Measurement of Corneal Thickness by Laser Doppler Interferometry

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The laser Doppler interferometry (LDI) technique, which was recently developed for axial eye length measurement, has been modified to measure the corneal thickness of the human eye in vivo. High accuracy is achieved. The standard deviation of the technique is about 7 μm, and improvement by a factor of 5 is possible. First comparisons with a usual slit lamp pachometer show a general agreement but a systematic difference of about 20 μm. Possible reasons for this discrepancy are discussed. Finally, the new method is compared to standard optical and ultrasound pachometry from a theoretical point of view, and advantages and drawbacks of the various techniques are discussed. Invest Ophthalmol Vis Sci 33:98-103, 1992.

Materials and Methods

Description of the Method

The method of measuring intraocular distances by LDI is described in detail in a previous paper. Only a short summary is presented here with the main alteration that allows the measurement of CT.

Figure 1 shows a sketch of the instrument used in this work. A multimode laser diode emits a light beam (wavelength = 780 nm, power = 250 μW) with high spatial coherence but short coherence length (CL). (The HeNe laser and the single mode laser diode, as well as the infrared scope, are used only for alignment purposes.)

This beam passes a Michelson interferometer, which splits the beam in two parallel, coaxial beams: a reference beam 1, and a measuring beam 2, which is retarded with respect to beam 1 by twice the difference, d, of the interferometer arm lengths. In addition, the interferometer mirror of the measuring beam is shifted with constant speed, causing a Doppler shift of beam 2.

The Michelson interferometer replaces the originally used Fabry Perot interferometer. Because the reference arm and the measurement arm of the Michelson interferometer are separated spatially, the measurement arm can now be shorter, equal to, or longer than the reference arm. This enables an exact balance of the two interferometer arm lengths with the possibility of performing measurements in the vicinity of this balance, which is necessary for measuring short distances such as the CT. This was not possible with the Fabry Perot interferometer, because the frame of the interferometer plates prevented their closure to zero distance.

Both beams, 1 and 2, illuminate the eye via a beam splitter cube and are reflected at the anterior and the
posterior corneal surface. This introduces an additional path difference that is twice the optical thickness of the cornea.

The intensity of the superimposed reflected beams is detected by the photodetector and amplified and recorded as a function of the stepping motor position with a personal computer. If the total path difference between beam 2, reflected at the anterior, and beam 1, reflected at the posterior corneal surface, is less than CL, these beams will interfere and the intensity will be modulated by the Doppler frequency $f_D$.

From the stepping motor position, where a signal with $f_D$ is registered, the difference of the interferometer arm lengths, $d$, can be determined and the optical thickness $= d \pm CL/2$ is obtained. The accuracy of this technique depends on CL. The multimode laser diode has a CL of about 110 $\mu$m. By determining the center of the signal peak, the accuracy can be even better than CL/2. The position of the center of the peak is determined by a “mouse” controlled cursor readout on the personal computer. The accuracy of this distance readout is 0.5 $\mu$m, but because of the signal noise, the overall precision of CT measurement is about 10 $\mu$m.

To convert the optical thickness to the geometrical thickness, it must be divided by the group refractive index $n_g$ of the cornea. The value $n_g = 1.3856$, which is based on the phase refractive index $n$ at a wavelength of 550 nm and on the dispersion of water, was used.

In Vivo Measurements

In performing in vivo measurements, laser safety regulations must be met. The power of alignment and measurement lasers are the same as in the case of the axial eye length measurement, which was shown to be well within the safety limits.

Another important point with in vivo measurements is the alignment of the subject’s eye with the laser beam. In this work, the central CT is measured along the vision axis. This is achieved by asking the subject to look at the beam (the wavelength 780 nm is just visible; the beam appears to the subject as weak red spot). The diameter of the beam is about 2 mm. Therefore, the vision axis of the eye must be aligned with the center of the beam with an accuracy of $\pm 1$ mm. (In the case of larger deviation, no part of the reflected beam is reflected back parallel to the illuminating beam; therefore neither the IR scope nor the photodetector receives any light). This can be easily achieved by adjusting the subject’s head using a head rest that is commonly used with slit lamps, which is mounted on a x-y translation stage.

The geometry of the detection unit (a small aperture transmits light only within a narrow angle to the incident beam back to the detector) ensures that even with maximum misalignment of $\pm 1$ mm the position of the cornea, from which light is reflected into the photodetector (the position at which the CT is measured) does not deviate more than 0.3 mm from the point where the corneal surface is perpendicular to the vision axis. This deviation can be further reduced to about 0.1 mm by visually aligning the photodetector with the center of the interference fringes, which are produced by the overlapping beams of corneal and retinal reflection.

In vivo measurements were carried out on both eyes of 9 volunteer subjects, who provided full in-
formed consent. They suffered from no eye diseases, according to their knowledge. They were emmetropic or myopic, up to 10 diopters. In the case of CT measurements, none of them had to wear spectacles to get a signal of good quality.

Pachometer Measurements

A first comparison with a modified version of the widely used Haag-Streit type pachometer was performed. It was manufactured by Nikon company (Tokyo, Japan) and has two small light-emitting diode (LED) lights to assist in alignment. It was used with a Nikon zoom-photo slit lamp microscope FS-2 with a slit width of 50 \( \mu \text{m} \). The pachometer reading was converted to corneal thickness using a table supplied by the manufacturer.

Statistics

Six measurements or more were performed on each eye by LDI and the pachometer. Mean values and standard deviations were calculated for each eye and method separately. The results of the two methods were compared by a paired Student’s t-test after normal distribution evaluated by the Kolmogorov-Smirnov test.

Results

Figure 2 shows an example of a calibration measurement. The point of equal interferometer arm lengths is determined by replacing the cornea with a single interface (mirror). A distance of 3 mm is scanned by the measuring arm of the interferometer, from -1.5 mm to +1.5 mm. The signal intensity \( I \) (ordinate) is plotted as a function of the interferometer arm length difference \( d \) (abscissa). Because of the high intensity of the signal at \( d \) values close to zero, the graph is distorted in this region because of nonlinearities of the amplifier and the AC-DC converter, which makes an exact location of the signal maximum difficult. Therefore, the smaller, subsidiary peaks in distances of multiples of 1.1 mm from the main peak—they are a result of periodic repetition of the coherence function of the laser—are used for calibration of the balance of the interferometer arm lengths. This can be done to an accuracy of about 2 \( \mu \text{m} \) SD.

Figure 3 shows the result of a typical measurement of the optical thickness of a cornea (subject LS. R.). A distance of -1.5 mm to +1.5 mm is scanned. Besides the broad, distorted main peak and the subsidiary peaks of the periodic coherence function, two additional signal peaks are observed in equal distances from the main peak. (Because of the symmetry of the coherence function, the signal is symmetric at about the point \( d = 0 \).) Their distance to the main peak equals the optical thickness of the cornea. In this case, the optical thickness = 712 ± 10 \( \mu \text{m} \) (mean value of 6 measurements ± SD). The time required for one scan is about two seconds. Because two signals from the cornea are obtained during one scan, the measuring time for one signal is only one second.

The optical thickness of the other 17 corneas was measured in a similar way. The values are shown in Table 1, with the calculated geometrical thickness. The values of the pachometer readings also are included in Table 1 (mean values of 6 measurements). In 2 cases, only the right eye was investigated because of geometrical limitations of the pachometer (the subjects’ noses were too large).

The mean SD values of the single measurement are: optical thickness (LDI), 10 \( \mu \text{m} \); geometrical thickness (LDI), 7 \( \mu \text{m} \); geometrical thickness (pachometer), 15 \( \mu \text{m} \).

Discussion

We have shown that the LDI technique, which was recently developed for the measurement of the axial
Fig. 3. Measurement of the optical thickness, OT, of the cornea. I is plotted versus d. In addition to the main and the two subsidiary peaks, two peaks can be observed at a distance $OT = 712 \pm 10 \, \mu m$ from the main peak.

The CT measurement is performed along the vision axis perpendicular to the corneal surface. In the section on materials and methods, it was shown that deviations of measuring position from vision axis can be restricted to values of less than 0.3 mm without difficulty. These deviations can occur because of lateral eye motions of $\pm 1 \, \text{mm}$ during a single measurement or alignment differences between the individual measurements of a measurement series. Note that longitudinal eye motions along the optical axis during the measurement procedure cannot affect the result in any way. The reason is the simultaneous use of the two waves reflected at the two corneal interfaces.

Table 1. Corneal thickness (in micrometers) determined by LDI and OP

<table>
<thead>
<tr>
<th>Subject</th>
<th>OT (LDI)</th>
<th>GT (LDI)</th>
<th>GT (OP)</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.F.L.</td>
<td>754</td>
<td>544</td>
<td>527</td>
<td>17</td>
</tr>
<tr>
<td>A.F.R.</td>
<td>750</td>
<td>542</td>
<td>513</td>
<td>29</td>
</tr>
<tr>
<td>C.H.L.</td>
<td>749</td>
<td>540</td>
<td>506</td>
<td>34</td>
</tr>
<tr>
<td>C.H.R.</td>
<td>748</td>
<td>540</td>
<td>508</td>
<td>32</td>
</tr>
<tr>
<td>W.D.R.</td>
<td>717</td>
<td>518</td>
<td>514</td>
<td>4</td>
</tr>
<tr>
<td>L.L.</td>
<td>676</td>
<td>488</td>
<td>487</td>
<td>1</td>
</tr>
<tr>
<td>L.R.</td>
<td>679</td>
<td>490</td>
<td>458</td>
<td>32</td>
</tr>
<tr>
<td>K.L.</td>
<td>746</td>
<td>539</td>
<td>535</td>
<td>4</td>
</tr>
<tr>
<td>K.L.R.</td>
<td>733</td>
<td>529</td>
<td>522</td>
<td>7</td>
</tr>
<tr>
<td>H.S.R.</td>
<td>759</td>
<td>548</td>
<td>522</td>
<td>26</td>
</tr>
<tr>
<td>L.S.L.</td>
<td>726</td>
<td>524</td>
<td>490</td>
<td>34</td>
</tr>
<tr>
<td>L.S.R.</td>
<td>712</td>
<td>514</td>
<td>508</td>
<td>6</td>
</tr>
<tr>
<td>G.G.L.</td>
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<td>540</td>
<td>520</td>
<td>20</td>
</tr>
<tr>
<td>G.G.R.</td>
<td>754</td>
<td>544</td>
<td>518</td>
<td>26</td>
</tr>
<tr>
<td>P.H.L.</td>
<td>812</td>
<td>586</td>
<td>570</td>
<td>16</td>
</tr>
<tr>
<td>P.H.R.</td>
<td>814</td>
<td>587</td>
<td>572</td>
<td>15</td>
</tr>
</tbody>
</table>

$OT =$ optical thickness; $GT =$ geometrical thickness; LDI = determined by laser Doppler interferometry; OP = determined by optical pachometry.

Standard deviations: $OT$ (LDI) $\leq 10 \, \mu m$; $GT$ (LDI) $\leq 7 \, \mu m$; $GT$ (OP) $\leq 15 \, \mu m$.

Difference: $19 \, \mu m \pm 12 \, \mu m$ (mean value and standard deviation).

errors in CT values caused by these small deviations are negligible because the variation of CT within 0.3 mm off the vision axis is only about 0.1%, or 0.5 $\mu m$ for a cornea with CT = 500 $\mu m$. Therefore, the repeatability of measurement is very high if the patient is able to cooperate and has no problems with fixation of the beam. Microsaccades usually do not exceed an angle of $\frac{\pi}{2}^\circ$. The resulting deviation of the measuring position from the vision axis should therefore be less than 50 $\mu m$. Large eye motions can be observed via the IR scope during measurement, and the corresponding CT value will be excluded from the final result.

The standard deviation of the geometrical thickness was 10 $\mu m$ or less (mean value, 7 $\mu m$), which is a factor of about 3 smaller than in the case of the axial eye length measurement. There are two reasons for the higher precision in the case of CT. First, the pulsation of the eye length with the heart beat, which is in the order of a few micrometers, does not influence the measurement of CT. Second, small deviations of vision axis and measurement axis due to saccadic eye movements between individual measurements should have a greater influence on eye length results than on CT results.

Comparison with Pachometer Measurements

The LDI and pachometer methods show a general agreement of the results, but there is a systematic difference with high significance ($P < 0.0001$). The values obtained by LDI are about 19 $\mu m$ longer than the pachometer results. There are three possible reasons for this discrepancy:

1. The precise $n_\text{g}$ value of the cornea for a wavelength of 780 nm is not known. It was calculated assuming water dispersion. Although this approximation seems to be correct for aqueous and vitreous, it is...
probably wrong in the case of the cornea. A value of \( n_g = 1.4365 \) would yield an agreement between LDI and pachometer, but this value seems too high.

2. The discrepancy could be caused by a too low pachometer reading resulting from a smaller effective width of the illuminating slit on the posterior surface of the cornea than the true slit width. This effect could yield readings that are 30 \( \mu \text{m} \) too low.

3. The thickness of the tear film, about a few micrometers, is included in the LDI results.

The dominant error source is not yet clear. A careful measurement of the \( n_g \) value of the cornea for the wavelength in use (780 nm) will help clarify this point. If only relative values of CT are required, this difference is only of minor interest.

In the following section, the advantages and drawbacks of LDI and conventional optical and ultrasound pachometers will be discussed. The first point regards the precision of the different techniques. Our standard deviation of the reading of the optical pachometer was about 15 \( \mu \text{m} \), which is of the same magnitude as reported in the literature, where the values range from 12 to 14 \( \mu \text{m} \).\textsuperscript{4,5,19} According to the literature,\textsuperscript{1,6} this value can be reduced to about 5 to 8 \( \mu \text{m} \) by very experienced operators.

However, different studies on large numbers of eyes, carried out with this technique, reported mean CT values that differ by up to 60 \( \mu \text{m} \).\textsuperscript{5} The reasons for these discrepancies are probably different alignment methods of the two half-images formed by the beamsplitter of the pachometer\textsuperscript{5,6} and different slit width settings of the slit lamp during measurement.\textsuperscript{5} But even with the same alignment method and slit width, considerable inter-observer discrepancies occur. The CT values of the same eye, measured by different observers, differed by up to 20 \( \mu \text{m} \).\textsuperscript{6} The reasons for these discrepancies are probably differences in the perceptive properties of the observer and difficulties in defining exactly the "edges" of the bright bands of the optical section that need to be aligned in the two half images.\textsuperscript{6}

Problems with inter-observer discrepancies were not encountered using ultrasound pachometers.\textsuperscript{20} The standard deviations of measurements carried out with these instruments is reported to be of the order of 5 \( \mu \text{m} \).\textsuperscript{20,21} However, large differences in the readings of different instruments when measuring the identical point in the same eye were encountered. In measuring the central CT, the maximum differences were about 50 \( \mu \text{m} \). Measuring peripherally, deviations of up to 150 \( \mu \text{m} \) were encountered.\textsuperscript{21} Because all of the instruments were set at the same sound speed (1640 m/s) the reasons for these discrepancies are not clear. Another disadvantage of ultrasound pachometry, compared to conventional optical pachometry and LDI, is its need for mechanical contact between instrument and eye. Therefore, anesthesia is needed and the patient's comfort is reduced.

The large discrepancies in the results obtained by different observers or different instruments are the main limitations of existing pachometric techniques. They are cumbersome if the results of different studies are to be compared or if the same patient is examined several times, such as in the case of therapy control, by different observers or instruments. The application that probably generates the greatest demand for accurate CT measurements is refractive surgery. In this case, undercorrections, overcorrections, and even perforations can occur if data from different ultrasound pachometers are used.

The LDI method should not suffer from the problems mentioned above. The measurement is performed by matching two path differences, which is checked by an electronic system. It does not depend on measurements of absolute light intensities, only on the determination of the position of a signal peak. Therefore, the perceptive properties of the observer do not influence the results. Although it was not checked, an inter-observer variance probably will be avoided. Additional parameters that may influence the results, such as the slit width of the optical pachometer, do not exist with the LDI technique. Because the CT is read directly from another linear distance (the interferometer arm length difference \( d \)) there are no calibration problems that might be the error sources of the ultrasound pachometers. The only remaining error source of the LDI technique is the value of \( n_g \), which is used for the optical thickness to geometrical thickness conversion and which is not known precisely. But if different LDI instruments use the same value, the results should be identical. On the other hand, this problem exists with the ultrasound technique, too, because the true value of sound speed in the living human corneal tissue is not known with great accuracy.\textsuperscript{21}

The standard deviation of LDI is about 7 \( \mu \text{m} \) for the geometrical thickness. This is about the same magnitude as with the ultrasound technique and about half the value usually achieved with conventional optical pachometers. By replacing the multimode laser diode with a super radiant diode, which has a CL of only about 20 \( \mu \text{m} \), this value should be reduced by a factor of 5. In this case, the CL has approximately the same length as the light pulses of the femtosecond pulse laser used to measure the thickness of rabbit corneas.\textsuperscript{7} This, in principle, would mean equal accuracy but with the great advantage of lower cost with the LDI technique.

So far, only measurements of the central CT have...
been discussed. There are several applications in which the knowledge of the central CT is sufficient. Measurements of the central CT were suggested to be helpful in the diagnosis of several corneal disorders, such as in cases of chronic degenerations and endothelial dysfunctions, and for differentiating between different types of stromal dystrophy. Numerous studies indicate the importance of central CT measurements for determining the tolerance of the eye to different types of contact lenses. In this case, the swelling of the cornea resulting from edema caused by hypoxia is measured in the examination of new types of contact lenses. The application of these measurements also might be useful for determining which type of contact lens is tolerated best by a patient. These applications require several measurements over several hours. Therefore, a noncontact technique that can be performed by different observers without inter-observer variability, as with the LDI technique, would be very useful in these cases.

In other cases, especially for corneal refractive surgery, there is a demand for measuring CT at different positions of the cornea—centrally, paracentrally, and peripherally. The main advantage of the ultrasound pachometers is their ability to carry out these measurements. However, as already mentioned, the discrepancy between different instruments in performing peripheral CT measurements is even greater than for central CT measurements. Peripheral measurements are difficult using standard optical pachometers, but it has been shown that they are feasible with an electronic pachometer equipped with separate fixation lights that make angles of multiples of 5° with the central light. So far, LDI only has been used for central CT measurements, but, in principle, peripheral measurements are possible. Separate fixation lights as mentioned above could be attached easily to the instrument. If the patient has no fixation problems, the CT could be measured at different points of the cornea with the same high precision as the central CT. If one is not willing to rely on the cooperation of the patient, an eye tracking system or at least a photographic recording of the measurement position on the cornea (with the HeNe laser switched on as a pointing device and the camera triggered with the measurement) would need to be used.

**Key words:** biometry, pachometry, corneal thickness, laser Doppler interferometry, laser interferometry

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**References**