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Original article

Intrasession repeatability of pachymetry measurements with RTVue XR 100 optical coherence tomography in normal cornea

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Abstract

Purpose: To assess intra-observer reproducibility and repeatability of corneal pachymetry measurements with RTVue XR-100 anterior segment optical coherence tomography (AS-OCT) in normal cornea.

Methods: Eighty-four eyes of 84 healthy volunteers were enrolled for this study. A single examiner performed 3 successive corneal pachymetry mappings with RTVue XR-100 AS -OCT in a single session. One eye was randomly selected for the analysis. Intrasession intraexaminer reproducibility and repeatability were calculated for the minimum corneal thickness (MCT), central corneal thickness (CCT, central 0–2 mm), pericentral (2–5 mm) and peripheral (5–6 mm) annular zones of cornea, in the pachymetry mapping protocol by intraclass correlation coefficient (ICC), coefficient of variation and test retest variability.

Results: The mean CCT was 497.08 ± 32.83 μm and MCT was 490.28 ± 32.87 μm. ICC was 0.994 for CCT and 0.983 for MCT in central 2 mm zone. ICC in the pericentral 2–5 mm zones and 5–6 mm zone was lower than that in central 2 mm zone, but were still over 0.961 in 2–5 mm zone and had ICC of 0.85 in 5–6 mm zone.

Conclusion: In normal cornea, corneal thickness measurements produced highly repeatable pachymetry measurements at the central and paracentral zones (up to 6-mm diameter) which could be because of the high resolution and faster image acquisition with RTVue XR-100 OCT.

Keywords: Pachymetry, Repeatability, AS-OCT

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Introduction

Measurement of the corneal thickness is essential in the preoperative assessment of corneal refractive surgery procedures, astigmatic keratotomy, phototherapeutic keratectomy and lamellar keratoplasty. It is also important in monitoring patients with corneal edema, keratoconus, and contact lens related problems and for the visualization of abnormal pattern in pellucid marginal degeneration.[1]

Precise quantitative measurements of the central corneal thickness (CCT) and minimum corneal thickness (MCT) can provide useful information for such clinical conditions. Measurement of thinnest corneal thickness or MCT is essential for the preoperative evaluation in deep anterior lamellar keratoplasty for partial trephination, collagen cross-linking and intrastromal ring placement. CCT measurement has become a part of risk assessment in management of glaucoma.[2] Hence, in clinical practice, it is mandatory to have devices which measure CCT, MCT and peripheral corneal thickness.

Ultrasound pachymetry (USP) is the most widely used technique to measure CCT.[3]

However, being a contact method, it can cause discomfort to the patient, has a risk of possible iatrogenic injury, and

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requires topical anesthesia and its measurement precision depends on the operators' skill. These drawbacks have led to the development of non-contact methods for corneal thickness measurements.

Commercially available RTVue XR-100 optical coherence tomography (OCT, Optovue, Fremont, California, USA, Avanti edition, software version 2014.2) provides the clinician with non-contact method to assess CCT and measurement of the pericentral corneal thickness in annular zone up to 6 mm. It has an axial resolution of 5 μm, transverse resolution of 15 μm and a depth resolution of 5 mm. It uses diode laser (840 nm) as a light source and because of its high resolution, provides better delineation of anterior and posterior surface of cornea with the computer tracing algorithm. It takes 70,000 A-scans/s and has the cornea –anterior module (CAM) which helps in anterior segment imaging by taking 6 mm scans of cornea for pachymetric analysis. The high scan speed may minimize the effect of eye movement during data acquisition which improves the repeatability of pachymetry maps. Previous study has shown that the CCT measurements obtained with the OCT are lower than those of USP, but have good reproducibility.[4]

The aim of this study was to measure intrasession, intra-examiner repeatability and reproducibility of MCT, CCT (0–2 mm), and pericentral (2–5 mm) and transitional (5-6 mm) annular ring corneal thickness measurements using RTVue XR-100 OCT pachymetry mapping protocol.

Material and methods

A total of 84 healthy volunteers were enrolled for this prospective cross-sectional study. The study was conducted according to tenets of the Declaration of Helsinki for the use of human participants in biomedical research. Review board approval was not required for this study.

After informed consent, all subjects underwent complete ophthalmic examination including visual acuity, slit lamp, intraocular pressure measurement and fundus evaluation. Subjects with corneal pathology, ocular disease, history of contact lens wear, ocular trauma or ocular surgery were excluded from the study. All the scans were performed by a single experienced examiner and the measurements were performed between 3 pm and 5 pm to minimize the effect of diurnal variation on corneal thickness. One eye was randomly selected for the analysis.

RTVue XR -100 OCT with CAM-L (low - magnification corneal lens adaptor) anterior segment OCT pachymetry mapping protocol was used for measurement of corneal thickness. Each eye was scanned 3 times in a single visit with a gap of 3 min between each scan. An external illumination (2 goose neck cables with 735 nm LED) was used for illumination of the pupil. Subjects were asked to look at the internal fixation target and the scan was obtained when a bright, well centered infrared image of the central cornea was visualized and displayed on the real time OCT video image on the screen and the circular overlay. The operator positioned the corneal vertex at the center of the scan image to obtain the maximum, bright vertex flare reflection within 0.5 mm of the center of the scan and it was ensured that the scan is perpendicular to the corneal surface.

The OCT software automatically delineates anterior and posterior corneal boundaries in the cross-sectional images along the 8 meridians. The pachymetry numerical data map consists of 3 annular zones, subdivided into 8 equally placed radial sectors by 8 radial lines (6 mm length) with equally spaced meridians centered on the corneal vertex reflection subtending 45° angle each. Each radial line is composed of 1024 A scans and the entire map contains high definition 8192 A-scans acquired in 0.32 s. Average corneal thickness values are provided for the 3 sectors, which is, central 2 mm zone, surrounded by 8 annular zones in the 2–5 mm diameter (pericentral) and 5–6 mm diameter (transitional). It also gives minimum corneal thickness (MCT) value. In each sector (superior, superotemporal, temporal, inferotemporal, inferior, inferonasal, nasal and superonasal) pachymetry value was recorded from 2–5 mm diameter and 5–6 mm diameter.

Only scans with the good demarcation of anterior and posterior corneal boundaries and good measurement reliability rating with signal strength index (SSI) > 60, were included for the analysis. Images with artifacts due to eyelid margin, decentered images due to eye movement and images with poor corneal apex reflection were discarded.

Statistical analysis

Repeatability and reproducibility were analyzed using Statistical Package for the Social sciences (SPSS Inc., software version 15, Chicago, IL, USA). Intraclass correlation coefficient (ICC) is a measure of consistency for a data set, where a value of 1 represents perfect agreement, while 0.8 to 0.99 represents almost perfect agreement. Coefficient of variation (CV) is defined as the ratio of the standard deviation (SD) of the repeated measurements to the mean, where a lower value indicates high repeatability. Test retest variability measures interval within which 95 % of the difference between measurements is expected to lie.

Results

The mean age ± standard deviation of study participants was 38.24 ± 8.7 years (range, 22–56 years). There were 35 males and 49 females. The mean CCT was 497.08 ± 32.83 μm and the mean MCT was 490.28 ± 32.87 μm. The mean corneal thickness measurements and 95% confidence interval of various scan sectors is summarized in Table 1.

The ICC, CV and repeatability for each region are shown in Table 2. ICC was high for most of the sectors, ranging from 0.994 for CCT to 0.85 for superior nasal (5–6 mm) zone. CV ranged from 6.6% for CCT to 7.3% for superior (5-6 mm) zone. CCT and MCT measurements showed the best intraoperator repeatability. Test retest repeatability ranged from 2.3 μm for CCT to 15.3 μm for superior nasal (5-6 mm) zone.

The central 2 mm zone showed the best intra examiner and intrasession repeatability which relatively decreased from pericentral 2–5 mm zones to transitional 5–6 mm zones.

Discussion

The clinical utility of any instrument depends strongly on the reproducibility of its measurements and a good reproducibility means that the measurements obtained are not dependent on the operator.

Table 1. Pachymetric measurements at different corneal locations as measured by RTVue –XR 100 optical coherence tomography.

Parameters	Minimum (in μm)	Maximum (in μm)	Mean + standard deviation (in μm)	95 % confidence interval (lower bound-upper bound)
Central corneal thickness (Diameter < 2 mm)	446	549	497.08 ± 32.83	486.6–506.9
Minimum corneal thickness	439.7	539.3	490.28 ± 32.87	479.9–500.1
Pericentral zone (Diameter = 2–5 mm)				
Superior	467.3	600.7	527.72 ± 37.17	515.7–539.0
Superior temporal	456.7	590	515.88 ± 36.11	503.8–526.4
Temporal	451.7	569	503.25 + 33.74	491.6–512.2
Inferior temporal	449.3	560	502.2 ± 33.38	491.1–512.1
Inferior	447	560.7	507.88 ± 34.66	497.0–518.5
Inferior nasal	452	563.7	514.84 ± 34.5672	504.4–525.7
Nasal	458.3	572.7	521.53 ± 34.82	510.6–532.5
Superior nasal	470.7	589.7	528.68 ± 36.12	517.2–539.9
Transitional zone (Diameter = 5–6 mm)				
Superior	494	644	560.18 ± 40.83	546.4–572.3
Superior temporal	474.3	626.7	541.44 ± 38.86	527.5–552.3
Temporal	466	593.3	521.07 ± 34.98	508.6–531.3
Inferior temporal	466	579.7	520.43 ± 34.62	509.1–531.6
Inferior	464.7	587.3	529.9 ± 36.47	518.7–541.6
Inferior nasal	470	592	539.27 ± 36.55	528.2–550.5
Nasal	476.7	605.3	547.86 ± 36.18	535.6–558.6
Superior nasal	492.7	637	557.86 ± 37.38	544.9–568.7

Table 2. Intraobserver repeatability for pachymetric measurements at different locations by RTVue XR-100 optical coherence tomography.

Parameters	Test retest variability (μm)	Intraclass correlation coefficient (95 % Confidence interval)	Coefficient of variation (in %)
Central corneal thickness	2.35	0.9945 (0.991–0.997)	6.6
Minimum corneal thickness	4.3	0.983 (0.972–0.990)	6.7
Pericentral zone (Diameter = 2–5 mm)			
Superior	5.75	0.976 (0.961–0.986)	7.0
Superior temporal	5.18	0.980 (0.967–0.988)	7.0
Temporal	5.04	0.978 (0.964–0.987)	6.7
Inferior temporal	4.7	0.980 (0.967–0.989)	6.6
Inferior	4.35	0.984 (0.974–0.991)	6.8
Inferior nasal	5.08	0.979 (0.964–0.988)	6.7
Nasal	6.97	0.961 (0.935–0.977)	6.7
Superior nasal	6.85	0.965 (0.941–0.979)	6.8
Transitional zone (Diameter = 5–7 mm)			
Superior	7.38	0.968 (0.947–0.982)	7.3
Superior temporal	7.48	0.964 (0.941–0.979)	7.2
Temporal	7.95	0.950 (0.918–0.971)	6.7
Inferior temporal	7.49	0.955 (0.924–0.973)	6.6
Inferior	5.97	0.974 (0.956–0.985)	6.9
Inferior nasal	6.36	0.970 (0.951–0.983)	6.8
Nasal	11.95	0.898 (0.835–0.939)	6.6
Superior nasal	15.26	0.850 (0.763–0.909)	6.7

Repeatability and reproducibility of the pachymetry measurements obtained are dependent on factors such as short acquisition time of measuring device, variation in corneal thickness along the neighboring points, consistency of positioning the scan over the same points during scanning, and the number of sampling points for each region.

RTVue XR-100 OCT has better axial resolution (5 μm) compared to previous generation of OCT, allowing for deeper penetration, clearer delineation of anterior and posterior corneal boundaries, higher reflectivity from the outer most and deepest layer of the cornea, which improves edge detection and overall width calculation and hence a better repeatability is expected with this new device. It also enables continuous monitoring of the subject's eye during pachymetry scanning with the use of the real time corneal cross-sectional video monitor and corneal reflection i.e. vertical flare from the vertex, which further assists in confirming proper centration. It has fast acquisition speed of 0.32 s, which reduces the scanning time and therefore minimizes both patient and machine related motion artifacts resulting in higher accuracy and predictability.

Li et al.[5] reported CCT intrasession repeatability of 4.9 μm and 5.8 μm with Visante OCT (Carl Zeiss Meditec, Dublin, CA) and SL-OCT (slit lamp OCT; Heidelberg Engineering, Dossenheim, Germany) respectively in 25 healthy subjects. They also showed intersession reproducibility of 6.3 μm with Visante OCT and 7.6 μm with SL-OCT. The axial-scan density used in their study was lower and they used a horizontal scan line (15 mm with 215 axial scans in SL OCT and 16 mm with 256 axial scans in Visante OCT) for CCT measurement.

Mohamed et al.[6] showed intrasession CVs of 0.3% (central), 0.4% (2–5 mm) and 0.5% (5–7 mm) and intersession CVs of 0.5% (central) and 0.6% (2–5 mm) for corneal thickness using Visante AS-OCT.

They reported the ICC to be 0.998 for CCT, 0.996 for the (2–5 mm) corneal zone and 0.994 for the transitional zone (5–6 mm) in 27 healthy eyes.

Prakash et al.[7] used RTVue OCT (Optovue, Fremont, California, USA) in their study and reported a corneal thickness intersession reproducibility of 2.1 μm (central), 1.84 μm for MCT and 3.59 μm (2–5 mm pericentral). ICC was 0.999 for CCT and MCT and 0.995 for paracentral 2–5 mm zone. However, they reported the repeatability of average corneal thickness in the pericentral 2 to 5 mm zone and not in the each individual section of the pericentral 2 to 5 mm zone.

Huang et al.[8] assessed intraoperator repeatability of CCT, TCT and midperipheral corneal thickness measurements at corneal apex in 66 healthy volunteers using RTVue OCT.

Intraobserver repeatability was found to be the worst in superior 5 mm zone among the superior, nasal, inferior and temporal zones.

Another study assessed intra-examiner repeatability of corneal pachymetry maps in 72 eyes from 72 healthy volunteers using RTVue OCT with CAM.[9] Intraexaminer ICC was 0.994 (95% CI 0.991–0.996) for CCT and varied from 0.964 in superior -temporal pericentral zone to 0.978 in nasal and superior-nasal zone.

In our study, the ICC of corneal thickness measurement in the central 2 mm zone was 0.994.

Although the ICCs in the pericentral 2 to 5 mm zone were slightly lower than those in the central 2 mm zone, the ICCs were still over 0.961 in all the pericentral 2 to 5 mm zones and over 0.85 in the transitional 5–6 mm zone. Our results showed repeatability of 2.3 μm for CCT measurements and 4.3 μm (inferior) to 7 μm (nasal) repeatability for pericentral corneal thickness measurements and 6 μm (inferior) to 15.3 μm (superior nasal) in 5–7 mm zone. A change in corneal thickness in the 2–5 mm zone greater than 6.97 μm and 15.3 μm in 5–6 mm zone, would therefore be more likely to represent actual change rather than measurement error with the instrument.

Our results agree with the previous studies[8,9] which report more variation of midperipheral corneal thickness measurement than that for CCT measurement. The reason that RTVue XR -100 OCT showed variable intra-examiner repeatability in different scanning zones, could be due to the characteristics of the cornea, number of points measured in each zone and spacing of radial lines. The corneal central 2 mm zone is more or less planar but curved in the pericentral 2 to 6 mm zone and hence the OCT may be fast enough to overcome the eye motion artifact in the central 2 mm zone but not in the pericentral 2 to 5 mm and transitional 5-6 mm zone.[9] The difference in reproducibility of area between each scanning meridian was more obvious in the pericentral 2 to 5 mm and transitional 5–6 mm zone compared with the central 2 mm zone because the points measured also decrease from the center to the periphery of the cornea, where the radial lines are more spaced compared to the central pericentral zone.

Limitation of our study is that the participants in this study had clinically normal corneas; hence, the results obtained cannot be applied to patients who have undergone refractive surgery or have corneal pathology. Errors with scan positioning and alignments, especially in the areas of thinning (as in keratoconus), could result in higher variability of measurements.

Second, the ''pachymetry map'' protocol of RTVue OCT scans in only eight meridians, and derives the thickness in each sector by sampling interpolating points along these meridians.

Hence, the small areas of localized thickness variation between the sampled lines may not be reflected in the map. Third, the RTVue XR-100 OCT provides a pachymetry map of the central 6 mm diameter cornea, which is a limitation for measurement of corneal thickness in diseases which involve peripheral cornea, such as pellucid and Terrien's marginal degeneration. Fourth, the inter-observer reproducibility was not evaluated in our study.

In conclusion, the pachymetry mapping protocol of RTVue XR-100 OCT provides high-resolution, qualitative and quantitative imaging of the normal cornea and demonstrated good intra-observer repeatability in the central and pericentral zones obtained with the pachymetry mapping protocol because of clear fixation target, continuous video monitoring of the subject's eye to allow proper and consistent positioning for scanning over the same points during different scanning sessions. This can be useful to assess corneal thickness and monitor patients with corneal disease, such as abnormal thickening or thinning, and in longitudinal studies. Because of the high reproducibility, if the operator correctly follows the operating guidelines, the device could become operator-independent. Future studies in pathologic corneas using this device will further enhance the clinical utility of this advantage that OCT seems to have in normal corneas.

Conflict of interest

Authors declare that there is no conflict of interest.

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