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RAPID AND PRECISE *IN VIVO* MEASUREMENT OF HUMAN CORNEAL THICKNESS WITH OPTICAL LOW-COHERENCE REFLECTOMETRY IN NORMAL HUMAN EYES

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ABSTRACT

An optical low-coherence reflectometer is used for rapid noncontact measurements of the human corneal thickness *in vivo*. Thickness measurements on ten volunteers show a standard deviation of 3.4 μm. The experiments reveal that the optical reflectometer benefits from a 2.5 fold enhancement of the measurement precision and a 2.8 fold reduction in measurement time compared to a standard clinical ultrasonic pachometer. © *1998 Society of Photo-Optical Instrumentation Engineers.* [S1083-3668(98)00303-7]

Keywords optical distance measurement; optical position measurement; optical low-coherence reflectometry; optical interferometry; corneal pachometry; corneal thickness.

1 INTRODUCTION

Optical low-coherence reflectometry (OLCR) has been reported to be a highly sensitive technique for measuring optical powers in the sub-fW range.[1–3] It has been used to investigate optical properties of industrial[4–9] and biological samples.[10–16] In diffusive media the longitudinal resolution of this technique is limited to the coherence length of the broadband source.[10–18] In contrast, specularly reflecting media have been shown to be scanned at a precision significantly below the resolution given by the coherence length of the optical source.[4–9,19–21] However, due to their low scan speed, a precision in the range of 0.5 nm[9] to typically 1 μm is obtained only for fixed samples.

To avoid motion artifacts in *in vivo* measurements the scan speed of optical low-coherence reflectometers has to be adapted to the motion of the subject under test. We recently reported a fiber reflectometer with a rotating glass cube[19,20,22] resulting in a high scan speed and scan repetitiveness. Based on this delay technique a precision of one micron has been achieved when corneal tissue of enucleated porcine eyes was measured before and after excimer laser keratectomies.[20]

The precise measurement of the corneal thickness is an important parameter in experimental and clinical conditions. For the routine measurement of corneal thickness optical slit beam[23–25] or ultrasound pachometers[26–28] are most widely used today. Ultrasonic corneal pachometry (USCP) offers a precision of about 6–14 μm[29] and is considered sufficient for routine purposes. However, in USCP a contact with the corneal surface is required, and the lateral positioning error of the ultrasonic probe is at least 1 mm. Interferometric techniques, and in particular the technology of OLCR may offer an improved alternative for the measurement of corneal thickness[21,30–36] with a precision of 1.6 μm[34] to 0.3 μm.[36]

In this article, we describe an OLCR instrument being attached to a slit lamp for biomicroscopic control to measure the central human corneal thickness in ten volunteers. The visual control offered by the slit lamp permits precise and rapid positioning of the measuring beam of the reflectometer on the cornea under test. The OLCR-thickness measurements on ten volunteers reveal a relative precision of 3.4 μm. The reflectometer shows a scan repetition rate of 15 Hz being several times faster than that reported in the high-precision measurements in Ref. 36. Furthermore, in contrast to the reflectometers in Refs. 35 and 36 operated at the safety limit of 200 μW, a power of 8 μW incident onto the cornea is sufficient for our measurements. To compare quantitatively the results of optical reflectometry with a standard clinical measurement tech-

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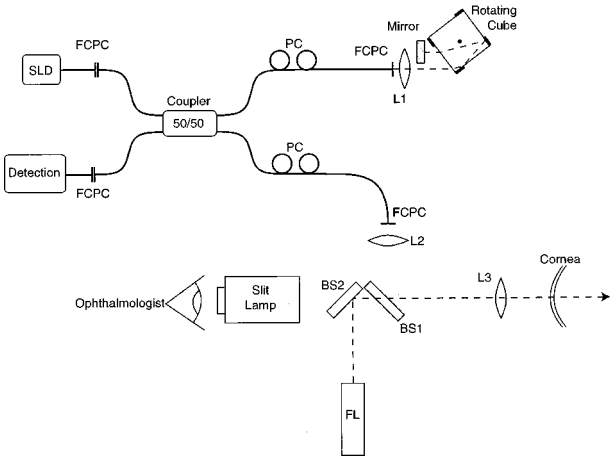

Fig. 1 Schematic diagram of the experimental setup. SLD: Superluminescent diode; FCPC: FCPC connector; PC: Polarization controller; L1, L2, L3: Lenses; BS1, BS2: Beam splitters; FL: Fixation laser.

nique the corneal thicknesses of the same ten volunteers are subsequently measured using an ultrasonic pachometer.

2 SETUP OF THE OPTICAL REFLECTOMETER

In Figure 1 the setup of the slit-lamp integrated optical low-coherence reflectometer is presented. The emission around 850 nm of a pigtailed superluminescent diode (SLD) is guided to the sample and reference arms by the use of a 50/50 single mode fiber coupler. The free beam in the reference arm is focused onto the reference mirror with a lens (L1) of 4.5 mm focal length. The light in the referential arm is delayed by a rotating glass cube of 30 mm diameter. The optical principle of the rotatory delay line is thoroughly described in Ref. 22.

The glass cube is rotated by the use of a dc motor. The rotation axis of the cube is fixed due to ball bearings. The angle between the cube facets and the rotation axis is matched to within 0.03° to allow for perpendicular incidence of the reference beam onto all four cube facets. The rotation frequency of the cube of 3.67 Hz leads to a scan repetition rate through the cornea of 14.7 Hz and an average scan speed of 0.5 m/s. Hence, the short duration of a single scan through the cornea being ≈ 1 ms limits the measurement error due to different types of eye movements such as microsaccades and tremor to significantly less than 1 μm.

The sample arm bulk optic consists of a collimating lens (L2) with a focal length of 30 mm followed by a focusing lens (L3) with a focal length of 60 mm. This optic leads to a focus diameter of the SLD of 10 μm on the sample. The sample arm optic can be placed in front of the center of the objective lens of a Haag–Streit BQ 900 slit lamp by the use of a beam splitter (BS1). The introduction of the low-coherence beam into the optical path of an ophthalmic slit lamp allows for simultaneous observation of the patient's eye and repetitive corneal thickness measurements by an ophthalmologist. The spatial translation of the focus position of the measuring beam is established with the joystick of the slit lamp. The longitudinal distance between the focus and the patient's cornea is controlled with the help of visible pilot lasers to match the optical path length of the sample arm to that of the reference arm. Furthermore, coherent signal detection is obtained only when the return path of the reflected light coincides approximately with the path of the incoming light. To accomplish the latter condition the visual axis of the patient has to be matched to the axis of the incident SLD beam. The angular tolerance of the cornea orientation, $\Delta\varphi$, at that a coherent signal can be detected is proportional to

$$\Delta\varphi \propto NA \cdot \frac{f_{L2}}{f_{L3}}, \tag{1}$$

where NA is the numerical aperture of the single mode fiber, and f_{L2} and f_{L3} are the focal lengths of the collimating and focusing lenses, respectively. A visible fixation laser (FL) is introduced into the sample arm with a beam splitter (BS2). By watching the on-axis fixation laser being collimated on the cornea the patient is able to orientate his cornea for the detection of the front corneal surface. In general, only minor transverse adjustments of the slit lamp are then required to be performed by the ophthalmologist to collect both corneal signals.

Using adjustment screws on the base plate of the cube, the rotation axis of the cube is orientated perpendicularly to the reference beam to provide an equal sensitivity for all four cube facets. At a power of 8 μW incident on the cornea a maximum sensitivity of -82 dB is measured for all four facets. This value is close to the shot-noise limit of -84 dB. The longitudinal scan range with a 3 dB sensitivity loss is about 3 mm. The sensitivity loss over the scan distance is caused by the scan speed variation of $\pm 17\%$ and the rather narrow bandwidth used in the filter electronics. Longer scan ranges can be obtained with larger filter bandwidths. However, enlarging the filter bandwidth leads to a decrease of the maximum sensitivity.

The detection unit consists of Si photodiode, a preamplifier, a filter, a rectifier, and a low-pass filter with a bandwidth of 60 kHz. The low-pass filter generates two envelope signals corresponding to the two reflections from the front and back surface of the cornea. The uncertainty of thickness measurements is mainly given by the precise identification of the centers of the two envelope signals. The location of an envelope center with respect to the scan distance is determined by the use of a motor-coupled encoder and a phase-locked loop. An optical shaft encoder has an incremental resolution of 512 counts per revolution. Each increment is inter-

polated with a phase-locked loop by a factor of 256 leading to a division of the scan into angular steps of 47.9 μrad. Slight short- and long-term speed variations of the motor in the range of 2% are taken into consideration due to a phase comparator in the phase-locked loop. The angular position of a signal is determined by counting the number of angular steps performed from the envelope center to the reference point at 0° given by the index channel of the encoder. The longitudinal position is calculated from the formula describing the scan length as a function of the scan angle. In the formula the effects of cube decentering and unequal cube facet lengths on the scanned distance are taken into account. Considering that the scan length change in air due to a cube rotation from 0° to 45° corresponds to 19 mm, the length measurement accuracy of the reflectometer is limited to ± 0.58 μm for a single scan.

3 *IN VIVO* OLCR AND USCP MEASUREMENTS

Ten corneas from ten healthy patients without a history of previous eye disease or contact lens wear are measured using an optical low-coherence reflectometer and a standard clinical ultrasonic pachometer. In contrast to ultrasound the optical technique is a noncontact measuring method that is applied to nonanesthesized corneas.

The relatively high measurement repetition rate of 15 Hz offered by the optical reflectometer enables the ophthalmologist to gather 20 scans through the human cornea in a time of typically 30 s. In Figure 2 the averages of the geometric central human corneal thicknesses derived from the 20 scans are shown for the ten volunteers. The geometric thickness is obtained by assuming the refractive index of the cornea to be 1.376 according to Ref. 37. Subsequently after the OLCR measurements 20 consecutive measurements of the central corneal thickness are performed on the same volunteers using an ultrasonic pachometer (DGH-1000) with a transducer frequency of 20 MHz and an assumed sound speed of 1620 m/s. A systematic deviation between the OLCR and USCP measurements is found. The experiment shows that each OLCR-thickness measurement lies below the corresponding USCP measurement. The deviations range from 23.7 to 41.2 μm. On average the OLCR measurements are 30.7 μm below the corresponding USCP measurements. The average deviation of 30.7 μm corresponds to a relative difference of 5.7% between OLCR- and USCP-thickness measurements (100% = 534.6 μm = average thickness of the ten OLCR measurements). This finding is consistent with that reported in Ref. 38 where the thicknesses measured with a DGH-1000 pachometer lay systematically above the true thicknesses of four test blocks of 0.4, 0.5, 0.6, and 0.7 mm.

The thickness measurements shown in Figure 2 are used to evaluate the precision of the OLCR and

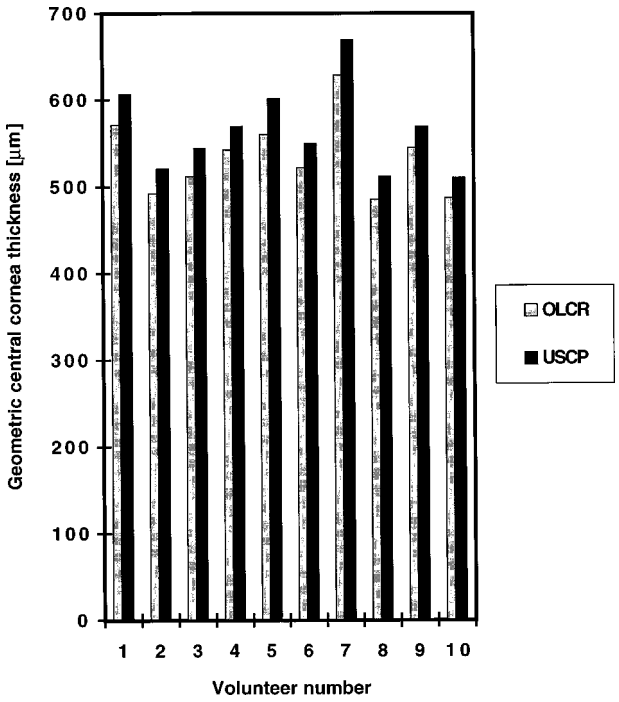

Fig. 2 Geometric central cornea thickness measurements as a function of ten volunteers for OLCR and USCP.

the USCP measurement methods. In Figure 3 the intraobserver standard deviations of the thickness measurements on ten different volunteers are depicted. For each volunteer the standard deviation for the OLCR and USCP measurements are calculated from the 20 thickness values. The standard

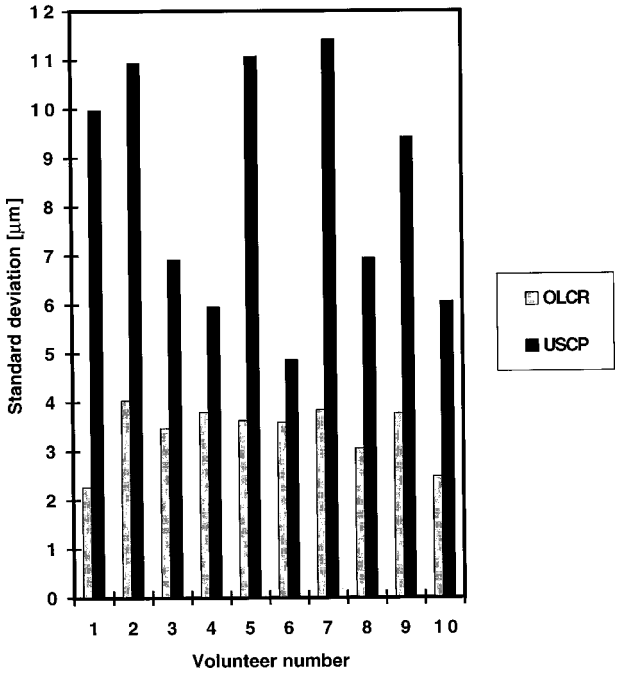

Fig. 3 Standard deviations of the central cornea thickness measurements as a function of ten volunteers for OLCR and USCP.

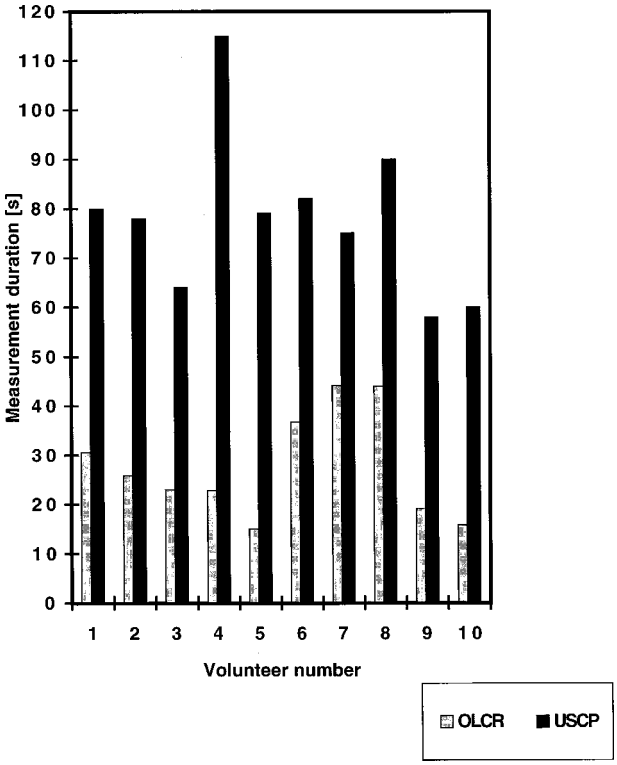

Fig. 4 Measurement times for the central cornea thickness measurements as a function of ten volunteers for OLCR and USCP.

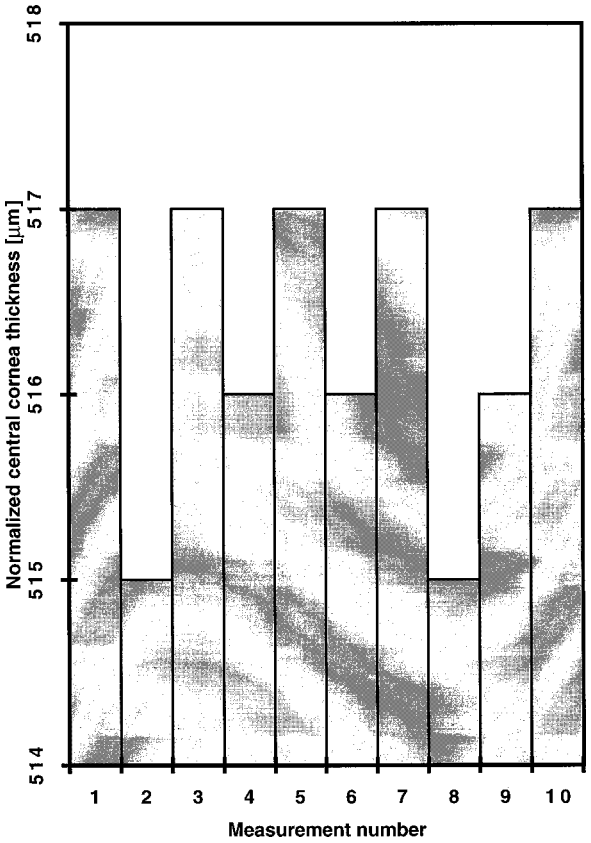

Fig. 5 Central cornea thicknesses as a function of ten independent measurements on the same volunteer.

deviations of the OLCR measurements range from 2.3 to 4.0 μm. The average of the 10 standard deviations amounts to 3.4 μm.

To compare the precision of the optical with that of the acoustic measurement technique the standard deviations resulting from the 20 USCP scans performed on each volunteer is calculated. The intraobserver standard deviations of the ultrasonic measurements are shown in Figure 3. The standard deviations of the ultrasound measurements lie within a range from 4.9 to 11.4 μm. The averaged standard deviation is 8.4 μm.

The times required for the optical and acoustic measurements shown in Figures 2 and 3 are measured. The optical and acoustic measurement times are compared in Figure 4. The times for the OLCR measurements are automatically recorded with a PC program. The times required for one OLCR measurement consisting of 20 scans range from 15.0 to 44.1 s. Within this time the positioning and alignment of the measuring beam with respect to the patient's eye due to translatory movements of the slit lamp is included. The mean value of the measurements on the ten subjects amounts to 27.7 s. The corresponding USCP measurements consisting of 20 scans each last between 58 and 115 s. The mean value is 78.2 s. The time required for USCP is manually recorded.

In additional OLCR experiments which are not quantified here, paracentral and peripheral corneal thickness measurements are performed by turning the slit lamp together with the sample arm of the reflectometer around the volunteer's eye to obtain perpendicular incidence of the measuring beam onto the cornea. The range of such measurements is expanded as far as the limbus.

In the last experiment 10 consecutive OLCR measurements on the same volunteer are carried out by the same ophthalmologist. The reflectometer was calibrated with a glass plate of known thickness and refractive index. After each measurement the volunteer moves his eye out of the measurement range of the reflectometer to provide 10 independent corneal measurements. The physical lengths of the central cornea are plotted in Figure 5 for the 10 measurements. One physical length measurement corresponds to the average of the 10 scans centered around the average of 20 scans. The 10 length measurements range from 515 to 517 μm. The standard deviation calculated from the 10 length measurements amounts to 0.8 μm. The uncertainty of the index of refraction of the cornea leads to a systematic error for the physical length measurement. However, a comparable systematic error in absolute thickness measurements occurs also in ultrasonic pachometry due to the inherent incertainty of the velocity of the ultrasonic wave in the human cornea.

4 CONCLUSIONS

Measurements on ten volunteers show that the optical low-coherence pachometer is 2.5 times more precise and 2.8 times faster than a standard clinical ultrasonic pachometer. The averaged intraobserver uncertainty of one corneal thickness measurement performed with the optical reflectometer is $\pm 3.4\ \mu$m. On average one OLCR thickness measurement lasts 28 s. In contrast to ultrasound the optical instrument has the additional advantage to be a noncontact measuring method without the need for cornea anesthesia. The rapid and precise optical pachometer reported here bears the potential for very precise routine measurement of corneal thickness. As a consequence, even minor changes of corneal thickness can now be reproducibly measured, giving corneal pachometry with OLCR an improved resolution for future clinical applications.

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