Comparison of Central Corneal Thickness Measurement Using Non-Contact and Contact Pachymetry Devices in Normal Eyes

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Purpose: To compare central corneal thickness (CCT) in normal population using contact and non-contact pachymetry devices and to assess the intra operator repeatability of measurement with each device.

Materials and Methods: This prospective, cross sectional comparative study evaluated 30 healthy subjects fulfilling the inclusion criteria reporting in AFIO Rawalpindi. CCT was measured in both eyes of subjects using noncontact specular microscope, Dual Scheimpflug analyzer and contact ultrasound pachymeter by a single investigator at the same time of the day. Pearson's correlation coefficient test was performed to ascertain correlation between pachymetry devices. Intra operator repeatability was analysed using within subjects coefficient of variation/repeatability (CoV) and intra class correlation coefficient (ICC).

Results: Sixty eyes of 30 male subjects were analysed. Mean age of study population was 31.03 ± 10.30 years. Mean CCT values were 536.48 ± 35.77 µm, 498.62 ± 34.70 µm and 526 ± 37 µm with Dual Scheimpflug Analyzer, Specular microscope and Ultrasonic pachymeter respectively (p < 0.01). There was significant linear co relation between all measurement modalities (r = 0.804 to r = 0.949) (p < 0.01). Intra operator repeatability was excellent for all devices as indicated by low CoV values (< 0.80%) and high ICC values (> 0.90).

Conclusion: All three devices showed excellent intra operator repeatability for CCT measurement making them reliable tools for CCT measurement.

Key Words: Central Corneal Thickness, Pachymetry, Repeatability, Microscopy.

Corneal thickness is a sensitive indicator of corneal hydration and patency of corneal endothelial pump. Accurate central corneal thickness (CCT) measurement (Pachymetry) has diagnostic and therapeutic implications in various conditions like ectatic corneal dystrophies (Keratoconus, Pellucid marginal degeneration), contact lens related problems, dry eyes, diabetes mellitus, glaucoma and refractive surgery (LASIK).1,2 An ideal method of pachymetry should be accurate, safe, repeatable, reproducible, easy and quick to perform.3 Over a period of time, many methods have been devised for pachymetry such as ultrasound pachymetry, ultrasound bio microscopy, slit scanning corneal topography, confocal microscopy, optical biometry, Scheimpflug system, specular microscopy, spectral domain OCT and very high frequency ultrasound scanner (VHFUS).2,3

For years, ultrasound pachymetry remains the gold standard method for measurement of CCT due to...
its high degree of intra operator and inter operator reproducibility.4 But the potential disadvantages of this method include possibility of probe malplacement and malalignment, inadvertent indentation leading to slightly thinner readings, patient’s discomfort, need for topical anaesthesia, epithelial damage and risk of infection.1,4,8 In the current era, newer non-invasive methods of pachymetry have been thoroughly evaluated for accuracy, precision, repeatability, reproducibility, and agreement between these new devices and gold standard ultrasound pachymeter. Many studies have demonstrated acceptable repeatability and reproducibility of various non-contact pachymetry equipments and conformed agreement between CCT measurements with non-contact methods and contact ultrasound methods.1,4, 7,9,10

The objective of this study was to compare CCT measurements in healthy volunteers using contact ultrasound pachymeter, noncontact Dual Scheimpflug analyzer and non-contact specular microscope and to assess the intra operator repeatability of measurement with each device.

MATERIAL AND METHODS

This prospective, cross sectional comparative study enrolled 30 consecutive healthy subjects (Staff members, candidates for medical examination and attendants of patients) reporting in Armed Forces Institute of Ophthalmology (AFIO) Rawalpindi between 21 June 2013 to 30 Aug 2013. Subjects with ocular or systemic disease, history of ocular surgery or trauma, intraocular pressure (IOP) > 21 mm Hg, refractive error ≥ ± 1.5 dioptres, contact lens wearers and those using any topical ocular medications were excluded. The study was conducted in accordance with the ethical considerations given in Helsinki declaration and written and informed consent was obtained from each subject before examination. Comprehensive ophthalmic examination including visual acuity, refraction, slit lamp examination and fundus examination was carried out in each subject.

CCT was measured in both eyes of subjects using noncontact specular microscope (SP 3000 P; Topcon, Japan), Dual Scheimpflug analyzer (Galilei™ G4; Ziemer, Switzerland) and contact ultrasound Pachymeter (IOPac® Advanced; Reichert). All the readings were taken by a single investigator at the same time of the day between 1000 – 1400 hours to avoid diurnal variation of pachymetry readings. For each subject all the measurements were performed within a 45 minute period. CCT readings were first taken by non-contact method (Specular microscope or Dual Scheimpflug Analyzer). Ten readings were recorded for each eye with a gap of 30 seconds after each reading and fresh alignment of equipment was done each time. Following measurements with both non-contact equipments, cornea was anaesthetized with topical 0.5% Proparacaine Hydrochloride (Alcaine) eye drops and 10 readings on each eye were taken with ultrasound pachymeter by placing the sterile ultrasound probe perpendicular to the centre of cornea and asking the patient to blink before each new reading. All the measurements were endorsed on a pre-devised proforma.

Statistical analysis of the data was done using SPSS version 13.0. All the data were tested for normality before analysis. Descriptive statistics i.e. means ± standard deviation (SD) for quantitative variables and frequencies and percentages for qualitative variables were used. Inter device differences were analysed using paired sample ‘t’ test. Pearson’s correlation coefficient test was performed to compare the mean CCT values obtained from non-contact equipment with contact ultrasound pachymeter. A p value of ≤ 0.05 was considered significant. Intra operator repeatability was analysed using within subjects coefficient of variation / repeatability (CoV) and intra class correlation coefficient (ICC). CoV was defined as the SD values divided by the mean result. The lower the CoV and higher the ICC the more repeatable the measurements were. For repeatability assessment 10 readings of right eye of 10 randomly selected subjects were used.

RESULTS

Sixty eyes of 30 healthy volunteer male subjects fulfilling the inclusion criteria were analysed. Mean age of study population was 31.03 ± 10.30 years (Range: 16- 50 Years) with 33.33% of subjects were in 3rd decade of life. Mean CCT values were 536.48 ± 35.77 µm , 498.62 ± 34.70 µm and 526 ± 37 µm with Galilei™ G4 Dual Scheimpflug Analyzer , SP 3000 Specular microscope and IOPac Advanced Ultrasound pachymeter respectively (p < 0.01). Mean CCT values for right and left eyes were comparable for each measurement modality (p > 0.05) (Table 1). Inter device comparison results showed that mean CCT values obtained by specular microscope and ultrasound pachymeter were 7.05% and 1.90% lower.
than Galilei analyzer values, while CCT measurement obtained by specular microscope were 5.25% lower than those from ultrasound method (p < 0.01). There was strong linear co relation between all measurement modalities with Pearson co relation coefficient ranging from r = 0.804 to r = 0.949 (p < 0.01) (table 2).

The coefficient of variation (CoV) and Intra class correlation coefficient (ICC) for CCT measurement from different methods is given in table 3. Agreement for successive measurements performed was excellent for all devices as indicated by low CoV values (< 0.80%) and high ICC values (> 0.90). Galilei Dual Scheimpflug analyzer produced lowest CoV (0.406%) and Specular microscope gave highest ICC values (0.996) indicating a high degree of intra operator repeatability of these equipments.

DISCUSSION
Importance of CCT measurement in various domains of ophthalmology including diagnosis of glaucoma, cataract and refractive surgery cannot be undermined. Availability of a precise and accurate non-contact pachymetry device with high intra operator repeatability eliminates the need of conventional ultrasonic pachymeter with its potential contact hazards. Most of the studies on CCT measurements in Pakistan have been done using various contact ultrasound pachymeter. Mean CCT values in our study were 526.27 ± 37 µm using ultrasonic pachymeter that were comparable to CCT values of 535.68, 531.08 and 540.60 µm quoted in various studies on Pakistani population.\textsuperscript{11-13} In our study, mean CCT values using Galilei Dual Scheimpflug analyzer, SP-

### Table 1: Central corneal thickness (CCT) measurements (n = 30).

<table>
<thead>
<tr>
<th>Method</th>
<th>Mean ± SD (µm)</th>
<th>Range (µm)</th>
<th>95% CI (µm)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Galilei G4 (Rt Eye)</td>
<td>538.03 ± 40.22</td>
<td>44.7 - 661.5</td>
<td>523.64 - 552.42</td>
<td>0.442</td>
</tr>
<tr>
<td>Galilei G4 (Lt Eye)</td>
<td>534.92 ± 31.31</td>
<td>491.1 - 652.7</td>
<td>523.72 - 546.12</td>
<td>0.398</td>
</tr>
<tr>
<td>SP - 3000 (Rt Eye)</td>
<td>499.30 ± 34.44</td>
<td>452.3 - 608.4</td>
<td>485.98 - 511.62</td>
<td>0.398</td>
</tr>
<tr>
<td>SP - 3000 (Lt Eye)</td>
<td>497.94 ± 35.52</td>
<td>452.3 - 615.3</td>
<td>485.23 - 510.65</td>
<td>0.450</td>
</tr>
<tr>
<td>IOPac (Rt Eye)</td>
<td>525.78 ± 35.45</td>
<td>481.7 - 641.6</td>
<td>513.09 - 538.47</td>
<td>0.450</td>
</tr>
<tr>
<td>IOPac (Lt Eye)</td>
<td>526.76 ± 39.09</td>
<td>480.7 - 661.2</td>
<td>512.77 - 540.75</td>
<td>0.450</td>
</tr>
</tbody>
</table>

### Table 2: Inter device comparison of CCT measurements (n = 60).

<table>
<thead>
<tr>
<th>Method</th>
<th>Mean Paired Difference</th>
<th>Pearson Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specular - Galilei</td>
<td>-37.85 ± 22.06</td>
<td>0.000</td>
</tr>
<tr>
<td>Ultrasound - Galilei</td>
<td>-10.20 ± 22.69</td>
<td>0.001</td>
</tr>
<tr>
<td>Specular - Ultrasound</td>
<td>-27.64 ± 11.65</td>
<td>0.000</td>
</tr>
</tbody>
</table>

*Mean Inter device Difference  **Paired sample ‘t’ test

### Table 3: Repeatability assessment of CCT measurements (n = 10).

<table>
<thead>
<tr>
<th>Method</th>
<th>CoV</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Galilei Analyzer</td>
<td>0.406%</td>
<td>0.992</td>
</tr>
<tr>
<td>Specular Microscope</td>
<td>0.768%</td>
<td></td>
</tr>
<tr>
<td>Ultrasound Pachymeter</td>
<td>0.569%</td>
<td>0.995</td>
</tr>
</tbody>
</table>
3000 Specular microscope and Ultrasonic pachymeter were 536.48 ± 35.77 µm, 498.62 ± 34.70 µm and 526 ± 37 µm respectively. A lot of work has been published in international literature regarding CCT measurement by different devices in various ethnic and racial groups (table 4). Most of the results from these studies are comparable to our results, whereas, observed differences from our results may possibly be due to racial differences, variation in study settings and measurement methods. Overall, inter device comparison in our study showed mean paired differences of CCT values being statistically significant between devices (p < 0.01). However, pairwise comparison of all devices demonstrated significantly strong linear correlation with Pearson correlation coefficient ranged from r = 0.804 to r =0.949. Study by Ou TH et al, showed significant good linear correlation between ultrasound pachymeter – Orbscan II (r = 0.793, p < 0.001) and ultrasound pachymeter – SP 3000 specular microscope (r = 0.890, p < 0.001) for CCT measurement in eyes with glaucoma or glaucoma suspect.5 However, CCT values obtained by Galilei dual Scheimpflug analyzer were comparable with our results. In our study, CCT values obtained by specular microscope were significantly lower than both ultrasound pachymeter and Galilei analyzer (p = <0.01). But this pattern of significantly lower CCT measurements obtained by specular microscopy as compared to other modalities had been reported in other studies as well.1,5,14,15 The difference between specular microscope pachymetry and other two methods used in our study was probably due to different operating principles. The non-contact specular microscopy is based on reflection of light, while ultrasonic pachymetry depends on reflection of ultrasonic waves from anterior and posterior corneal surfaces and Galilei dual Scheimpflug analyzer uses two rotating Scheimpflug cameras 180 apart along with placido imaging.

Comparing repeatability of the instruments is essential because it reflects amount of agreement that is possible between instruments. We used coefficient of variation (CoV) and intra class correlation coefficient (ICC) to ascertain intra operator repeatability and our results suggested excellent agreement of repeated measurements for all devices as indicated by low CoV values (< 0.80%) and high ICC values (> 0.990). In our study Galilei analyzer produced lowest CoV (0.40%) and specular microscope gave highest ICC (0.996) indicating high

### Table 4: CCT Measurement data reported in literature.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Eyes</th>
<th>Country</th>
<th>Ultrasonic Pachymeter</th>
<th>Specular Microscope</th>
<th>SD OCT</th>
<th>Corneal Tomography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ogbuehi KC et al (14)</td>
<td>32</td>
<td>KSA</td>
<td>560 µm</td>
<td>520 µm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bao F et al (15)</td>
<td>70</td>
<td>–</td>
<td>539.01 µm</td>
<td>513.66 µm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wond AC-M et al (16)</td>
<td>74</td>
<td>Hong Kong</td>
<td>555.11 µm</td>
<td>–</td>
<td>523.21 µm</td>
<td></td>
</tr>
<tr>
<td>Almibrad TM et al (1)</td>
<td>114</td>
<td>KSA</td>
<td>546.69 µm</td>
<td>518.53 µm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Piotrovik I et al (3)</td>
<td>28</td>
<td>Poland</td>
<td>555.74 µm</td>
<td>–</td>
<td>537.92 µm</td>
<td></td>
</tr>
<tr>
<td>Ladi SJ et al (4)</td>
<td>92</td>
<td>India</td>
<td>541.83 µm</td>
<td>–</td>
<td></td>
<td>541.27 µm</td>
</tr>
<tr>
<td>Shafiq I et al (7)</td>
<td>108</td>
<td>Pakistan</td>
<td>542.04 µm</td>
<td>–</td>
<td></td>
<td>537.44 µm</td>
</tr>
<tr>
<td>Faramarzi A et al (17)</td>
<td>100</td>
<td>–</td>
<td>496.97 µm</td>
<td>–</td>
<td></td>
<td>524.06 µm</td>
</tr>
</tbody>
</table>

lower CCT values (524 ± 36 µm) compared with Galilei (542 ± 26 µm) and Pentacam (544 ± 26 µm).18 However, CCT values obtained by Galilei dual Scheimpflug analyzer were comparable with our results. In our study, CCT values obtained by specular microscope were significantly lower than both ultrasound pachymeter and Galilei analyzer (p = <0.01). But this pattern of significantly lower CCT measurements obtained by specular microscopy as compared to other modalities had been reported in other studies as well.1,5,14,15 The difference between specular microscope pachymetry and other two methods used in our study was probably due to different operating principles. The non-contact specular microscopy is based on reflection of light, while ultrasonic pachymetry depends on reflection of ultrasonic waves from anterior and posterior corneal surfaces and Galilei dual Scheimpflug analyzer uses two rotating Scheimpflug cameras 180 apart along with placido imaging.

Over a period of last decade, various computerized corneal tomography devices were developed based on the principle of placido disc and slit scanning (Orbscan II), single rotating Scheimpflug camera (Pentacam) and dual Scheimpflug and placido disc (Galilei) that provide more reliable pachymetry data apart from providing accurate curvature and topographic analysis of cornea. In a study by Crawford AZ et al Orbscan II measured significantly lower CCT values (524 ± 36 µm) compared with Galilei (542 ± 26 µm) and Pentacam (544 ± 26 µm).18 However, CCT values obtained by Galilei dual Scheimpflug analyzer were comparable with our results. In our study, CCT values obtained by specular microscope were significantly lower than both ultrasound pachymeter and Galilei analyzer (p = <0.01). But this pattern of significantly lower CCT measurements obtained by specular microscopy as compared to other modalities had been reported in other studies as well.1,5,14,15 The difference between specular microscope pachymetry and other two methods used in our study was probably due to different operating principles. The non-contact specular microscopy is based on reflection of light, while ultrasonic pachymetry depends on reflection of ultrasonic waves from anterior and posterior corneal surfaces and Galilei dual Scheimpflug analyzer uses two rotating Scheimpflug cameras 180 apart along with placido imaging.

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degree of repeatability of these instruments. Weerawat K et al, reported high intra operator repeatability (ICC = 0.985) for CCT measurement by ultrasonic pachymeter that was comparable to our repeatability results using ultrasonic pachymeter (ICC = 0.995). Various studies demonstrated high intra operator repeatability of various non-contact pachymetry devices (Galilei, Orbscan, specular microscope and SD OCT) and ultrasonic pachymeter for CCT measurement as reflected by low CoV (between 0.33 – 0.93 %) and high ICC values (> 0.978). 3-4,10,15,18

Discrepancies between studies may be due to several factors, including statistical method, subject characteristics, and the definition of acceptable agreement. Subject characteristics also may influence the interpretation of agreement. One of the limitations of our study was that we examined both eyes of each subject. Although this increases the sample size, it raises the fundamental issue of inter eye correlation. The use of both eyes of each subject therefore may account for some of the differences reported between studies. In the current study, the pachymetry values obtained by the Galilei, Specular microscope, and ultrasonic pachymeter were sufficiently disparate that the 3 devices could not be considered equivalent. As the true gold standard for CCT measurement is not yet established, it is difficult to conclude which device obtains the most accurate measurements, and therefore it is not possible to recommend one device absolutely over the others at the present time.

CONCLUSION
Both non-contact devices showed excellent intra operator repeatability for CCT measurement that was comparable to contact method in normal eyes making them reliable tools for CCT measurement providing better patient comfort. Although, all three devices showed strong linear correlation, they are not inter changeable as mean CCT measurement values differ significantly between instruments.

REFERENCES
14. Ogbuehi KC, Osubagwu UL. Repeatability and interobserver reproducibility of Artemis - 2 high -


