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Real-time pachymetry during photorefractive keratectomy using optical low-coherence reflectometry

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Abstract. Optical low-coherence reflectometry (OLCR) was used as a noncontact method to measure the central corneal thickness of three patients intraoperatively during photorefractive keratectomy. Continuous on-line measurements were performed on the intact cornea immediately before the beginning of surgery, after the removal of the corneal epithelium, during laser tissue photoablation, and for 3 min after the ablation process. Corneal thinning due to evaporation was studied on a separate patient with the OLCR instrument, and it was found to be −0.14 μm/s during the first 5 min after epithelium removal. This baseline corneal thinning rate was used as a fit parameter to calculate actual from measured ablation depths. The measurements showed a maximum difference of ±10 μm between planned ablations (34–92 μm) and measured ablation depths. [DOI: 10.1117/1.1412438]

Keywords: noncontact corneal pachymetry; optical low-coherence reflectometry; optical coherence tomography; photorefractive keratectomy.

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1 Introduction

The cornea is the most anterior optical component of the eye, which accounts for two thirds of its total refractive power of about 60 diopters (D). For surgical correction of refractive errors of the eye, the use of lasers to reshape the corneal surface [photorefractive keratectomy (PRK)] by controlled and precise corneal stromal tissue removal[1,2] has been a major advancement in the field of refractive surgery. In PRK, an excimer laser operating at 193 nm is used to change the corneal curvature in an optical zone of 5–7 mm diameter for up to 10 diopters of refractive power (equivalent to about 100 μm of ablation depth in the corneal center) with a precision that is unattainable with conventional surgery. The controlled removal of stromal tissue reduces the optical power of the cornea and leads to the correction of myopia.

The excimer laser is usually calibrated before treatment is initiated by performing a fluence test that allows the calculation of the current ablation rate per pulse for corneal tissue (usually about 0.2 μm per pulse). Corneal photoablation algorithms are based on the assumption of (i) a constant rate of tissue removal per pulse, (ii) identical ablation rates of corneal tissue in different individuals or corneal layers, and (iii) and a constant ablation rate over time during the ablation process. As clinical results indicate, however, PRK and other photorefractive treatments do not yet achieve the correction desired in all cases. Postoperative studies show that only 70%–90% of patients lie within ±1 diopter of the desired amount of correction. In higher myopic corrections particularly the percentage of miscorrected patients is rather high. The suboptimum results obtained in 10%–30% of the patients are usually attributed to variations in epithelial and stromal wound healing including scar formation and, possibly, to small intersession changes of the ablation rate over a 1 day period.[2]

The capacity to ablate stromal layers in the micron range has called for methods to measure the corneal thickness with high precision. Commonly used clinical methods for obtaining corneal thickness measurements on patients are ultrasound,[3] optical slit-lamp pachymetry,[4] and specular microscopy.[3] Ultrasound pachymetry—a method requiring contact between the transducer and the corneal tissue—is the routine method used for corneal thickness measurement today. Obviously, continuous measurement of corneal thickness during photoablation with this method has not been possible. Additionally, the precision of ultrasound pachymetry does not exceed 5–10 μm, so it is not yet precise enough for the requirements of trend monitoring in excimer corneal photoablation.

Recently, a novel noncontact pachymetry technique based on optical low-coherence reflectometry (OLCR)[5–7] or optical coherence tomography (OCT)[8–10] was reported. OLCR is a one-dimensional scanning method whereas OCT is known as a measurement technology for two- or three-dimensional imaging. OLCR has been reported to deliver *in vivo* central corneal thickness measurements of typically 1 μm (Refs. 11 and 12) or submicrometer reproducibility.[7]

An OLCR device integrated into the excimer laser was used to continuously measure central corneal thickness in patients undergoing PRK before, during, and after laser ablation. To our knowledge this is the first report of an intraoperative

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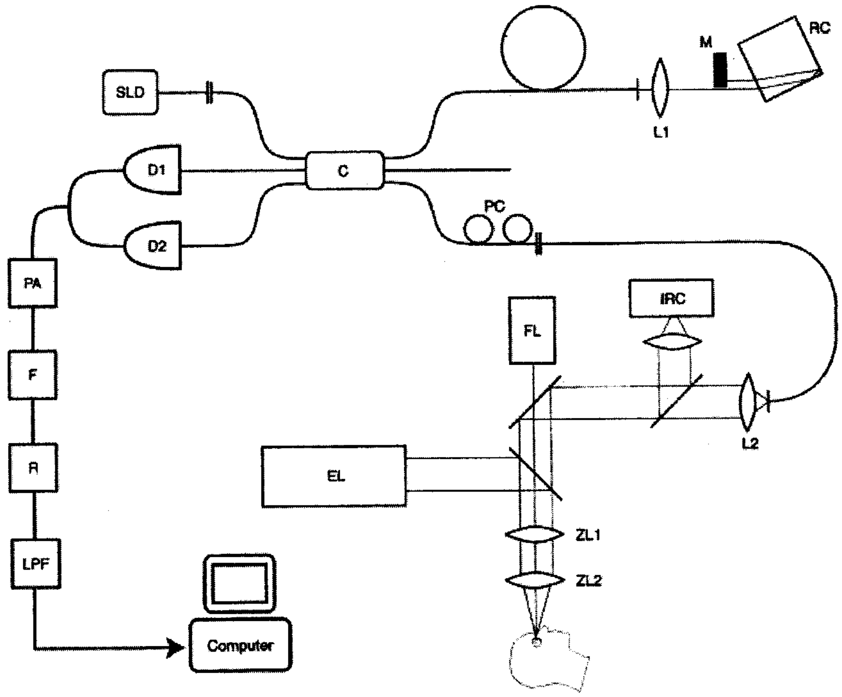

Fig. 1 Schematic of the excimer-laser integrated reflectometer. SLD: Superluminescent diode; C: 3×3 fiber coupler; L1, L2: lenses; RC: rotating cube; M: mirror; PC: polarization controller; IRC: infrared camera; FL: fixation laser; EL: excimer laser; ZL1, ZL2: zooming lenses; D1, D2: photodiodes; PA: preamplifier; F: filter; R: rectifier; LPF: low-pass filter.

clinical application of this method in refractive excimer surgery.

2 Experimental Setup

The fiber-optic pachymeter is illustrated in Figure 1. The measurement principle of the optical pachymeter is described in Ref. 13. The optical source is a superluminescent diode (SLD) operated continuously with a full width at half maximum (FWHM) spectral width of about 50 nm centered at 1310 nm.

After passing through a 3×3 fiber coupler (C) the optical signal is divided into three arms of the interferometer. The upper arm is the reference arm. It has an optical single mode fiber, a focusing lens (L1), a mirror (M), and an optical path length variator provided by a rotating cube (RC). The reference beam is retroreflected from the mirror (M) back into the fiber. The sample arm consists of a sample arm fiber, a polarization controller (PC), several lenses, mirrors, and dichroic beam splitters. The lens (L2) is used to couple the sample beam into the arrangement of the excimer laser system. The position of the patient's cornea is controlled by an infrared camera (IRC) detecting the center of the patient's pupil to control the excimer beam orientation with an eye tracking mirror. As the SLD measurement beam travels through the eyetracking mirror, its position is controlled accordingly. A red fixation laser (FL) is used to orientate the visual axis of the patient and to establish normal perpendicular incidence of the measurement beam on the corneal surface of the patient. The excimer laser (EL) (Schwind) is operated at a pulse rate of 13 Hz to ablate the patient's cornea. Two zooming lenses (ZL1, ZL2) are used to change the diameter of the photorefractive excimer laser beam on the patient's cornea. Due to the refractive index differences occurring at the air-to-cornea and cornea-to-anterior chamber interfaces, the measurement beam is reflected from the anterior and posterior corneal surfaces back into the laser optics and the sample arm fiber. An interferogram occurs only when the difference between the optical path lengths between the reference and sample arms is less than the coherence length of the SLD. The PC is adjusted to maximize the interference signals detected by two photodiodes (D1, D2). The electrical signals are processed by a preamplifier (PA), a filter (F), a rectifier (R), a low-pass filter (LPF), and an analog-to-digital converter placed within a personal computer. Patient data and measurement data are monitored on a computer screen. The fiber of the middle arm of the interferometer is not used. However, in combination with a photodetector the middle arm could be used to control the optical power of the SLD.

The optical low-coherence reflectometer presented shows a combination of several beneficial features comprising sufficient sensitivity (~65 dB), a high depth scanning speed (0.6 m/s), a high measurement repetition rate (18 Hz), a long measurement range (4.5 mm), low optical power incident on the patient's cornea (15 μW), and a nearly arbitrary working distance. The laser (EL) was operated according to the manufacturer's instructions.

3 Experimental Results

In this experimental study a total of four eyes of Caucasian patients was included. The average age of the patients was 34 (range of 27–45) years. One patient underwent only a measurement to determine the corneal thinning induced by evaporation of fluid from the corneal stroma (see Figure 2). In addition, the central corneal thickness of three patients with myopia (−8.5, −3.0, and −3.3 D) was measured before epi-

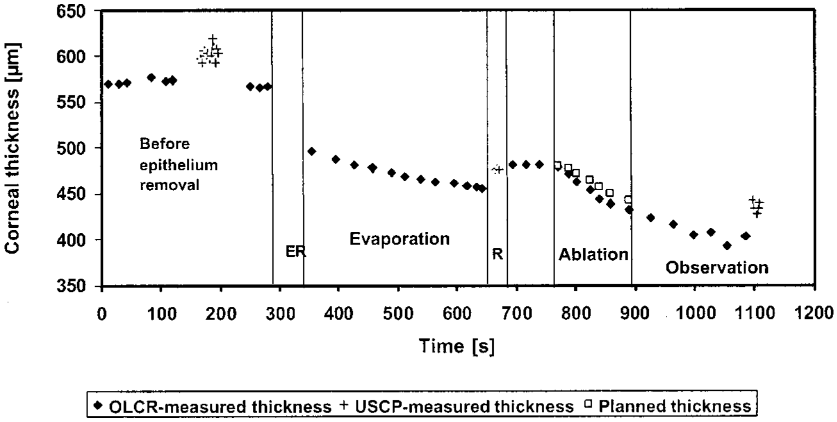

Fig. 2 Central corneal thickness measured during the entire myopic PRK (birth date 8/9/66, male). Immediately after the epithelium removal a period of 5 min is measured where no surgical intervention occurred. ER: Epithelium removal; R: rinsing.

thelium removal, after epithelium removal, during a short period of nonintervention by the surgeon (evaporation), during laser photoablation, and for another short period after termination of the treatment (see Figures 4–6). During the course of photoablation measurements, the cornea was left dry with no rinsing or moistening.

Each single measurement point shown in Figures 2–7 is an average of 20 consecutive thickness scans. The median based average and the standard deviation of 20 scans each are calculated in real time and displayed on a monitor. Each measurement (scan series) was started manually after completing the previous one. The time between two measurements was measured with manual stop watches. All treatments and measurements were performed by one surgeon. The refractive index of the cornea used for the thickness measurements is 1.376.[14]

Figure 2 shows the central corneal thickness measured with OLCR and ultrasonic corneal pachymetry (USCP). Both OLCR and USCP measurements were performed three times: before epithelium removal (BER), after the evaporation period after brief rinsing of the cornea (R), and at the end of the postoperative observation period before removing the lid speculum and applying eye drops for postoperative treatment (observation). The USCP measurements were systematically higher than the OLCR measurements, as has been reported previously.[12] During the period before epithelium removal the average corneal thickness measured with OLCR was 571 μm (a range from 566 to 574 μm) compared to 602 μm (a range from 594 to 619 μm) obtained with USCP.

The OLCR pachymetry was feasible during nearly the entire operation and consisted of initial measurements before epithelial removal, not during epithelial removal, then the preoperative dry phase after epithelial removal (evaporation), the laser ablation process (ablation), and a postoperative time period called the observation period (observation). The evaporation period following epithelium removal (ER) comprises 12 OLCR measurements. It spans 288 s from the first to the last of these 12 measurements. During the time period earmarked as evaporation there is no surgical intervention. The OLCR measurements during this time period are used to determine corneal thinning due to evaporation. A very short corneal rinsing (R) and consecutive wiping of the corneal surface with a microsponge after the evaporation period led to an immediate increase of the central corneal thickness from 455 to 482 μm, a limited tissue rehydratation. During preparation of the ablation and during the ablation phase, OLCR measurements were obtained continuously. In the observation phase after the end of the excimer action, OLCR measurements were also possible.

The average standard deviation of all 31 OLCR measurements documented throughout the various phases of the entire process (recorded during the first 900 s) was $1.2 \pm 0.3\,\mu$m. The standard deviation showed no significant differences in the four patients measured in this article.

The standard deviation measured in the region of 1 μm means that for our system the accuracy of the thickness measurements is significantly better than the depth resolution of OCT systems used, e.g., for retinal imaging. The depth resolution in diffuse media such as the human retina is given by the coherence length of the measurement light source (typically 10–20 μm for superluminescent diodes). The result of this is that in diffuse media the longitudinal position of a reflection site cannot be resolved with accuracy better than the coherence length. So, for OCT, a depth resolution in diffuse media of 10–20 μm is usual.

However, reflection sites enclosing a highly transparent inner structure (such as the cornea) can be localized in depth with accuracy better than the coherence length, provided that the reflection sites are longitudinally separated from each other by a distance larger than the coherence length. In this special case, the depth resolution is given by the accuracy at which the peak of an interference envelope generated by a reflection site can be detected. (The length of such an interference envelope is equal to the coherence length.) The normal human cornea is highly transparent and its typical thickness of 500 μm exceeds the coherence length of the superluminescent diode used. So, if the above conditions are fulfilled, the reflection sites from the front and back corneal surfaces can be measured with accuracy better than 20 μm. Also, in our measurement system, the depth resolution is not limited by the source spectrum, but rather by the stability of the optical delay line used in the interferometer. Therefore, because the stability of the cube rotation obtained in our in-

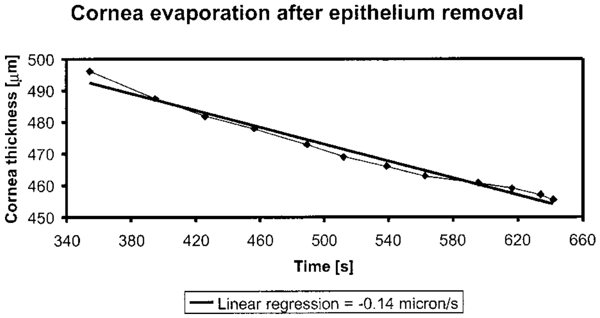

Fig. 3 Corneal thinning due to evaporation after epithelium removal vs time.

terferometer is very high, the accuracy attained with the pachymeter is much less than the 20 μm of the OCT system, and more in the region of 1 μm.

The transverse resolution is given by the core diameter of the single mode fiber optics, the magnification of the delivery optics, and the longitudinal measurement range. For our pachymeter the transverse resolution is typically 50–100 μm, depending on the longitudinal position of the patient's cornea with respect to the longitudinal focus position of the measurement beam.

To determine the effect of evaporation on thinning of the stroma without epithelium, we used the measurement data of Figure 2. In Figure 3 only the 5 min time period marked in Figure 2 as evaporation is depicted. Corneal thinning was monitored for 288 s without any surgical intervention. During these 288 s the central corneal thickness decreased from 496 to 455 μm. Using a curve fit based on linear regression, the preoperative stromal thinning rate (STR-1) per time was calculated to be -0.14 μm/s.

However, the measurement points in Figure 3 indicate that the corneal thinning is not constant. The preoperative stromal thinning rate is largest, -0.21 μm/s, immediately after epithelium removal while the stroma still has a high water content; this rate decreases over time and 4 min after epithelium removal it is only -0.11 μm/s. So, a value of -0.14 μm/s should be considered average for a duration of about 5 min.

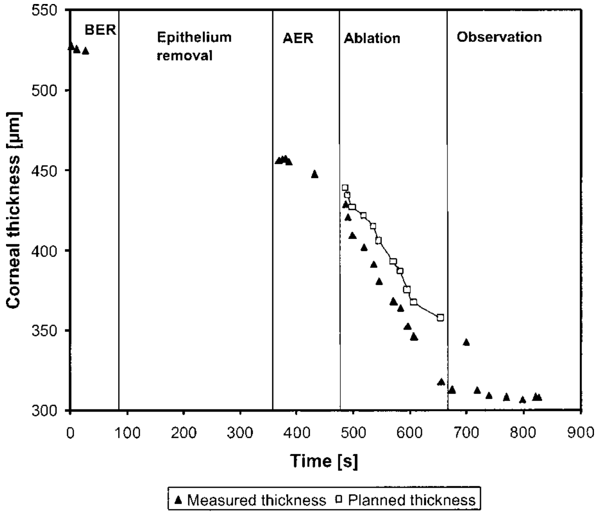

Fig. 4 Central corneal thickness measured during the entire myopic PRK (birth date 1/15/52, female). Planned ablation depth=92 μm corresponding to −8.5 D; ablation depth performed=91 μm corresponding to 388 pulses. BER: Before epithelium removal; AER: after epithelium removal.

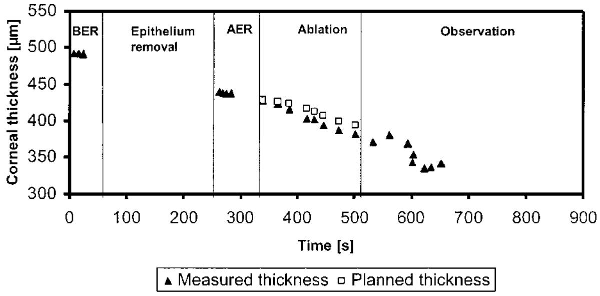

Fig. 5 Central corneal thickness measured during the entire myopic PRK (birth date 1/22/70, male). Planned ablation depth=34 μm corresponding to −3.0 D; ablation depth performed=34 μm corresponding to 145 pulses. BER: Before epithelium removal; AER: after epithelium removal.

However, at this stage of research it is not clear if a temporally variable thinning rate may have a measurable influence on the postoperative outcome of refractive surgery. To clarify this postoperative studies have to be carried out that correlate the intraoperatively measured thinning rate due to evaporation and the postoperative visual acuity of the patients.

A second evaporation rate (STR-2) can be calculated from the postoperative observation phase: Here the rate was -0.03 μm/s in patient 1, -0.2 μm/s in patient 2, and -0.09 μm/s in patient 3.

In patients 1–3, the OLCR measurements were carried out over the entire surgical procedure (see Figures 4–6).

Patient 1 (Figure 4) was intended to receive myopic correction of -8.5 D. Before epithelium removal a center corneal thickness of 526 μm was measured using the OLCR instrument. The corneal thickness was 457 μm after epithelial removal, giving a calculated epithelial thickness of 69 μm. During a 64 s period marked "AER" the center cornea thickness was reduced from 457 to 448 μm without any surgical intervention, equivalent to a STR-1 of -0.14 μm/s. The PRK was then performed with 388 laser pulses ablating a planned stromal depth of 92 μm (0.23 μm/pulse). The center corneal thickness immediately before the first and after the last laser pulse was measured to be 429 and 318 μm, respectively, giv-

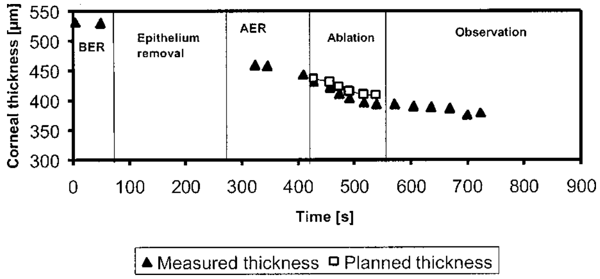

Fig. 6 Central corneal thickness measured during 10 entire myopic PRK (birth date 10/27/67, male). Planned ablation depth=37 μm corresponding to −3.3 D; ablation depth performed=37 μm corresponding to 157 pulses. BER: Before epithelium removal; AER: after epithelium removal.

ing an uncorrected thickness change of 111 μm and a corrected thickness change of 87 μm using a preoperative stromal thinning rate (STR-1) of -0.14 μm/s during an ablation period of 171 s.

During posttreatment observation that lasted 153 s the center corneal thickness further decreased from 313 down to 308 μm, resulting in a STR-2 of -0.03 μm/s. One measurement around 700 s was assumed to be an outlier.

In patient 2, who was receiving myopic correction of -3.0 D (Figure 5) the initial corneal thickness was measured to be 492 μm as calculated from three measurements before epithelium removal. The center corneal thickness measured immediately after epithelium removal was 440 μm, resulting in an epithelial thickness of 52 μm. In a time period of 76 s between the end of epithelium removal and the beginning of laser ablation corneal thinning of 12 μm due to evaporation was measured, giving a STR-1 of -0.16 μm/s. The planned ablation depth in this patient was 34 μm with 145 pulses required (0.23 μm/pulse). The center corneal thickness immediately before the first and after the last laser pulse was measured to be 428 and 382 μm, respectively, giving an uncorrected thickness change of 46 μm and a corrected thickness change of 23 μm using a preoperative stromal thinning rate (STR-1) of -0.14 μm/s.

During the postoperative observation period of 2 min the center corneal thickness was measured to further decrease from 371 to 342 μm, giving a STR-2 of -0.2 μm/s.

In patient 3, who was undergoing myopic correction of -3.3 D, the initial cornea thickness was 531 μm (see Figure 6). The epithelial thickness was derived as 71 μm from the consecutive stromal pachymetry of 460 μm. During a 86 s period between the end of epithelium removal and the beginning of ablation we measured thinning of the stroma of 17 μm, resulting in a STR-1 of -0.20 μm/s. The planned ablation depth in this patient was 37 μm requiring 157 pulses (0.24 μm/pulse). The uncorrected thickness change during ablation was measured to be 38 μm, equivalent to a corrected thickness change of 22 μm. During the observation interval after the laser treatment (150 s), the center corneal thickness further decreased from 394 down to 380 μm, corresponding to a STR-2 of -0.09 μm/s.

4 Correlation Between Planned and Measured Ablation Depths

Figure 7 shows the differences between measured center corneal thinning and planned ablation depths for the three patients given in Figures 4–6. The differences are shown without and with the introduction of a fit accounting for baseline stromal thinning due to evaporation. The *x* axis shows the ablation time. The origin of the *x* axis is defined as the beginning of the laser ablation. The positive *y* axis represents data in which the measured corneal thinning exceeds the planned ablation depth. In Figure 7 only the time window noted in Figures 4–6 as ablation is shown. The nonfitted values are marked by closed diamonds for patient 1, closed rectangles for patient 2, and closed triangles for patient 3. For the first 80 s the differences between the planned ablation depth and the thinning measured increase steadily over time. After about 80 s the increase is lower. For patients 1 and 2 the difference is measured as being reduced for certain time periods. Omitting the last measurement point of patient 1 the maximum difference between planned and measured ablation depth is 25 μm.

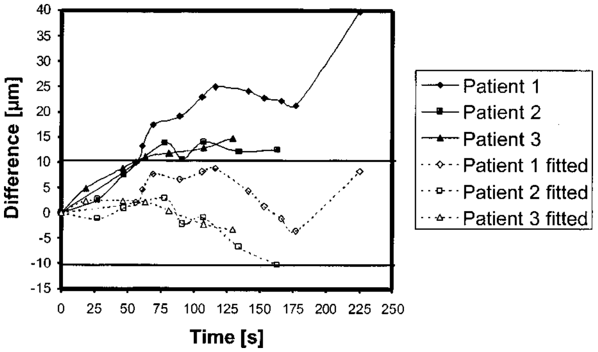

Fig. 7 Difference between measured and planned ablation depths. Fit based on corneal thinning of –0.14 μm/s.

Stromal total thinning during ablation thus is constantly measured to be much higher than expected. This is due to the evaporation effect, which has to be accounted for when the measured and the intended stromal ablation are monitored.

The fitted (open) data points in Figure 7 show a better comparison of measured and planned ablation. The fit used in Figure 7 is based on the results obtained with the first patient (Figures 2 and 3). In the fit corneal thinning due to evaporation of -0.14 μm/s is used. Each closed data point is corrected and corresponds to the amount of time that has elapsed since delivery of the first laser pulse. For example, the *y* coordinate of a closed data point at an *x* coordinate of 100 s would be corrected by subtraction of 100 times 0.14 μm, yielding 14 μm. For that reason a fitted data point always lies below its corresponding closed data point. As a result, the fitted thickness measurements are in much better agreement with the planned ablation than the nonfitted values. The fitted values do not exceed a difference between fitted measurements and planned ablation depths of ± 10 μm. Tolerance of ± 10 μm corresponds to a correction uncertainty of ± 0.7 D. Tolerance of about ± 0.7 D is typical for the 1 year post-op refractive outcome provided by PRK. This means that the OLCR measurements presented in this article are not in contradiction with the postoperative experience of PRK.

The residual difference of 10 μm may be attributed to corneal thinning being not exactly constant during the ablation process, to interindividual differences in stromal evaporation, to measurement errors, to variations in stromal laser ablation influenced by changes in corneal temperature and water content, and to short-term fluctuations in environmental laser absorption properties.

5 Conclusions

The noncontact method OLCR is used to measure the center corneal thickness with micrometer precision during laser ablation of the corneal stroma. OLCR seems to be a useful, easy to handle device with which the surgeon can monitor online the stromal ablation at a single point in the center of the cornea. By establishing pre- (STR-1) and postablation (STR-2) corneal thinning rates, the influence of time on corneal stromal water evaporation was established (which may be important for rather time demanding single small spot scanning techniques). OLCR allows online detection of interindividual and intra- and intersession variations of the amount of corneal tissue removed. This method can be applied to patients undergoing PRK or other photorefractive treatments such as laser *in situ* keratomileusis (LASIK) or laser epithelial keratomileusis (LASEK). Using OLCR, a yet unknown percentage of miscorrections may be detected online during PRK and LASIK. By establishing feedback control, the actual laser ablation parameters may in the future be automatically calculated online. More research is underway to investigate the correlation among corneal evaporation, corneal water content, tissue reaction during photorefractive treatments, intended and measured central ablation depths, as well as intended and measured refractive outcomes.

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