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Comparison of Central Corneal Thickness Measurements by Optical Coherence Tomography, Non-Contact Specular Pachymetry and Ultrasound Pachymetry in Patients with Primary Open Angle Glaucoma

KEYWORDS

Pachymetry, Primary open angle glaucoma.

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ABSTRACT

Purpose: To compare the central corneal thickness (CCT) measurements of non-contact methods, namely, Optical Coherence Tomography (OCT) and Non-Contact Specular Microscopy (NCSM) with those of the gold standard contact method i.e. ultrasonic pachymetry (UP) and to assess agreement between three devices in eyes with primary open angle glaucoma (POAG).

Material and methods: This study included 142 eyes (71 patients) with POAG. CCT was measuredinitially by non-contact methods followed by the contact method. An average of 3 readings was taken for each eye.

Results : The mean CCT values by OCT, NCSM, US PACHY were 507.53±34.22, 498.07±33.64 & 514.90±32.65 µm respectively. All the methods showed good reliability, significant correlation ($p < 0.001$).Bland Altman analysis showed good agreement.

Conclusion : All three methods are reliable, reproducible, have significantcorrelation with each other, can be used interchangeably with the application of correction formulae.

INTRODUCTION

Measuring Central Corneal Thickness (CCT)

Central Corneal thickness (CCT) measurements can be performed using either ultrasonic based or optic based technology[1], the procedure being referred to as Pachymetry. One of the most common approaches to the Pachymetry is ultrasound. Ultrasound (US) uses the "Doppler Effect" to determine thickness. Many previous studies have shown the contact method i.e. Ultrasound Pachymetry(UP) as Gold standard. The other advantage of contact method being that it is independent of media opacities. But being a Contact method it has risks of iatrogenic infections and epithelial micro-trauma, error due to incorrect probe placement. Whereas the non- contact methods i.e. Optical Coherence tomography(OCT) &Non-Contact Specular Microscopy(NCSM) are easily Reproducible, avoids the associated risk of contact methods, but are expensive and need greater technical skill and cooperation**.**

NCSM provides specular images and measures the focal distance, from which the corneal thickness can be calculated. This non-contact Specular microscope analyses the endothelium in addition to measuring the corneal thickness for not just the central but also the mid-peripheral cornea in all four quadrants up to 3 mm from the center[2]. Noncontact specular microscopy is reported to have more consistent inter-user readings, but gives a significantly lower reading than those generated by ultrasound Pachymetry. Besides, non-contact specular microscopy provides information of both central and peripheral cornea thickness, and also allows for evaluation of endothelial cell density simultaneously[2].

Optical coherence tomography (OCT) works on the principle of light reflection at optical interfaces: the "low-coherence interferometry" method. In this method, the low coherence light source used is a super luminescence diode which emits light of band width of 20-25 nm (near infrared). OCT results have an advantage that they cannot be biased by the incorrect placement of a probe as with the ultrasonic pachymetry. Besides, it allows high resolution cross-sectional imaging of the cornea in vivo, a feature that may be of special interest for quantification and localization of corneal abnormalities such as stromal scarring or edema. This particular feature makes the OCT comparable to ultrasound bio microscopy and very high frequency (VHF) ultrasound (like UBM- Ultra-biomicroscopy), making imaging possible even in cases like hydrops where ultrasound measurement fails.

Importance of CCT in Glaucoma

Apart from corneal diseases, CCT plays an important role in estimating the reliability of intraocular pressure measurements. Ehlers et al. have shown that CCT affects applanation tonometry measurements. Recent studies have disclosed the role of CCT in diagnosing glaucoma, as patients with ocular hypertension were found to have increased CCT. This may lead to falsely elevated intraocular pressure measurements, whereas patients with low tension glaucoma were noted to have decreased CCT, resulting in falsely low intraocular pressures measured[3].

Ocular Hypertension Study by Gordon et al reported that each 40µm decrease in CCT is associated with a relative risk of 1.71 for development of Primary Open Angle Glaucoma (POAG).In fact, progression of visual field loss in primary open angle glaucoma is highly correlated with thinner values of central corneal thickness[4].
A meta-analysis by Doughty and Zaman showed that a 10% change in CCT may result in an approximately 3.4 mm Hg change in intraocular pressure. Moreover, there is evidence supporting that CCT is an independent risk factor for the development and progression of glaucoma[1].

MATERIALS AND METHODS

The study was a Prospective, comparative, observational, cross-sectional, hospital-based study. The patients included in the study were diagnosed cases of POAG, Age >20 years and those giving consent. Patients with corneal pathologies, scarring, opacities, with previous history of intraocular surgery were excluded. A total of 71 patients (n=142 eyes) diagnosed with Primary Open Angle Glaucoma were included in the study.

A thorough history and examination of the patients enrolled for the study was recorded including the socio-demographic profile i.e. age, gender, socioeconomic status, education status. Clinical examination included uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA) on Snellen's chart, automated refraction, Intraocular Pressure (IOP) measurement, Slit Lamp Biomicroscopy of the anterior segment of the eye, and fundus examination by Direct Ophthalmoscopy. Gonioscopy was done in all known cases of primary open angle glaucoma (POAG) using Goldmann's 2 mirror gonioscope to document the open angle. Visual fields were charted by the Humphrey Field analyzer. Strategy used was Swedish Interactive Threshold Algorithm (SITA) central 30-2 threshold test.

This was followed by Central Corneal Thickness (CCT)

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measurements; first by the non-contact methods (specular microscope and OCT) followed by the contact method using ultrasound to avoid any effect of inadvertent trauma. An average of three readings was taken from OCT machine and Specular Microscope. Following this, topical anesthetic agent Proparacaine 0.5% was instilled and after 80 seconds of instillation an average of 3 readings was taken with the ultrasound pachymeter probe. In 132 eyes, all 3 methods were used and in 10 eyes 2 of the 3 methods were used for CCT measurements.

Instruments

1) Anterior segment OCT

It was performed using **Carl Zeiss Cirrus Tm HD Spectral Domain OCT** machine – Anterior segment 5 line raster scan.

2) Specular pachymetry

Secular pachymetry was performed by using **TOPCON SP 2000 P** specular microscope with image net 2000 database. Using this instrument, tracking of the cornea and endothelium are fully automatic, requiring minimal interventions by the operator.

3) Ultrasonic pachymetry

It is done using **QUANTEL MEDICAL POCKET II ULTRASONIC PACHYMETER** allowed for measuring and mapping corneal thickness.

Data collection and analysis

Standardized proforma was used to record observation.

All patient parameters were entered in computer friendly data entry form and an excel sheet was prepared. **Statistical analysis** was done using suitable statistical software for comparison between three methods of pachymetry. The tests used were: one way ANOVA test, Bonferroni test for multiple comparisons, paired t test, Pearson's correlation coefficient, reliability tests using Cronbach's alpha and Intraclass coefficient, Levene's test, Bland Altman analysis and linear egression for assessing agreement between the methods. Softwares used were: SPSS version 17, Med calc version 17, Graph pad prism version 7.02.

RESULTS

A total of 41 males and 30 females were included in the study. M:F ratio was 57.7% (n=41):42.3% (n=30). Meanage was 56.39 years (Range: 21-80 years).

The minimum and maximum CCT values in µm by OCT, NCSM, US PACHY were 408 & 650, 394 & 650, 420 & 660 respectively. The mean CCT values (in µm ± SD) by OCT, NCSM, US PACHY being 507.53±34.22, 498.07±33.64 & 514.90±32.65 respectively. The co-efficient of variability being 6.74%, 6.75% and 6.34% for OCT, NCSM and US PACHY respectively. The mean of differences for OCT and NCSM being 9.44±12.78, for OCT and US PACHY being 7.11±12.16, for NCSM and US PACHY being 16.25±10.27. The student paired t test and also the Pearson correlation test showed that OCT and NCSM, OCT and US PACHY, NCSM and US PACHY have significant correlation with each other with p values for all the three methods being <0.001, the r values being 0.929, 0.963, 0.952 respectively for the pairs.

Reliability

The three methods were found to be interchangeably reliable for the measurement of CCT. reliability for CCT measurements was calculated for OCT and NCSM in comparison to the gold standard US PACHYMETRY. The reliability percentage of the OCT and NCSM as compared to US PACHY was 98.27% and 98.73% with Cronbach's alpha for OCT and US PACHY being 0.966 and for NCSM and US PACHY being 0.975. No significant difference for the measurement of CCT by all the method was found between the right and the left eye.

Regression analysis

Showed that both OCT and NCSM could be used interchangeably with UP by the following formula**e**

US PACHY = 66.69 + 0.883 * OCT	US PACHY = 60.064 + 0.912 NCSM

Agreement

Agreement between the devices was assessed using the **Bland Altman analysis**. All the methods showed good level of agreement with each other. Among the three methods, US pachymetry had the best agreement with OCT with the least difference in means.

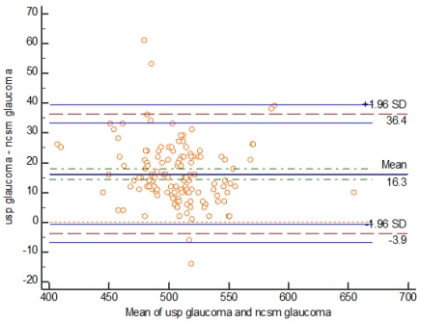

Figure 1: Bland-Altman plot for US PACHY and NCSM in POAG eyes and the 95% limits of agreement (LoA) (mean difference ± 1.96 SD)

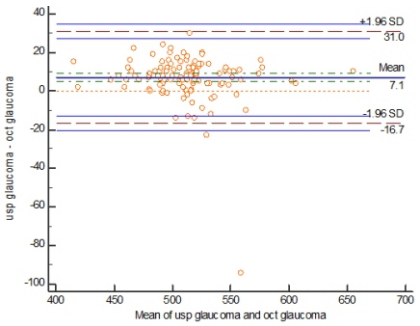

Figure 2: Bland-Altman plot for US pachymetry and OCT in POAG eyes and the 95% limits of agreement (LoA) (mean difference ± 1.96 SD)

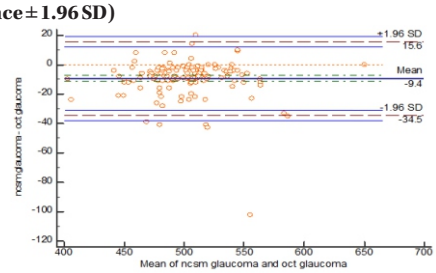

Figure 3: Bland-Altman plot for OCT and NCSM in POAG eyes and the 95% limits of agreement (LoA) (mean difference ± 1.96 SD)

Global indices of perimetry

In our study we compared the global indices of perimetry namely VFI (visual field index), MD (mean deviation) and PSD (pattern standard deviation) with central corneal thickness measured by different methods. Pearson correlation coefficient showed that the CCT measurement by any of the three methods does not correlate with the global indices of perimetry or the visual field defects. The scatter plots were made and R2 Linear was also calculated the values of which proved no statistical correlation between CCT measurements by all the three methods when compared to the global indices of perimetry even though they showed an inverse trend where VFI and PSD were concerned.

Intraocular pressure and CCT

Also the correlation of the CCT measured by the three methods with

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intraocular pressure was calculated using Spearman's **rho ' '** which showed that only US PACHY has significant correlation with IOP and to some extent NCSM but not with OCT.

DISCUSSION

CCT is a powerful predictor for development of POAG. Also its association with severity of POAG and degree of damagehas been proven. CCT measurements affect and alter IOP value measurement/ estimation. Various formulae propose adjustments in IOP estimation based on CCT values. However, as CCT measurements themselves change from instrument to instrument and hence accuracy of IOP measurement may also get affected.

In a study by Malah et al[5] and Fujioka et al[6], pachymetry showed positive association with IOP measurement by GAT (Goldman applanation tonometry) whereas in our study only USP had significant correlation with IOP. This discrepancy may be attributed to the fact that in our study we used non-contactAir-Puff tonometry and could not use Goldman applanation tonometer which is a standard tonometer. In previous study by Papadiya et al[7], a definite inverse relationship was found between CCT and damage to the visual fields whereas our study inverse correlation (not significant) was found between global indices of perimetry and CCT.

Ultrasound pachymetry is the gold standard for pachymetry. But its direct contact with cornea as well as possible pressure effects related and probe related errors in pachymetric measurements necessitate the need for evaluation of other non-contact pachymeters for their precision and agreement with the gold standard. Hence, one needs to develop formulae where the other non-contact methods may reliably predict the actual CCT values

Considering the limitations of these three instruments and the differences between them, even though in our study we found good correlation, reliability and agreement between OCT, NCSM and USP, the methods cannot be used simply interchangeably with each other in clinical practice without suitable correction formulae.

However, when the correction factors applied, non-contact methods of pachymetry (OCT and NCSM) gave similar results as those of Ultrasound pachymetry. We suggest that OCT and NCSM can be used interchangeably with Ultrasound pachymetry with application of correction factors.

It's advisable to use these non contact methods of central corneal thickness measurements instead of making the patients suffer from disadvantages of direct corneal contact like epithelial micro trauma, risk of infections as well as interoperator bias resulting due to probe placement and possible errors of measurements due to applanation effects of probe, use of anestheticdrops, displacement of tear film and misalignment of probe in case of ultrasound pachymetry.

CONCLUSION

Our study concluded that among the threemodalities, Ultrasound gives the highest value of CCT for a given cornea and Specular Microscopy gives the least, OCT lies in between. All three modalities show statistically significant correlation in pachymetric measurements. NCSM and OCT showed good reliability as compared to gold standard US pachymetry. All the three devices had good agreement with each other. Using certain proposedformulae, one may use the values from one instrument to predict those of another.
The use of these non-contact methods along with applied correction factors will be of great importance in the treatment of glaucoma where accurate CCT measurement plays a key role in proper management of glaucomaandprevention of glaucoma blindness.

References:

1) Bayhan HA, Aslan Bayhan S CI. Comparison of central corneal thickness measurements with three new optical devices and a standard ultrasonic pachymeter. 2014. Int J Ophthalmol. 2014;2:302–8.
2) Bovelle R, Kaufman SC, Thompson HW, Hamano H. Corneal thickness measurements with the Topcon SP-2000P specular microscope and an ultrasound pachymeter. Arch Ophthalmol (Chicago, Ill 1960) 1999;117(7):868–70.
3) Bechmann M, Thiel MJ, Neubauer a S, Ullrich S, Ludwig K, Kenyon KR, et al. Central corneal thickness measurement with a retinal optical coherence tomography device versus standard ultrasonic pachymetry. Cornea. 2001;20(1):50–4.
4) Correa-Perez ME, Lopez-Miguel A, Miranda-Anta S, Iglesias-Cortinas D, Alio JL, Maldonado MJ. Precision of high definition spectral-domain optical coherence tomography for measuring central corneal thickness. Invest Ophthalmol Vis Sci . 2012;53(4):1752–7.
5) El-Malah MA A-HN. Comparative measurement of central corneal thickness using Pentacam, ocular response analyzer, and ultrasound pachymetry devices for normal, glaucomatous, and keratoconic eyese. J Egypt Ophthalmol Soc. 2014;1(107(1)).
6) Fujioka M, Nakamura M, Tatsumi Y, Kusuhara A, Maeda H, Negi A. Comparison of PentacamScheimpflug camera with ultrasound pachymetry and noncontact specular microscopy in measuring central corneal thickness. Curr Eye Res . 2007;32(2):89–94.
7) Papadia M, Sofianos C, Iester M, Bricola G, Mete M, Traverso CE. Corneal thickness and visual field damage in glaucoma patients. Eye (Lond). 2007;21(7):943–7.