for imaging and has a resolution of 10 µm while the resolution of ultrasound is about 50 to 100 µm.

In conclusion, we found that the IOP estimates of PT were relatively independent from CCT both in patients with and without previous LASIK. On the other hand, the analysis showed that the IOP estimates of GAT were indeed influenced by CCT in all patients, both with and without LASIK. We found that they were positively correlated with CCT in eyes with and without previous LASIK.

Although the present study did not involve a direct mea-

surement of IOP by manometry, IOP estimates by using PT may be a useful adjunct to the clinical evaluation of the patients seen in glaucoma clinics. Especially when the full extent of nerve damage or progression of the optic neuropathy is not consistent with the IOP measurements obtained by GAT or for evaluating patients after laser keratorefractive surgery, we recommend the use of PT as a complementary IOP assessment method. We also recommend measuring CCT in those patients. In our clinic, we routinely measure the retinal nerve fiber layer thickness by OCT as a part of the initial work-up of patients referred to us as glaucoma suspect or as early glaucoma, and also obtain CCT measurements by the same device at the same session.

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