Ultrasound and Partial Coherence Interferometry With Measurement of Central Corneal Thickness

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ABSTRACT

PURPOSE: To compare noncontact pachymeter measurements with ultrasound pachymeter measurements and assess their reproducibility.

METHODS: Central corneal thickness was measured in 104 eyes of 56 patients with three laser interference pachymeters (OCLR [Haag Streit, Köniz, Switzerland], OCP [Aoptics AG, Lübeck, Germany], and ACMaster [Carl Zeiss Meditec, Jena, Germany]) and an ultrasound pachymeter (Tomey AL2000 [Tomey Corp, Nagoya, Japan]).

RESULTS: Compared to the ultrasound measurements, the mean difference for the laser interference pachymeter measurements were +8.8 μm (standard deviation [SD] 5.68) for the OCLR, −8.0 μm (SD 5.39) for the OCP, and −0.12 μm (SD 5.88) for the ACMaster. Reproducibility could only be estimated as not all of the devices allowed access to individual measurements. For all laser interference devices, reproducibility was estimated to be approximately 2 μm. Ultrasound measurements yielded a reproducibility of approximately 3.4 μm.

CONCLUSIONS: Although ultrasound pachymeter measurements differed significantly from OCLR and OCP measurements, agreement was considered good because the mean differences were <10 μm, and the results can be regarded as clinically interchangeable. [J Refract Surg. 2006;22:665-670.]

In recent years, the importance of accurately measuring corneal thickness in glaucoma and refractive surgery patients has increased. In patients with glaucoma, knowledge of the central corneal thickness is essential to avoid continuous mis-measurement of intraocular pressure by corneal applanation.1-5 In refractive surgery such as LASIK, corneal thickness measurements are obtained as a standard safety measure.6-13 However, measuring corneal thickness with ultrasound pachymeters is limited by several major problems. First, because the probe is in direct contact with the cornea, topical anesthesia is mandatory. Second, contact measurements shortly after surgical refractive procedures are not desirable. Third, the handheld ultrasound probe limits the accuracy of measurements.

Several noncontact pachymeters have been introduced recently.11-14 Along with rotating Scheimpflug cameras and specular microscopy, several laser interference (partial coherence interferometry) devices have been developed that have been reported to provide fast, reliable, noncontact measurements with micrometer precision.6,11,15-18 Inter- and intraobserver variabilities are well known for the clinical standard method of ultrasound pachymetry.19 The objective of this study was to compare three different noncontact pachymeters with an ultrasound pachymeter to assess their agreement, especially regarding the clinical interchangeability of the different methods.

PATIENTS AND METHODS

Data were collected on 104 eyes in 56 patients who were undergoing corneal thickness measurement as part of their

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Dr Haigis’ research is funded in part by Carl Zeiss Meditec, Jena, Germany. Dr Much has no proprietary interest in the materials presented herein.

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Received: June 29, 2005
Accepted: February 20, 2006
Posted online: May 15, 2006

Journal of Refractive Surgery Volume 22 September 2006 665
routine clinical examination, primarily as screening for glaucoma. Patient age ranged from 22 to 91 years, with an average age of 56 years and a median age of 59 years. Slit-lamp examination was performed before corneal thickness measurements were obtained. Only measurements of patients without any known or apparent corneal illness or ocular surgery within the previous 12 months were collected. All measurements were obtained by a single investigator. In addition to the routinely obtained ultrasound measurements, non-contact measurements were obtained with three laser interference pachymeters. All non-contact measurements were performed before the ultrasound measurement to avoid any disturbance or swelling of the corneal surface caused by the contact measurement. All measurements were performed within a 45-minute interval. Partial coherence interferometry measurements were obtained with patients in a sitting position and fixing either on the measuring beam itself or a target beam aligned with it. Ultrasound measurements were obtained by measuring the geometric center of the cornea with patients supine.

**LASER INTERFERENCE PACHYMETER MEASUREMENTS**

Measurements were obtained first with the Optical Coherence Pachymeter (OCP) (4optics AG, Lübeck, Germany), which uses a 1300-nm laser beam. The default group refractive index for this device is set to \( n_g = 1.3684 \). The desktop device obtains 400 individual measurements on every examination, from which 120 are selected internally. An average is computed and presented to the examiner. Because this device requires a relatively long measuring process, patients were measured only once.

The Optical Low Coherence Reflectometer (OLCR) (Haag Streit, Künzli, Switzerland) was used second. The OLCR is a slit-lamp mounted device that also applies a 1300-nm measuring beam. The group refractive index in this device is set to \( n_g = 1.330 \). Ten measurements per reading are processed internally, and the mean and standard deviation of the five best-agreeing measurements are displayed. Mean and standard deviation of those five measurements are accessible. Three measurements with this device were obtained for every patient, and the mean and standard deviation of these were used for all further calculations.

The ACMaster (Carl Zeiss Meditec, Jena, Germany) was used next to obtain measurements. The ACMaster is an optical low coherence reflectometry anterior segment biometry device with pachymetry capabilities measuring at 850-nm wavelength. The group refractive index is set to \( n_g = 1.3616 \). The examiner is given full access to every individual measurement. The device allows 20 subsequent measurements, from which the average and standard deviation of the central corneal thickness as well as other parameters are extracted. The maximum of 20 measurements were made for every patient. Only measurements that showed a signal to noise ratio of 8:1, which is twice as high as the internal level of acceptance in this device, were accepted by the examiner. Outliers were excluded if they deviated >3% from the computed average.

**ULTRASOUND PACHYMETER MEASUREMENTS**

Ultrasound pachymeter measurements were obtained with the Tomey AL2000 (Tomey Corp, Nagoya, Japan). This device uses a 20-MHz handheld ultrasound tip. Corneal ultrasound velocity was originally set to 1640 m/s. However, for this study, the results were normalized to an ultrasonic velocity of 1620 m/s, as this was regarded to be the most plausible value. The cornea was anesthetized with oxybuprocaine 0.4%, and 10 measurements were obtained by placing the probe in the center of the cornea manually. The probe was lifted between each measurement. Average and standard deviation for these measurements were calculated.

**REPRODUCIBILITY**

The assessment of reproducibility was complicated by the way the four devices differ in their mode of calculating the actual output-result. The ultrasound device is capable of displaying 10 subsequent measurements. This number of measurements was taken and the standard deviation was calculated. Our result for reproducibility represents the average of these 104 standard deviations.

The ACMaster yields access to the individual measurements as well, and results were obtained accordingly. The OLCR chooses 5 of 10 measurements for every release, and the OCP uses 120 from a total of 400 single measurements. Both of these devices present a single figure without the possibility of accessing individual measurements. Furthermore, each set of measurements is gathered within only seconds and therefore omits sources of error such as slight changes in alignment between measurements. Therefore, reproducibility was estimated by gathering three complete measurements for each patient with the OLCR; obtaining additional measurements seemed unacceptable to the volunteering patients. As the OCP used for this study required a time-consuming input of patient data for every measurement, repeating the procedure in every patient seemed excessive. Thus, gathering of reproducibility data was limited to 17 eyes in 9 different patients each measured 10 times subsequently. Ten measurements were chosen in accordance to the ultrasound device. The reproduc-
Figure 1. Bland-Altman plot showing the difference versus the average of measurements for the OLCR and the ultrasound pachymeter, with mean difference (solid line) and two standard deviation intervals (broken line).

Figur 2. Bland-Altman plot showing the difference versus the average of measurements for the ACMaster and the ultrasound pachymeter, with mean difference (solid line) and two standard deviation intervals (broken line).

Figure 3. Bland-Altman plot showing the difference versus the average of measurements for the OCP and the ultrasound pachymeter, with mean difference (solid line) and two standard deviation intervals (broken line).

Reproducibility values for the OCP and OLCR were calculated according to the method described.

**Statistical Analysis**

In agreement with the publications of Bland and Altman, the differences between the newer partial coherence interferometry methods and standard ultrasound were plotted against their average (Figs 1-3), and the mean difference was computed. To assess the estimated limits of agreement, the 95% confidence intervals (CI) for the mean difference was calculated.

In addition, after controlling the data with the one sample Kolmogorov-Smirnov test for normality, the different sets of measurements were compared using paired, two-tailed Student t tests. The level of significance was set at P<.05.

**Results**

All 104 eyes were measured using the OCP, OLCR, ACMaster, and Tomey AL2000. Differences between partial coherence interferometry measurement and ultrasound were plotted against their average (see Figs 1-3); standard deviations and confidence intervals were computed. Mean central corneal thickness was 546.0±33.5 μm with the OLCR, 537.05±34.4 μm with the ACMaster, and 529.18±33.3 μm with the OCP. Ultrasound measurement with the Tomey AL2000 yielded a mean central corneal thickness of 537.18±32.0 μm. Thus, compared to ultrasound, the OLCR measured +8.8±5.68 μm (95% CI: +7.7 to +9.9 μm) (see Fig 1), the ACMaster measured −0.12±5.88 μm (95% CI: −1.2 to +1.0 μm) (see Fig 2), and the OCP measured −8.0±5.39 μm (95% CI: −7.0 to −9.1 μm) (see Fig 3).

Reproducibility was determined as described. The mean standard deviation was 1.44 μm for the OLCR,
2.07 μm for the ACMaster, and 3.36 μm for ultrasound, and the standard deviation was 2.36 μm for the OCP.

DISCUSSION

In this study, central corneal thickness measurements differed significantly for the OCP (P<.01), which measured on average 8.0 μm thinner than ultrasound, and the OLCR (P<.01), which measured 8.8 μm thicker than ultrasound. The ACMaster demonstrated the best agreement with the ultrasound pachymeter, measuring only 0.12 μm thinner than ultrasound; this difference was not statistically significant.

Optical coherence tomography devices have been compared previously to ultrasound pachymeters. These studies found optical coherence tomography measured central corneal thickness as significantly lower than ultrasound (24 μm, 31.9 μm, and 49.4 μm), which is in agreement with our results. However, these studies did not use optical coherence pachymeters; instead, they used optical coherence tomography devices that were designed primarily to produce tomographic images of either the retina or the cornea and then were altered to meet this specific purpose. Ultrasonic velocity settings were given in two studies only, in which the setting was 1640 ms in contrast to 1620 ms as in our study. In our study, reproducibility was estimated to be approximately 2 μm, which is distinctly less than in the other studies. Yet the OCP device, other than previously examined ones, was designed specifically for central corneal thickness measurements.

Only a few studies have used the OLCR. Gillis and Zayen compared the device with ultrasound, with the OLCR measuring approximately 5 μm thicker than ultrasound. This is in agreement with our results, as well as with those reported by Bohnke et al, who compared OLCR integrated into an excimer laser with ultrasound. Differences may be due to different ultrasound settings or different group refractive indices. The corneal ultrasonic velocities used for these studies are not known.

Only one study yielded results that do not agree with our results. In testing an OLCR prototype, Genth et al found significantly larger corneal thickness values (mean difference 15 μm) with ultrasound. The ultrasonic velocity in their study was set to 1640 ms, and the refractive index used was 1.4467 in contrast to 1.330 built in the OLCR device used in our study. Adjusting the group refractive index as well as ultrasound settings according to the ones used in our study would lead to thicker measurements with the OLCR and hence less disagreement between the studies.

Only a few studies have compared the ACMaster with other pachymeters, and studies comparing the ACMaster with ultrasound have not been published. The ACMaster and ultrasound pachymeter achieved good agreement in our study. This agreement likely is due to the fact that the calibration of the ACMaster was based on ultrasound measurements using a velocity setting of 1620 ms as was acknowledged by the Zeiss development department.

In this study, agreement between the different partial coherence interferometry devices and the ultrasound pachymeter was good. The remaining slight disagreements between these pachymeters are possibly due to two technical details. First, in partial coherence interferometry measurements, the alignment of the eye follows the optical axis as the subject fixates on either the measuring beam itself or a target beam that is aligned with it. The actual measurement is taken at the intersection of this axis with the cornea. This is not necessarily the center of the cornea as it is measured with the handheld ultrasound probe.

The second and probably more important difference between the devices is the setting for the corneal group refractive index and the corneal sound velocity. Both factors are subject to scientific discussion. The sound velocity of 1620 ms used in this study was chosen in accordance with a meta-analysis of the literature by Thijssen et al. The corneal group refractive index is a factor necessary to calculate the actual corneal thickness from the so-called optical path length that is primarily measured by the optical coherence method.

As mentioned, different group refractive indices have been used by the manufacturers. Thus, disagreements between the measurements are due in part to different settings. By adjusting the individual group refractive indices, the different pachymeters can be set for maximum agreement in a specific clinical setting. Of course, changes of the ultrasound setting for v (corneal sound speed of sound) would produce similar results. Setting the ultrasound device to 1640 ms would result in average measurements of 543.81±32.5 μm (compared to 546.00±33.5 μm for the OLCR, 537.05±34.4 μm for the ACMaster, and 529.18±33.3 μm for the OCP).

Reproducibility of central corneal thickness measurements has been assessed in several studies. The use of ultrasound pachymeters has been thoroughly examined, showing reproducibility ranging from 2.4 to 4.88 μm, which agrees well with the 3.37 μm achieved over 10 readings in our study.

Studies regarding the reproducibility of the OLCR and OCP are relatively few. Gillis and Zayen achieved 0.49 μm repeatability, which is better than the 1.44 μm obtained in our study. However, in their study, the standard deviation was computed from multiple readings in every examined subject rather than from the
internal calculation of the device. According to our observations, this internally calculated standard deviation, used mainly to control quality of measurement, is lower than the standard deviation over multiple readings. This might be due to slight changes in alignment between multiple measurements. Studies on the reproducibility of the ACMaster are few as well and generally are in accordance with the reproducibility of approximately 2 μm as measured in our study.27,28

In general, this study was designed primarily to obtain details on the inter-system comparability of the four devices. Due to the different modes of measurement and the varying method of processing the results internally, sometimes with limited access to the examiner, the comparability of the assessed reproducibility is limited.

The corneal thickness measurements with the ultrasound pachymeter differed significantly from the OCLR and OCP measurements. However, as the differences were in the low micrometer range, agreement was still considered to be good, and it seems reasonable to regard the results of the tested pachymeters as clinically interchangeable. All of the tested partial coherence interferometry pachymeters offer simple and convenient noncontact measurement of central corneal thickness with micrometer precision.

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