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Original article

Central corneal thickness measurement by Fourier domain optical coherence tomography, ocular response analyzer and ultrasound pachymetry

Shu-Wen Chang [a, b, c, *], Po-Fang Su [d], Andy Y. Lo [d], Jehn-Yu Huang [c]

[a] Department of Ophthalmology, Far Eastern Memorial Hospital, Ban-Chiao District, New Taipei City, Taiwan
[b] Department of Community Health Development, Far Eastern Memorial Hospital, Ban-Chiao District, New Taipei City, Taiwan
[c] Department of Ophthalmology, National Taiwan University Hospital, Taipei, Taiwan
[d] Lo's Eye Clinic, Changhua City, Changhua County, Taiwan

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ABSTRACT

Purpose: To assess the repeatability, reproducibility, and agreement of central corneal thickness (CCT) measured by non-contact Fourier domain optical coherence tomography (FD-OCT; OptoVue) with the other two contact devices, ocular response analyzer (ORA; Reichert Ophthalmic Instruments) and Ultrasound Pachymetry (USP; DGH Technologies).

Methods: This observational cross-sectional study measured CCT sequentially using FD-OCT, ORA and USP. The first 16 volunteers (32 eyes) received three measurements by two independent examiners in a single session to determine intra-observer repeatability and inter-observer reproducibility. An additional 27 volunteers (54 eyes) received one measurement by the same examiner. The measurements of all 86 eyes were analyzed for the difference, correlation, and agreement among the three devices.

Results: FD-OCT measured the thinnest while USP measured the thickest CCT (548.6 ± 28.3 μm, 556.9 ± 28.8 μm, and 560.0 ± 28.8 μm by FD-OCT, ORA, and USP, respectively, $p < 0.001$). The mean differences (lower/upper limit of agreement) for CCT measurements were 8.4 ± 7.6 μm (−6.5/23.2) between ORA and FD-OCT, 11.4 ± 7.3 μm (−2.8/25.7) between USP and FD-OCT, and 3.1 ± 5.1 μm (−6.9/13.1) between ORA and USP. The intra-class correlation coefficients were above 0.98 for all tested groups. FD-OCT had the lowest intra-examiner variability (coefficient of repeatability of 0.64%) and lowest inter-examiner variability (coefficient of reproducibility of 1.16%).

Conclusion: FD-OCT, ORA, and USP demonstrated good inter-observer reproducibility and intra-observer repeatability. The three measurements were highly correlated; however, systematic differences between the three tested devices did exist. FD-OCT was a reliable and examiner-independent method in CCT measurement.

1. Introduction

Accurate central corneal thickness measurement (CCT) has clinically significant implications in glaucoma diagnosis and follow up.[1–8] The accuracy of corneal thickness measurement is also important in the evaluation of endothelial safety of newly emergent surgery modality,[9] dry eye therapy effect,[10] disease progression,[11] and refractive surgery evaluation.[12] Measurement of corneal thickness per se or monitoring its temporal alteration is considered as an overall functional evaluation of the corneal endothelium before and/or following intraocular surgery[11,13] and penetrating keratoplasty,[14,15] as well as in cases of prolonged contact lens wear[16] when *in vivo* confocal microscopy and specular microscopy are not possible.

Factors such as tear film thickness, topical eye drops used before examination including anesthetics and fluorescein, duration of contact lens wearing, diurnal variation, and pre-existing corneal pathologies or previous surgeries may influence corneal thickness

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* Corresponding author. Department of Ophthalmology, Far Eastern Memorial Hospital, Number 21, Section 2, Nanya South Road, Banciao District, New Taipei City 220, Taiwan.
E-mail addresses: swchang@mail.femh.org.tw, swchang2007@ntu.edu.tw (S.-W. Chang).

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measurement.[17,18] A corneal thickness measurement instrument less influenced by the tear film thickness that could be examined without topical anesthetics would thus provide more valuable and consistent information. There are many modalities available for corneal thickness measurement. Conventional ultrasonic pachymetry (USP) with a 10-MHz probe has been the gold standard with the advantages of ease of use, portability, low cost, and wide availability. Despite its high degree of inter-observer reproducibility and intra-observer repeatability, this technique is still operator dependent. Misalignment, corneal indentation, and variations in placing the probe all influence the final measurement. Furthermore, the requirement for cornea–probe contact and the resultant increased patient discomfort, risk for epithelial erosion, and transmission of infection have led to the development of several non-contact methods using various optical principles such as Scheimpflug imaging (Pentacam; Galilei Dual Scheimpflug Analyzer),[19–21] optical low-coherence reflectometry pachymeter,[22] slit-scan pachymetry (Orbscan),[20] and optical coherence tomography (Visante AS-OCT, RTvue-100 OCT).[21,23,24] Pentacam and Orbscan are clinically practical methods in corneal thickness measurement for refractive surgery. By contrast, AS-OCT measures the corneal thickness from linear cross-sectional images. It underestimates corneal thickness compared with USP, Pentacam, and Orbscan in unoperated eyes, although there is good repeatability and reproducibility among these instruments.[23,25] However, these results cannot be used interchangeably due to different design methodologies in previous studies.

Fourier Domain optical coherence tomography (FD-OCT; RTVue-100/CA, OptoVue, Fremont, CA, USA) is a newly emerged noncontact optical device capable of illustrating both retinal and corneal thickness and pathologies. For anterior segment measurement in FD-OCT, the information in an entire A-scan is acquired by a charge-coupled device (CCD) camera simultaneously. The A-scan acquisition rate is limited by the CCD camera frame transfer rate and the computer calculation time to perform the Fourier transform of the CCD-acquired raw data into A-scan information. It takes 26,000 A-scans per second, with a frame rate of 256–4096 A-scans per frame. The ocular response analyzer (ORA; Reichert Ophthalmic Instruments, Depew, NY, USA) is a new instrument designed to measure intraocular pressure (IOP) and the corneal-compensated IOP measurements obtained by the ORA are proposed to be independent of the corneal biomechanical properties. It is equipped with 20-MHz ultrasonic pachymetry (range 200–999 μm, accuracy ± 5 μm, display resolution ± 1 μm) for corneal thickness measurement. Both FD-OCT and ORA have gained more popularity in recent years. However, FD-OCT and ORA are usually owned by retinal and cornea/glaucoma specialists, respectively. Comparison of corneal thickness measurement by the two devices would provide interchangeable information to most ophthalmologists for their daily practice.

In the present study, FD-OCT with low magnification cornea lens adapters (CAM-L), ORA and 10-MHz ultrasound pachymetry (USP; DGH-500 Pachette, DGH Technologies, Exton, PA, USA) were compared for their repeatability, reproducibility, and agreement of CCT between methods.

2. Methods

2.1. Patients

This prospective study followed the tenets of the Declaration of Helsinki, and the protocol was reviewed and approved by the Institutional Board of our hospital. Informed consent was obtained from the patients before inclusion. Forty-three healthy young volunteers (17 male and 26 female) were randomly selected for the study from patients who visited the outpatient clinic.

2.2. Measurements

All measurements were taken between 10 AM and 4 PM (at least 2 hours after awaking), when corneal thickness is considered stable. Corneal thickness measurements were conducted in the sequential order of FD-OCT, ORA, and USP. Room illumination was set at 233–236 lux (TES-1339; TES Electrical Electronic Corp., Taipei, Taiwan). Patients who had a history of previous ocular surgery, ocular abnormalities other than cataract or refractive error, or were unable to cooperate in the examination were excluded. Contact lens wearers were asked to cease lens wearing for 1 week prior to data collection. Informed consent was obtained from all participants.

The FD-OCT RTVue-100/CA is a special version of the RTVue system that includes two cornea lens adapters, that is CAM-L (low-magnification cornea lens adapter) and CAM-S (high-magnification cornea lens adapter), for imaging the cornea and anterior chamber. Both lenses can be used to measure corneal flap or stromal thickness but only CAM-L can provide a corneal thickness map. We thus selected CAM-L for this study. In pachymetry map mode, the instrument has a scanning range of 8 mm × 6 mm and scanning depth of 2 mm. In this defined area, a total of 8 × 1024 scans were performed in 0.32 seconds (operator's manual). For examination, the patients were positioned with a headrest and external illuminations [two short goose neck cables with 735 nm light-emitting diode (LED)] were used for pupil illumination. To allow more precise alignment, the examiner observed a real-time image of the patient's eye on the video monitor. The cross-hair indicating the center of area of interest was centered on the pupil center. As soon as the image was perfectly aligned, the patients were asked to keep their eyes open during image capture. At the end of measurement, FD-OCT displayed a value of CCT that was an average of the central 2 mm of the cornea. This was different from ORA and USP, which showed the thickness of cornea at the point of contact. Each FD-OCT measurement was completed within 1 minute.

Five minutes after FD-OCT measurement, the cornea was anesthetized with topical 0.5% proparacaine hydrochloride (Alcaine, Alcon, Belgium) and CCT was measured with the ORA. For corneal thickness measurement by ORA, the ultrasound probe was placed manually as perpendicular as possible to the cornea at the pupil center, while the patient was instructed to fixate on a distant target. After contact with the cornea, the device automatically took several hundred measurements of corneal thickness (operator's manual). After measuring, three values were displayed: (1) mean corneal thickness; (2) thinnest corneal thickness; and (3) standard deviation (SD) of measurement. Measurement was repeated if the SD was >1.0. Each ORA measurement took 1–2 minutes in cooperative patients and >5 minutes in uncooperative patients.

Five minutes after ORA measurement, five consecutive measurements of the CCT were made using 10-MHz UPS in a manner similar to ORA. Every five measurements by USP took about 2 minutes. The lowest and highest values were excluded. The mean of three measurements was calculated for further analysis.

Volunteers underwent measurement sessions with the following protocol. For a total of 43 volunteers (86 eyes), the first 16 (32 eyes) were examined three times with each instrument. Two measurements were performed by Examiner 1 (PFS) with a further measurement by Examiner 2 (AYL) in a single session to determine intra-observer repeatability and inter-observer reproducibility of each device. The examiners completed their examination on one instrument before measuring the volunteer with a different device. The patients were asked to take their faces away from the chinrest between the measurements. The remaining 27 volunteers (54 eyes) were examined with each instrument by Examiner 1 only. The first measurement performed on all 43 volunteers (86 eyes) by