Published in final edited form as:

Optom Vis Sci. 2016 November ; 93(11): 1356–1363. doi:10.1097/OPX.0000000000000987.

Simulated Keratometry Repeatability in Subjects with & without Down Syndrome

Ayeswarya Ravikumar, PhD, Jason D. Marsack, PhD, FAAO, Julia S. Benoit, PhD, and Heather A. Anderson, OD, PhD, FAAO

University of Houston, College of Optometry, Houston, Texas

Abstract

Purpose—To assess the repeatability of simulated keratometry measures obtained with Zeiss Atlas topography for subjects with and without Down syndrome (DS).

Methods—Corneal topography was attempted on 140 subjects with DS and 138 controls (aged 7 to 59 years). Subjects who had at least 3 measures in each eye were included in analysis (DS: $n=140$ eyes (70 subjects) and controls: $n=264$ eyes (132 subjects)). For each measurement the steep corneal power (K), corneal astigmatism, flat K orientation, power vector representation of astigmatism (J_0 , J_{45}), and astigmatic dioptric difference were determined for each measurement (collectively termed keratometry values here). For flat K orientation comparisons, only eyes with >0.50 DC of astigmatism were included (DS: $n=131$ eyes (68 subjects) and control: $n=217$ eyes (119 subjects)). Repeatability was assessed using 1) group mean variability (average standard deviation (SD) across subjects), 2) coefficient of repeatability (COR) 3) coefficient of variation (COV), and 4) intraclass correlation coefficient (ICC).

Results—The keratometry values showed good repeatability as evidenced by low group mean variability for DS vs control eyes ($0.26D$ vs $0.09D$ for all dioptric values; 4.51° vs 3.16° for flat K orientation); however, the group mean variability was significantly higher in DS eyes than control eyes for all parameters ($p < 0.03$). On average, group mean variability was $2.5\times$ greater in the DS eyes compared to control eyes across the keratometry values. Other metrics of repeatability also indicated good repeatability for both populations for each keratometry value, although repeatability was always better in the control eyes.

Conclusions—DS eyes showed more variability (on average: $2.5\times$) compared to controls for all keratometry values. Although differences were statistically significant, on average 91% of DS eyes had variability $< 0.50D$ for steep K and astigmatism, and 75% of DS eyes had variability < 5 degrees for flat K orientation.

Keywords

Repeatability; simulated keratometry; Down syndrome; corneal topography

Corneal topography has been used extensively for mapping the surface of the cornea and assists in the diagnosis of corneal conditions such as keratoconus (KC), pellucid marginal degeneration and astigmatism. It is a commonly used measurement before refractive surgery to detect KC suspects, as well as in the management of patients with KC. In order to look for the development or progression of disease (e.g. KC), one is interested in change in corneal morphology over time. However, if measurements within a single session are highly variable, then it could be hard to know what constitutes real change versus normal variability in the measurement. While simulated keratometry from topography is not the only aspect of the topography map one would use to screen for disease, it is a useful component that can easily be compared from one capture to the next as a measure of repeatability of the topography scan. As stated by Vas et al¹ “Measurements are considered reliable if they are stable over time in stable subjects, show adequate levels of measurement variability, and are sensitive (precise) enough to detect clinically important change over time.”

Many studies have demonstrated the repeatability of topography measures for typical eyes and eyes with KC as reported in the discussion below, however, the variability of such measures have not been reported in patients with Down syndrome (DS). DS is a genetic condition associated with both structural and functional abnormalities. Several studies have reported that the eyes of individuals with DS have structural differences compared to aged matched populations without DS, such as thinner and steeper corneas,^{2–4} which may contribute to the observed higher incidence of refractive error,^{5, 6} as well as higher levels of astigmatism.^{3, 4, 7–10} Many studies have also reported a higher prevalence of KC in individuals with DS,^{11, 12} but it is not known if the structural differences in their thinner, more astigmatic corneas simply mimic KC, represent an incomplete (form fruste) KC, or is a truly progressive form of the disease.

Given that patients with DS may be at increased risk for certain corneal diseases, such as KC, understanding the variability expected with repeated measures of topography in this population is important to detect actual change over time. There are two reasons one would expect more variation in topography measurements in DS eyes: 1) they are likely to have more astigmatic and possibly more distorted corneas than the general population and 2) they may have less cooperation for measurements than the general population –related either to behavioral difficulties in cooperation due to intellectual disability, or related to reduced visual acuity^{13–15} (a common finding in this population) creating difficulty with fixation. Therefore the purpose of this study is to evaluate the repeatability of simulated keratometry values from topography measurements in DS eyes in comparison with age-matched individuals without DS.

METHODS

Subjects

Subjects with Down Syndrome—Individuals with DS were recruited from the Down syndrome Association of Houston (DSAH) or from Special Olympics Lions Club International Opening Eyes (SOLCIE) vision screening events in Texas. Individuals with DS with nystagmus, strabismus, any corneal or lenticular opacities, and/or poor fixation were excluded from participation (n = 10). Subjects with a previous history of ocular

surgeries were also excluded ($n = 2$). Ultimately, measurements were collected from 140 subjects with DS (44% female) aged 8 to 55 years (mean = 25 years $\pm$ 9 years). While no formal assessment of developmental ability was made of the participants in this study, all recruited subjects with DS were either actively involved in organized athletics (SOLCIOE) or adult education (DSAH) and were capable of sitting down and following instructions to complete topography measures. Thus we believe this sample of individuals likely represents the moderate to high functioning subsets of the Down syndrome population.

Control Subjects—Control subjects were recruited from the University of Houston faculty, staff, students, their friends and family. Optometry students, faculty with optometric doctorates, and clinic patients were excluded in an attempt to form a more general sample of the population. In addition, individuals who had previously undergone refractive surgery were excluded from participation. One hundred thirty eight age and sex-matched control subjects without DS (50% female) aged 7 to 59 years (mean = 25 years $\pm$ 10 years) participated in the study.

Protection of Human Subjects

This study followed the tenets of the Declaration of Helsinki and was approved by the University of Houston Committee for the Protection of Human Subjects. Parental/guardian permission was obtained from all subjects with DS recruited from the Down syndrome Association of Houston events. A consent waiver was approved for all subjects with DS recruited from SOLCIOE vision screenings given that the measurements were obtained as a part of a free vision screening to which the participants had already given consent and the measurements were collected without individually identifying information. Informed consent was obtained from all adult control subjects and parental permission and subject assent obtained for all control subjects less than 18 years of age.

Measurement of Corneal Topography

Corneal topography measurements were obtained using the Zeiss Atlas 9000 corneal topographer (Carl Zeiss Meditec, Inc. Jena, Germany). The examiner attempted to capture a minimum of four measurements per eye, although some subjects with DS had fewer successful captures due to difficulty in cooperation. Simulated keratometry measurements consisting of flat and steep corneal power (D) separated by 90° over a 3mm diameter and their corresponding angular orientation were exported. Corneal astigmatism magnitude was calculated as the difference between steep and flat K powers and the meridian associated with the flattest K was termed the axis of corneal astigmatism.

Quality Assessment of Topographic Images

As described in a previous publication of this dataset¹⁶, a cornea and contact lens specialist with over 40 years of clinical experience who was masked to the purpose of the study and the study population assessed the quality of each topography image obtained from subjects with DS. This step was taken due to concerns about the potential for poor quality due to poor fixation or subject movement during capture in this population. The specialist reviewed all outputs from the topographer for each measurement, including axial, tangential, and elevation maps, as well as the image of the topographic mires. The specialist was also

permitted to compare multiple measurements simultaneously to identify potential outliers. The specialist was instructed to use stringent criteria when rating images and to rate images based upon capture quality only (sharpness of the mires, occlusion of the cornea by the lid or eyelashes) and not based upon any potentially observed corneal abnormalities (corneal dystrophy, suspected KC or irregular astigmatism). The specialist rated each individual image as good (no concerns about quality), moderate (some concerns about quality which may impact interpretation, such as minor focusing concerns or minor tear film abnormalities), and poor (bad quality due to observations such as complete lid obstruction, blurred mires, or misdirected gaze).

Given that the control subjects did not have difficulty cooperating for measurements, there was less concern about the quality of images captured from control subjects and thus an unmasked study investigator assessed the quality of the control subject images to alleviate the time-intensive task of the specialist from reviewing thousands of additional images. This decision was justified by demonstrating that the masked specialist and unmasked examiner graded a subset of control images similarly, as described in a previous publication of this same dataset¹⁶.

For analysis of measurement repeatability, only subjects with three images of at least moderate quality per eye were included (i.e. subjects with fewer than three moderate or good quality images per eye were excluded). ‘Good’ quality measurements were selected first and if a subject did not have three ‘good’ measurements, ‘moderate’ measurements were then used. The exclusion of ‘poor’ quality images and the preference to include ‘good’ quality measures was adopted to mirror the process likely to occur in clinical practice. In other words, if a clinician does not feel a capture is of reasonable quality, they would rightly dismiss the accuracy of the information. This study is interested in speaking to the repeatability of measures that a clinician is likely to accept and consider as reasonably accurate in the management of a patient.

Power Vector Analysis

Sphere, cylinder and axis components of a spherocylindrical prescription are not independent. Thus representing a spherocylindrical lens in vector notation (M , J_0 and J_{45}) as described by Thibos et al,¹⁷ is advantageous because it allows one to represent both the magnitude and orientation information associated with the cylinder power. In this notation M represents the mean spherical equivalent, J_0 describes a vertically oriented Jackson Cross-Cylinder for which positive values indicate *with the rule* astigmatism (minus cylinder axis 180) and minus values indicate *against the rule* astigmatism (minus cylinder axis 090), and J_{45} describes an obliquely oriented Jackson Cross-Cylinder for which positive values indicate a minus cylinder axis at 045 degrees and negative values indicate a minus cylinder axis at 135 degrees. For this study, vector notation was utilized to describe the corneal astigmatism as measured by topography by calculating J_0 and J_{45} vectors.

Dioptric Difference for Astigmatism from J_0 and J_{45} Vectors

To evaluate variability in of the three corneal astigmatism measures, the mean dioptric difference (expressed in vector notation) was calculated from the measures as defined below.

Astigmatic dioptric difference between each pairwise intra-subject measures time points was calculated applying a strategy described by Raasch et al¹⁸ to quantify test-retest variability of each pairwise intra-subject two time points in subjective refraction measures as

$$\Delta D_{ij} = \sqrt{(J_{0_i} - J_{0_j})^2 + (J_{45_i} - J_{45_j})^2} \quad (1)$$

where, D_{ij} = Astigmatic dioptric difference between the i^{th} and j^{th} time points, $i=1,2,3; j > i$ and $i \neq j$.

Mean astigmatic dioptric difference ($\Delta \bar{D}$) was calculated as the average of the three dioptric differences (D_{ij}) for each subject:

$$\Delta \bar{D} = \frac{1}{3} \sum_{i=1}^3 \sum_{j=1, j>i}^3 \Delta D_{ij} \quad (2)$$

Statistical Analysis

Statistical analyses were performed using Stata 13.1 (StataCorp, College Station, TX) and SAS 9.4 (SasInstitute, Cary, NC). All statistical tests were performed at the 0.05 level of significance. Subjects who had at least 3 measures in each eye were included in analysis (DS: n=140 eyes (70 subjects) and controls: n=264 eyes (132 subjects)). For flat K orientation comparisons, only eyes with >0.50 DC of astigmatism were included (DS: n=131 eyes (68 subjects) and controls: n=217 eyes (119 subjects)). To assess within-subject repeatability of corneal astigmatism magnitude, steep K power, flat K orientation, J_0 , and J_{45} , the within subject standard deviation (Sw), estimated from the residual variance in a 3-level variance components model, using the 3 repeated measures made on each eye of each individual and the coefficient of repeatability ($COR: 1.96 * 2 * Sw$)¹⁹ was reported. Coefficient of variation (COV) (the ratio of Sw to the mean of the 3 measurements)²⁰ was also calculated. As another measure of consistency, the intraclass correlation coefficient (ICC) (proportion of total variance that is attributable by the subject and eye level estimated using a 3-level variance component model)²¹ and 95% CI were reported. The ICC value is 1 in the absence of measurement error and is considered to be very good if the value is more than 0.90, moderate if 0.75 to 0.90, fair if 0.40 to 0.75 and poor if less than 0.40. The clustered Wilcoxon rank sum test²² was used to test whether keratometry measures differed across DS and control subjects accounting for inter-eye correlation. A linear mixed-effect regression was used to assess both the intra-subject variability and magnitude relationship of the keratometry measures, accounting for the clustered observations. Transformations were made where necessary to achieve linearity assumption. Descriptive plots such as scatter plots and cumulative frequency plots are also presented. All tested hypotheses and calculated metrics accounted for the dependency of the two eyes within an individual.

RESULTS

Variability in Topography Measures

Steep K Power, Flat K Orientation and Astigmatism—For steep K power (Figure 1A), variability increased significantly with increasing steep K power in DS eyes ($p=0.005$), but not in control eyes ($p=0.856$). Variability in flat K orientation (Figure 1B) decreased significantly with increasing astigmatism for both groups combined ($p<0.001$) and there were no differences in this relationship found between groups ($p=0.502$). Increased magnitude of astigmatism (Figure 1C) was found to be related to increased variability in DS ($p<0.001$) but not control eyes ($p=0.402$).

J_0 , J_{45} Vectors and Astigmatic Dioptric Difference—There was no significant relationship found among either group between the variability of the measures and magnitude of J_0 (DS: $p=0.094$; control: $p=0.226$) (Figure 1D). However, in control eyes the J_{45} variability was associated with its magnitude ($p=0.026$) (Figure 1E). For astigmatic dioptric difference (Figure 1F), the variability increased significantly with increasing astigmatism magnitude in DS eyes ($p<0.001$), but does not vary with astigmatism magnitude in control eyes ($p=0.525$).

Cumulative Frequency of Steep K, Astigmatism and Flat K Orientation—Figures 2A and 2B show the cumulative frequency percentage of variability of corneal steep K power, astigmatism magnitude, and flat K orientation for DS and control eyes. As noted in Figure 2A, approximately 91% of DS eyes and >99.2% of control eyes had variability 0.50D for both astigmatism magnitude (DS: 91.4%, control: 100%) and steep K (DS: 90.7%, control: 99.2%). 75% of DS eyes and 85% of control eyes had variability of flat K orientation 5 degrees (Figure 2B).

Table 1 displays repeatability analyses for all keratometry values for DS and control eyes. The columns on the left side of the table provide mean variability values by group (group mean of the average intra-subject standard deviations) and the right columns provide repeatability coefficients (*COR*, *COV*, *ICC*). We did not calculate *COV* for astigmatic vectors (J_0 , J_{45} and astigmatic dioptric difference) as the mean value of the variable is at or near zero. Overall, DS eyes showed more variability than the control eyes for all values. An estimate of 2.5× greater variability in DS versus control eyes is based on the average of the ratios of group mean variability for all values.

DISCUSSION

DS eyes showed more group mean variability (on average: 2.5×) compared to control eyes for all keratometry values. Although differences were statistically significant, on average 91% of DS eyes had variability 0.50D for steep K and astigmatism measures and 75% of DS eyes had variability 5 degrees for flat K orientation.

In general, one would conclude that the corneal parameters (corneal astigmatism, steep K power, Flat K orientation, J_0 and J_{45} , astigmatic dioptric difference) obtained from Zeiss Atlas topography for subjects with DS showed good repeatability, when applying the

standard interpretations of the various metrics for repeatability analysis (Table 1). However, it can be seen that they are not as repeatable as those measurements obtained from control eyes. Inspection of Table 1 also suggests that the *ICC* may not be as sensitive of a metric of repeatability in this case given that the majority of *ICC* values are excellent (>0.90) for both groups, despite the sizeable disparity in repeatability between the two groups.

The eyes of subjects with DS demonstrated a relationship of increasing measurement variability with increasing astigmatism and increasing steep K power which was not similarly observed in controls. The difference in trends between the two groups is likely attributed to the much larger range of astigmatism and steep K power in the subjects with DS, which has been previously reported.¹⁶

This study also demonstrated that for Flat K orientation, the variability (measurement uncertainty) decreases as the astigmatism magnitude increases in both DS and control eyes. This finding is not new and is consistent with previous findings, such as that of Kobashi et al²³, in which eyes with small amounts of astigmatism had greater differences in axis location. Kobashi et al limited the analysis to subjects who had $>1D$ of astigmatism because of uncertainty in eyes with lower astigmatism, whereas our study limited analysis to eyes with $>0.50 D$ of astigmatism, but the observed trend was consistent. This observation is also applied clinically in the stricter ANSI Z80.1 standards for verification of spectacles with larger amounts of cylinder power (axis must be within ± 2 degrees for $>1.50DC$), which reflects the recognition that axis determination is more precise for greater astigmatism and that the visual outcome is more dependent upon its precise orientation.

Comparison with other Studies

To compare our control data with other studies in normal eyes, the repeatability parameters were also calculated for mean K (average of steep K and flat K values). Our current results are comparable to the repeatability of other Placido disk-based corneal topographers^{23–27} as indicated in Table 2. In studies which reported intraobserver repeatability, the average of the 1st and 2nd observer is reported, as indicated by an asterisk in Table 2.

Savini et al²⁸ looked at the repeatability of Sirius topography measurements in post-surgical, KC and control eyes. To compare our findings from subjects with DS to the KC group, mean sim K was calculated in DS eyes. *COR* of sim K in KC and control eyes as reported by Savini et al was 0.41 and 0.29 respectively. In our current study, *COR* in DS and control eyes was 0.83 and 0.28 respectively. *COR* in our control group was similar to that reported by Savini et al, whereas in DS eyes it was double that of KC eyes suggesting that the increased variability in DS eyes reported in our study may be the result of factors other than corneal structure, such as behavioral limitations in fixation or cooperation for study measures. However, it should be noted that Savini et al did not include details about the severity of the disease of the KC eyes. *ICC* values of sim K in KC and control eyes as reported by Savini et al were 0.992 and 0.994. In our current study, the *ICC* values in DS and control eyes were 0.98 and 0.995 respectively. *ICC* values were very similar to that reported by Savini et al in both groups; however, as suggested above, the *ICC* may not be as sensitive as other metrics (*Sw*, *COR* and *COV*) for identifying differences in repeatability of corneal parameters obtained from corneal topography.

Limitations

As mentioned, there are multiple potential sources of variability in the measurement of DS eyes, one of which may be behavioral limitations for fixation. Although fixation was an issue for this population, the poorest quality images (as judged by the masked clinical examiner) were eliminated from this sample, and thus our sample is biased towards the variability of measures in cooperative patients with DS with moderate to good quality captures. In analyzing this data, we felt it most beneficial to report the repeatability of measurements that clinicians were likely to accept as adequate for interpretation, rather than to include all measures. We believed that if a clinician recognized an image as poor, it was not likely to be valued as a basis for comparison for change from year to year in the management of a patient, and thus we wanted to capture the variability in measurements that were likely to be deemed adequate by a clinical examiner.

A second study limitation is that additional clinical findings were not collected on these subjects, so we cannot speak to whether the subjects had corneal diseases. A comparison of corneal powers and astigmatism between subjects with DS and controls has already been reported from this dataset¹⁶ and thus it is known that the corneal parameters differed overall between these populations, although whether those are stable structural differences or the result of potentially progressive corneal disease remains unknown.

A third limitation is that the findings may not be generalizable to other topographers. However, a comparison of our repeatability measures on control subjects with studies utilizing different instruments (Table 2) suggests that variability may be relatively similar across multiple instruments, suggesting that variability of simulated keratometry measures may not be greatly instrument dependent in the typical population, but whether this holds true for individuals with DS remains unknown. The Zeiss Atlas topographer was selected for this study population due to its fast capture time, easy subject task (fixate a stationary red light), and longer working distance. We believe these characteristics made it compatible for examining this population. It remains to be seen if success of capture and repeatability would be as good with topographers that adopt a shorter working distance or have rotating components (e.g. rotating scheimpflug camera) that could be distracting.

While strength of this study was the inclusion of a non-clinical population of individuals with DS from the community, this testing environment restricted the ability to evaluate possible correlations between other clinical measures (e.g. visual acuity, developmental ability, etc.) and topography repeatability. Future studies to evaluate these potential relationships could be conducted in a clinical setting as well as with additional topographers to determine how the repeatability of the Zeiss Atlas compares to other instruments in this special population.

CONCLUSIONS

DS eyes showed more variability (on average: 2.5×) compared to controls for all keratometry values. Although differences were statistically significant, on average 91% of DS eyes had variability 0.50D for steep K and astigmatism, and 75% of DS eyes had variability 5 degrees for flat K orientation.

Acknowledgments

Funding: NIH EY024590, NIH T35EY07088-28

We would like to thank Rachel Knowlton B.A and Ralph Herring OD, MHA, FAAO for assistance in collection of corneal topography measurements and Norman Leach OD, MS, FAAO for assessing the quality of topography images in eyes with DS. We also thank the Down Syndrome Association of Houston and the Special Olympics for allowing us to recruit participants with DS at their events.

References

1. Vaz S, Falkmer T, Passmore AE, Parsons R, Andreou P. The case for using the repeatability coefficient when calculating test-retest reliability. *PLoS One*. 2013; 8:e73990. [PubMed: 24040139]
2. Haugen OH, Hovding G, Eide GE. Biometric measurements of the eyes in teenagers and young adults with Down syndrome. *Acta Ophthalmol Scand*. 2001; 79:616–25. [PubMed: 11782229]
3. Little JA, Woodhouse JM, Saunders KJ. Corneal power and astigmatism in Down syndrome. *Optom Vis Sci*. 2009; 86:748–54. [PubMed: 19390470]
4. Vincent AL, Weiser BA, Cupryn M, Stein RM, Abdolell M, Levin AV. Computerized corneal topography in a paediatric population with Down syndrome. *Clin Experiment Ophthalmol*. 2005; 33:47–52. [PubMed: 15670078]
5. Woodhouse JM, Griffiths C, Gedling A. The prevalence of ocular defects and the provision of eye care in adults with learning disabilities living in the community. *Ophthalmic Physiol Opt*. 2000; 20:79–89. [PubMed: 10829129]
6. Woodhouse JM, Pakeman VH, Clegg M, Saunders KJ, Parker M, Fraser WI, Sastry P, Lobo S. Refractive errors in young children with Down syndrome. *Optom Vis Sci*. 1997; 74:844–51. [PubMed: 9383798]
7. Fimiani F, Iovine A, Carelli R, Pansini M, Sebastio G, Magli A. Incidence of ocular pathologies in Italian children with Down syndrome. *Eur J Ophthalmol*. 2007; 17:817–22. [PubMed: 17932861]
8. Caputo AR, Wagner RS, Reynolds DR, Guo SQ, Goel AK. Down syndrome. Clinical review of ocular features. *Clin Pediatr (Phila)*. 1989; 28:355–8. [PubMed: 2527102]
9. Clegg M, Woodhouse JM, Stewart RE, Pakeman VH, Bromham NR, Gunter HL, Trojanowska L, Parker M, Fraser WI. Development of refractive error and strabismus in children with Down syndrome. *Invest Ophthalmol Vis Sci*. 2003; 44:1023–30. [PubMed: 12601024]
10. Haugen OH, Hovding G, Lundstrom I. Refractive development in children with Down's syndrome: a population based, longitudinal study. *Br J Ophthalmol*. 2001; 85:714–9. [PubMed: 11371494]
11. Walsh SZ. Keratoconus and blindness in 469 institutionalised subjects with Down syndrome and other causes of mental retardation. *J Ment Defic Res*. 1981; 25(Pt 4):243–51. [PubMed: 6460109]
12. Cullen JF, Butler HG. Mongolism (Down's Syndrome) and Keratoconus. *Br J Ophthalmol*. 1963; 47:321–30. [PubMed: 14189698]
13. Little JA, McCullough S, McClelland J, Jackson AJ, Saunders KJ. Low-contrast acuity measurement: does it add value in the visual assessment of down syndrome and cerebral palsy populations? *Invest Ophthalmol Vis Sci*. 2013; 54:251–7. [PubMed: 23233262]
14. Courage ML, Adams RJ, Reyno S, Kwa PG. Visual acuity in infants and children with Down syndrome. *Dev Med Child Neurol*. 1994; 36:586–93. [PubMed: 8034120]
15. John FM, Bromham NR, Woodhouse JM, Candy TR. Spatial vision deficits in infants and children with Down syndrome. *Invest Ophthalmol Vis Sci*. 2004; 45:1566–72. [PubMed: 15111616]
16. Knowlton R, Marsack JD, Leach NE, Herring RJ, Anderson HA. Comparison of Whole Eye versus First-Surface Astigmatism in Down Syndrome. *Optom Vis Sci*. 2015; 92:804–14. [PubMed: 26002006]
17. Thibos LN, Horner D. Power vector analysis of the optical outcome of refractive surgery. *J Cataract Refract Surg*. 2001; 27:80–5. [PubMed: 11165859]
18. Raasch TW, Schechtman KB, Davis LJ, Zadnik K. Repeatability of subjective refraction in myopic and keratoconic subjects: results of vector analysis. *Collaborative Longitudinal Evaluation of*

- Keratoconus (CLEK) Study Group. *Ophthalmic Physiol Opt.* 2001; 21:376–83. [PubMed: 11563425]
19. Bland JM, Altman DG. Measurement error. *BMJ.* 1996; 312:1654. [PubMed: 8664723]
20. Everitt, BS. *The Cambridge Dictionary of Statistics.* Cambridge, UK: Cambridge University Press; 1998.
21. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. *Psychol Bull.* 1979; 86:420–8. [PubMed: 18839484]
22. Rosner B, Glynn RJ, Lee ML. The Wilcoxon signed rank test for paired comparisons of clustered data. *Biometrics.* 2006; 62:185–92. [PubMed: 16542245]
23. Kobashi H, Kamiya K, Igarashi A, Ishii R, Sato N, Wang G, Shimizu K. Comparison of corneal power, corneal astigmatism, and axis location in normal eyes obtained from an autokeratometer and a corneal topographer. *J Cataract Refract Surg.* 2012; 38:648–54. [PubMed: 22342010]
24. Huang J, Savini G, Chen H, Bao F, Li Y, Chen H, Lu W, Yu Y, Wang Q. Precision and agreement of corneal power measurements obtained using a new corneal topographer OphthaTOP. *PLoS One.* 2015; 10:e109414. [PubMed: 25559203]
25. Mao X, Savini G, Zhuo Z, Feng Y, Zhang J, Wang Q, Chen H, Huang J. Repeatability, reproducibility, and agreement of corneal power measurements obtained with a new corneal topographer. *J Cataract Refract Surg.* 2013; 39:1561–9. [PubMed: 23860010]
26. Read SA, Collins MJ, Iskander DR, Davis BA. Corneal topography with Scheimpflug imaging and videokeratography: comparative study of normal eyes. *J Cataract Refract Surg.* 2009; 35:1072–81. [PubMed: 19465294]
27. Wang Q, Savini G, Hoffer KJ, Xu Z, Feng Y, Wen D, Hua Y, Yang F, Pan C, Huang J. A comprehensive assessment of the precision and agreement of anterior corneal power measurements obtained using 8 different devices. *PLoS One.* 2012; 7:e45607. [PubMed: 23049823]
28. Savini G, Barboni P, Carbonelli M, Hoffer KJ. Repeatability of automatic measurements by a new Scheimpflug camera combined with Placido topography. *J Cataract Refract Surg.* 2011; 37:1809–16. [PubMed: 21852068]

Figure 1.

The standard deviation of three repeated measures of steep K power (A), flat K orientation (B) astigmatism (C), J_0 (D), J_{45} (E) and astigmatic dioptric difference (F) as a function of the mean of three repeated measures of steep K (A), astigmatism (B, C & F), J_0 (D) and J_{45} (E) in diopters for both DS eyes (black diamonds) and control eyes (gray circles).

Figure 2.

Cumulative frequency percentage depicting the magnitude of variability of astigmatism and steep K power (A) and flat K Orientation (B) for eyes with and without DS. Percentages on (A) represent the average of the two frequencies for astigmatism and steep K at the 0.50D cut-off for DS and control eyes.

Table 1

Group mean variability and the repeatability of all keratometry values for DS and Control eyes.

Keratometry Value	Group	Group Mean Variability			p-Value	COR	Repeatability		
		Mean $\pm$ SD	Range	Ratio of DS/Control			COV	ICC	95% CI of ICC
Steep K (D)	DS	0.26 $\pm$ 0.35	0.01 to 2.28	2.89	< 0.001	1.22	0.93	0.96	0.951 to 0.972
	Control	0.09 $\pm$ 0.09	0.00 to 0.79						
Flat K orientation (Degrees)	DS	4.51 $\pm$ 7.02	0 to 61	1.43	0.024	23.42	11.31	0.98	0.977 to 0.988
	Control	3.16 $\pm$ 3.02	0 to 24						
Astigmatism (D)	DS	0.25 $\pm$ 0.40	0.02 to 3.20	2.78	< 0.001	1.31	27.48	0.84	0.794 to 0.877
	Control	0.09 $\pm$ 0.06	0.01 to 0.37						
J ₀ (D)	DS	0.12 $\pm$ 0.19	0.00 to 1.39	3.00	< 0.001	0.63	-	0.92	0.892 to 0.937
	Control	0.04 $\pm$ 0.04	0.00 to 0.19						
J ₄₅ (D)	DS	0.12 $\pm$ 0.11	0.00 to 0.89	2.40	< 0.001	0.47	-	0.90	0.875 to 0.927
	Control	0.05 $\pm$ 0.03	0.00 to 0.22						
Astigmatic dioptric difference (D)	DS	0.11 $\pm$ 0.16	0.00 to 1.07	2.75	< 0.001	0.53	-	0.67	0.605 to 0.737
	Control	0.04 $\pm$ 0.03	0.00 to 0.21						

COR = coefficient of repeatability calculated as $1.96 * 2 * S_w$

COV = coefficient of variation (Sw/mean ratio)

ICC = Intraclass correlation coefficient with 95% confidence interval

Table 2

Comparison of repeatability values with previous studies of simulated keratometry.

Keratometry Value	No of eyes	Study	Instrument	COR	COV	ICC
Steep K (D)	264	current study	Zeiss Atlas	0.36	0.30	0.99
	79	Huang et al (2015) *	OphthaTop	0.29	0.24	0.99
	35	Wang et al (2012) *	EyeSys Vista	0.35	0.29	0.99
			Medmont	0.22	0.17	0.99
	77	Mao (2013) *	Topolyzer	0.34	0.28	0.99
	57	Kobashi (2012)	Keratograph	0.30	0.24	0.99
Flat K orientation (Degrees)			Zeiss Atlas			0.98
	140	current study	Zeiss Atlas	8.75	4.71	0.99
Astigmatism(D)	57	Kobashi (2012)	Zeiss Atlas			0.98
	264	current study	Zeiss Atlas	0.29	10.53	0.97
J_0 (D)	57	Kobashi (2012)	Zeiss Atlas			0.96
	264	current study	Zeiss Atlas	0.15		0.98
	79	Huang et al (2015) *	OphthaTop	0.16		0.97
	77	Mao (2013) *	Keratograph	0.09		0.99
	57	Kobashi (2012)	Zeiss Atlas			0.92
	101	Read (2009)	Medmont	0.12		0.99
J_{45} (D)	264	current study	Zeiss Atlas	0.17		0.90
	79	Huang et al (2015) *	OphthaTop	0.12		0.92
	77	Mao (2013) *	Keratograph	0.08		0.98
	57	Kobashi (2012)	Zeiss Atlas			0.91
	101	Read (2009)	Medmont	0.12		0.95

* = values are average of 2 observers;

COR= coefficient of repeatability; COV= coefficient of variation and ICC = Intraclass correlation coefficient