

Effect of Cataract Surgery on the Refractive Index of the Cornea Estimated by Optical Pachymetry

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Purpose: To noninvasively estimate the refractive index (RI) of the central cornea along the antero–posterior direction before and after routine phacoemulsification.

Methods: Using 2 setups for a standard optical pachymeter, the ratio of observed optical section widths (OSWs) is a function of the RI. Thus, the corneal RI could be estimated using a calibration equating OSW ratios with known RI values. The OSW was measured by 2 observers for 1) normal subjects for estimating interoperator errors and effects of sex and age on the RI and 2) before and after patients underwent routine phacoemulsification.

Results: First, the average interoperator difference (Δ RI) was $+0.0005$ (SD = ± 0.0044 , 95% confidence limit, -0.0002 to $+0.0012$). The root mean square difference between measurements obtained by the observers was 0.0032 . There was a significant correlation between the Δ RI and the mean of each pair of measured values ($r = -0.172$, $n = 153$, $P = 0.003$). The mean RI (\pm SD) was 1.435 (± 0.005 , $n = 82$) for females and 1.429 (± 0.005 , $n = 71$) for males. There was no significant between-sex difference or association between the RI and age (mean age, \pm SD, and range, 44.31, 20.38, and 19–88 years, respectively). Second, the difference (y) between the preoperative (x) and postoperative RI was, $y = 0.844x - 1.203$ ($r = 0.694$, $n = 31$, $P \leq 0.001$) according to observer 1 and according to observer 2, $y = 0.755x - 1.108$ ($r = 0.681$, $n = 31$, $P \leq 0.001$).

Conclusions: The RI of the human cornea along the antero–posterior axis can be estimated using a modified application of tra-

ditional optical pachymetry. The average values for the corneal RI were higher compared with those reported in previous reports. The change in the RI after phacoemulsification could be predicted from the preoperative value.

Key Words: phacoemulsification, noninvasive, refractive index, cornea

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Advances in cataract surgery have reduced the overall impact on the corneal endothelium, but loss of endothelial cells has not been nullified.^{1–5} These cells actively maintain corneal hydration,^{6–10} and depreciation of their function ultimately leads to an increase in hydration. This will affect the overall refractive index (RI) of the cornea^{11–15} and could affect the residual postoperative refractive error. The RI of the human cornea is often quoted as 1.376^{16} or 1.377^{17} . Most reported estimates of the corneal RI were made using ex vivo samples. The measurements reported using in vivo material are the RI of the corneal epithelium,^{18,19} Bowman layer, and anterior stroma before and after excimer laser photoablation.^{15,18,20} There is no clear way of obtaining a reliable representative single value for the corneal RI using available data. Such a value could be critical in refining the precision of biometry and intra-ocular lens (IOL) power calculation. To the best of our knowledge, all human corneal RI values were obtained by contact refractometry before, and after, sectioning to reveal the stroma. There are no available data of the corneal RI estimates obtained by noninvasive methods applied to cases in vivo.

Optical pachymetry requires measuring the width of the corneal optical section observed by slit-lamp biomicroscopy.^{21,22} The dimensions of the observed optical section width (OSW) can be varied by changing the angle between the illumination and observation beams of the biomicroscope. The OSW enlarges when the angular separation between the 2 beams increases. The ratio of the OSW values obtained using 2 different, but fixed, values for the angular separation between the 2 beams has a linear relationship with the average RI along the antero–posterior direction of the cornea.²⁷ Thus, the RI could be estimated noninvasively using the OSW ratio obtained from 2 different angular separations between the 2 beams of a slit-lamp biomicroscope.

The aim of this study was three-fold: first, to reveal the feasibility of estimating the RI of the cornea over its antero–posterior depth by optical pachymetry; second, to determine

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This article is dedicated to the late Prof. Nikolai Sergienko for his insight, inspiration, enthusiasm, and encouragement of this project.

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whether the estimated RI of the cornea was sex- and age-related; and third, to ascertain the effect of uncomplicated cataract surgery on the estimated RI of the cornea.

MATERIALS AND METHODS

Estimation of the Corneal RI from Pachymetry Data

Figure 1 shows 2 setups for pachymetry. Corneal thickness (t) can be calculated²¹ using the Jaeger method when:

1. the incident beam is normal to the apex of the corneal surface and the corneal optical section is observed at an angle of θ degrees as follows:

$$t = \frac{a1}{\cos\theta \cdot \tan\left\{\sin^{-1}\left[\sin\left(\theta - \frac{a1}{r} \cdot \cos\theta\right)/RI\right] + \left(\frac{a1}{r\cos\theta}\right)\right\}} \quad (1)$$

2. the angle of the incident beam striking the apex of the corneal surface and the angle of the corneal optical section is observed are both equal to θ degree as follows:

$$t = \frac{a2}{2\cos\theta \cdot \tan\left\{\sin^{-1}\left[\sin\theta/RI\right] + \left(\frac{a2}{2r\cos\theta}\right)\right\}} \quad (2)$$

In both expressions, r = radius of corneal curvature, RI = refractive index, a1 and a2 = OSW values. Both Equations 1 and 2 reveal a linear numerical relationship between t and the OSW for typical r and RI values. The effect of variations in r on t calculation is negligible. Equations 1 and 2 can be treated as simultaneous equations because the ratio a2/a1 is a function of the RI. Therefore, an empirically derived calibration curve could be obtained permitting the RI to be derived from a2/a1 ratios.

Apparatus for Noninvasive In Vivo Estimation of the RI

A standard pachymeter (ophthalmocalibrometer OK-4 for the slit lamp SHL-2B, Nezhinsky State Enterprise NPK Progress, Ukraine) was used throughout this study. The working principles of the pachymeter are based on the Jaeger method, whereby the OSW of the cornea is observed and measured by manually operating a doubling device linked to a Vernier scale using the edge-to-edge method.²³⁻²⁵ The reading on the pachymeter doubling device Vernier scale is directly proportional to the actual OSW of the cornea. The slit-lamp incident beam was fixed at maximum brightness, kept as narrow as possible while allowing the optical section to remain visible and with the total magnification of $\times 35$ during the entire study. The doubling device was zeroed, the angle between the incident and observation beams was set at 45 degrees and both beams were locked (condition 1 in Fig. 1). The patient looked directly into the incident beam, the doubling device was adjusted, and the OSW scalar reading was recorded. The doubling device was zeroed, and the patient was asked to keep staring straight ahead. The incident beam was unlocked, the angle between the incident and observation beams was increased to 90 degrees and the incident beam was again locked (condition 2 in Fig. 1), the doubling device was adjusted and the OSW the scalar reading was recorded. The pachymeter was manufactured with a doubling device scale featuring corneal thickness values corrected for an RI of 1.377. All readings taken from the doubling device were converted to actual OSW values using the appropriate algorithms based on Equations 1 and 2.

Repeatability/Test-Retest Reliability of the Apparatus

The test-retest reliability of the procedure was checked by taking 10 repeat OSW measurements for each of the 2 optical setups of the pachymeter using a single rigid mono-curve contact lens and repeated the next day.

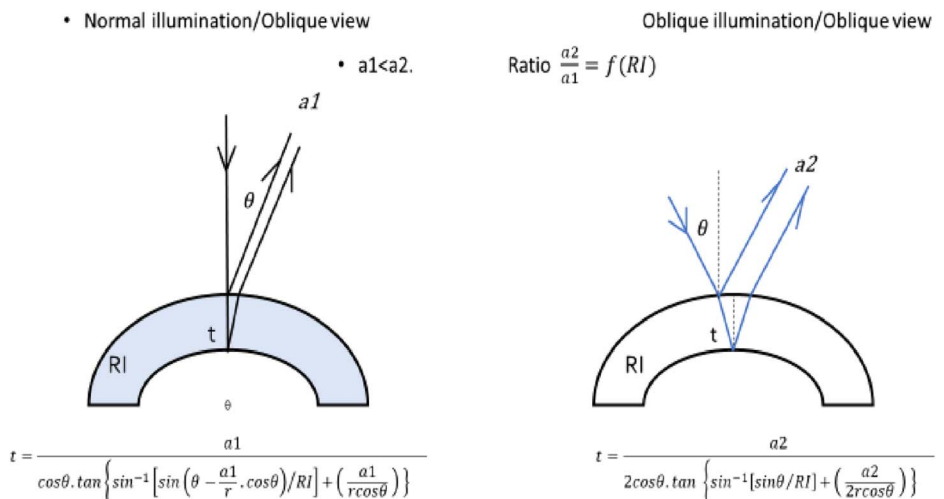


FIGURE 1. Two optical setups for pachymetry and the appropriate expressions that can be used to calculate corneal thickness (t); r is the surface radius of the cornea within the very center of the optical zone. The value of a1 is the width of the corneal optical section under normal illumination, and a2 is the counterpart under oblique illumination. Since t is a common value for any single cornea, it follows that refractive index (RI) can be calculated for known values of a1, a2 when θ is kept constant.

Calibration of the Apparatus for Estimating the RI

After familiarization and training, the pachymeter was calibrated by a trained operator using 7 moncurve contact lenses cut from rigid polymers. The RI of these lenses ranged from 1.415 to 1.446 (central thickness, 0.099–0.500 mm). The lenses were manufactured by an independent contact lens company that verified thickness and RI of each lens' material using methods compliant with the most recent International Organization for Standardization requirements. The lenses were masked by coding with random numbers. A randomly selected lens was suitably fixed, 10 individual measurements were made using the pachymeter under condition 1 then condition 2, and the process was repeated for the remaining lenses. The true specifications of the lenses were revealed after the OSW values and ratios were calculated for all 7 lenses.

Study Design of Clinical Investigation

The investigation was a prospective consecutive randomized masked observational study that was approved by the Commission on Ethics of Shupyk National Medical Academy of Postgraduate Education (Kyiv, Ukraine) and followed the tenets of the Declaration of Helsinki. All subjects signed consent forms after the aims and procedures of the investigation were fully explained. Other than the surgical cases, none of the subjects enrolled had any history of active or previous ocular conditions involving the anterior segment. Measurements were taken from each subject on a consecutive, case-by-case, basis.

Interoperator Error: Nonsurgical Cases

After the period of familiarization and training, 2 operators used the pachymeter to obtain OSW data from the right eye of 153 subjects (82 females and 71 males, age range 19–88 years). At all times, 3 repeat consecutive measurements were taken under condition 1 followed by 3 consecutive repeat measurements taken under condition 2. The average of the 3 consecutive measurements taken under the 2 conditions was archived and later subjected to further analysis. Each subject was checked by the second operator after a short break after data according to the first operator were recorded. At all times, operator 1 remained unaware of the results obtained by operator 2 and vice versa. The data were independently recorded by another member of the study team. The RI values were derived using the results from the calibration curve linking RI and the OSW ratios.

Surgical Cases

Adhering to the method described for nonsurgical cases, the same 2 trained operators obtained OSW data from patients just before and, between 1 week and 3 months, after phacoemulsification. Data were obtained, on a consecutive, case-by-case, basis from 20 females and 11 males (age range 23–89 years) who underwent routine uncomplicated surgery.

Description of Surgery and Postoperative Treatment

Surgery was performed by one surgeon (L.T.) under topical anesthesia through a 2.2-mm self-sealing clear corneal incision at the 12 o'clock position. A circular capsulorhexis of 5.0 mm was performed, followed by lens hydrodissection, phacoemulsification, and bimanual cortex removal. One type of hydrophobic acrylic 1-piece IOL was inserted into the capsular bag. The surgical wound was closed by stromal hydration. Surgery was completed with injections of dexamethasone (subconjunctival) and betamethasone (parabulbar). Postoperative treatment included drops of levofloxacin, dexamethasone, and indomethacin with gradual tapering, dexpanthenol gel, and a combination of trehalose and hyaluronic acid. IOP was within normal limits at all examinations postoperatively.

Statistical Analysis

The data were stored on an Excel spread sheet (Microsoft, Redmond, WA) and analyzed to determine 1) the reliability of the procedure (paired *t* test), 2) the significance of any correlation between the measured OSW ratios and the known RI of the contact lenses [Pearson correlation coefficient (*r*)], 3) the significance of any apparent differences between the results obtained by the 2 observers (method of Bland and Altman²⁶), 4) the significance of any apparent between-sex difference in the estimated RI (unpaired *t* test), 5) the significance of any apparent relationship between the estimated RI and subject age [Pearson correlation coefficient (*r*)], 6) the significance of any apparent change in the overall mean estimated RI after routine cataract surgery (paired *t* test), 7) whether there was any association between the change in the estimated RI after surgery and the estimated RI before surgery [Pearson correlation coefficient (*r*)], and 8) whether any change in the estimated RI after surgery was correlated with the time interval after surgery [Pearson correlation coefficient (*r*)]. The significance level was set at $P < 0.01$ for in vitro and $P < 0.05$ for in vivo data analysis.

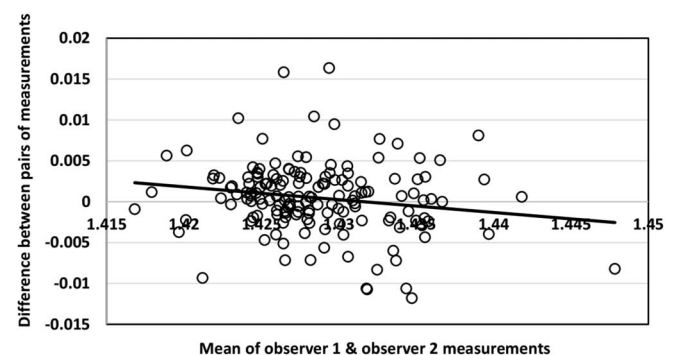


FIGURE 2. Bland and Altman plot comparing individual pairs of results obtained by the 2 observers. The differences between individual pairs of values obtained by observers 1 and 2 are plotted along the y-axis, and the corresponding average of the pairs is plotted along the x-axis. The correlation, *r*, from the regression analysis was -0.1717 ($n = 153$, $P = 0.0034$).

RESULTS

Reliability and Calibration of Apparatus

There were no significant intersessional differences in the estimation of the mean OSW and a2/a1 values ($P > 0.05$; these data are shown in Supplemental Table, Supplemental Digital Content 1, <http://links.lww.com/ICO/A690>). For the a2/a1 values, the SD divided by the mean reduced from over 25% to below 7% between the first and second sessions. The \pm SD values for the a2/a1 ratios for the calibration lenses ranged from ± 0.049 to ± 0.192 averaging at ± 0.135 (these data are shown in Supplemental Table, Supplemental Digital Content 2, <http://links.lww.com/ICO/A691>). The association between a2/a1 ratios and stated RI values was significant. The equation of the least squares regression line linking the RI with the measured a2/a1 was of the form:

$$RI = 1.3795 + 0.0268[a2/a1] (r = 0.9472, n = 7, P = 0.0012) \tag{3}$$

The 95% confidence limits were ± 0.0096 for the mean, ± 0.0179 for the slope and $\delta RI / \delta [a2/a1] = 0.0268$.

Interoperator Error

The RI estimates for all in vivo cases were determined using Equation 3. The Bland and Altman plot showing the differences between the calculated RI values obtained from the 2 observers is featured in Figure 2. The mean difference (ΔRI) between individual pairs of measurements was $+0.0005$ ($SD = \pm 0.0044$, 95% confidence limit, -0.0002 to $+0.0012$). The limits of agreement between the 2 observers ($\Delta RI \pm 1.96 SD$) was $+0.0005 \pm 0.0085$. The root mean square difference between individual pairs of measurements obtained by the 2 observers was 0.0032 . There was a significant correlation between the difference of values obtained by the 2 observers and the mean of each pair of values ($r = -0.1717$, $n = 153$, $P = 0.0034$).

Estimated RI and the Subject's Sex

The main descriptive results are shown in Table 1. There was no significant difference in the mean estimated RI values between males and females according to the results obtained by either operator ($P > 0.05$).

Estimated RI and the Subject's Age

These data are shown in Figures 3A and B. There was no significant correlation between the estimated RI and the subject's age ($P > 0.05$).

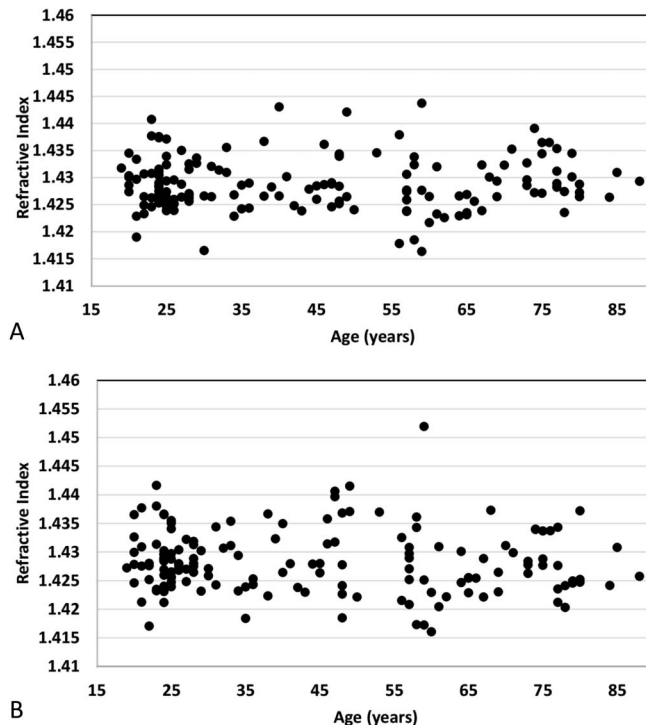


FIGURE 3. A and B, Relationship between age (x axis) and the estimated RI (y axis) of the cornea according to observer 1 (5a) and observe 2 (5b). There was no significant association between age and the RI.

Effect of Surgical Intervention on the Estimated RI

The key data are shown in Table 2. There was no significant difference in the mean RI estimated preoperatively and postoperatively according to observer 1 ($P = 0.286$). However, according to the measurements obtained by observer 2, there was a small albeit statistically significant ($P = 0.026$) increase in the mean (\pm SD, 95% confidence limit) estimated RI from $1.424 (\pm 0.004, 1.423-1.426)$ to $1.426 (\pm 0.003, 1.425-1.428)$. A significant association was revealed between the change in the estimated RI (y) and the preoperative estimated RI (x). These data are shown graphically in Figures 4A, B. The equation of the least squares regression line linking y with the RI was of the following form:

For observer 1, $y = 0.844x - 1.203$ ($r = 0.694$, $n = 31$, $P \leq 0.001$).

For observer 2, $y = 0.755x - 1.108$ ($r = 0.681$, $n = 31$, $P \leq 0.001$).

TABLE 1. Estimated RI, Gender and Interobserver Variation for the Normal Nonsurgical Cases

Gender	Observer 1			Observer 2			P		n
	Mean RI	\pm SD	95% CI	Mean RI	\pm SD	95% CI	Intergender	Interobserver	
Female	1.435	0.005	1.434–1.436	1.432	0.006	1.31–1.433	0.879 (observer 2)	0.199	82
Male	1.429	0.005	1.428–1.430	1.430	0.005	1.429–1.431	0.096 (observer 1)	0.744	71

TABLE 2. Estimated RI Before and After Phacoemulsification

n = 31	Observer 1			Observer 2			P	
	Mean RI	±SD	95% CI	Mean RI	±SD	95% CI	Interobserver	Intraobserver
Preoperative	1.426	0.004	1.425–1.428	1.424	0.004	1.423–1.426	0.061	0.286
Postoperative	1.427	0.004	1.426–1.429	1.426	0.003	1.425–1.428	0.275	0.026

There was no significant correlation between the change in the estimated RI and the time between surgery and the day the postoperative RI was estimated (observer 1: $r = 0.023$, $P > 0.05$; observer 2: $r = -0.141$, $P > 0.05$).

DISCUSSION

The mean interoperator error (Δ RI) from the data collected in vivo was $+0.0005$ (SD = ± 0.0044 , 95% confidence limit, -0.0002 to $+0.0012$), the root mean square difference between the individual pairs of measurements obtained by the 2 observers was 0.0032 , and the limit of agreement between the 2 operators was higher at ± 0.0085 . Figure 2 shows that the measurements obtained by the 2 observers were in general agreement, but there was a significant correlation between the difference of values obtained by the 2 observers and the mean of each pair of values ($r = -0.1717$, $n = 153$, $P = 0.0034$). The 2 observers

may have inadvertently adopted different interpretations of when doubling occurred at the 90-degree and 45-degree settings. However, the results in Tables 1 and 2 and Figures 3 and 4 do not reveal any significant interoperator differences when estimating the RI in females and males, in relation to patient age or after phacoemulsification. The RI values obtained from the 184 cases (153 normal and 31 surgical cases) were much higher than previous estimates for the human cornea ranging from 1.366 to 1.401.^{15–20,27} The error in determining the final step in the subjectively interpreted doubling of the observed optical section depends on the shape of the distribution of light scattered over the observed section.²⁸ The shape of this distribution is highly dependent on the width of the slit of light incident on the cornea. Widening the slit increases the visibility and the size of the observed optical section. This action leads to a systematic error when estimating the actual width of the optical section. The width of the incident slit beam was kept as narrow as possible while ensuring that the optical section remained visible. In addition, the observer's interpretation of the point when optical doubling of the viewed section occurs is governed by the Rayleigh criterion.²⁹ The criterion defines the point at which 2 luminescent objects either no longer appear separated or just appear separated in relation to the actual separation between the 2 objects. The width and characteristics of light spreading over the observed optical section in association with the Rayleigh criterion may impair the observer's subjective interpretation of doubling. This uncertainty could be the source of the lack of confluence, the divergence, between our results and previous estimates. This paradox did not occur during the calibration exercise because the calibration lenses do not backscatter light toward the observer. Using lenses, the observer sees bright specular reflection from the front and back surfaces separated by a dark space and the lens is perfectly still. For the subject, the observer sees specular reflection from the front and back surfaces separated by a light gray space and the subject is not perfectly still.

Traditional methods for estimating the corneal RI measure the RI of the immediate layer of tissue in direct contact with the refractometer. Furthermore, there is no absolute guarantee that the preparation of corneal tissue for invasive refractometry does not upset the natural level (the equilibrium) of intracorneal fluid. The inverse relationship between the stromal RI and water content^{11–15} is a clear indication of how the index can be altered by inadvertent shifts in water content alone. This is a systematic error adjusting the natural RI recording. The lower values reported for the corneal stromal RI in the contemporary literature result from the disruption inflicted on the cornea

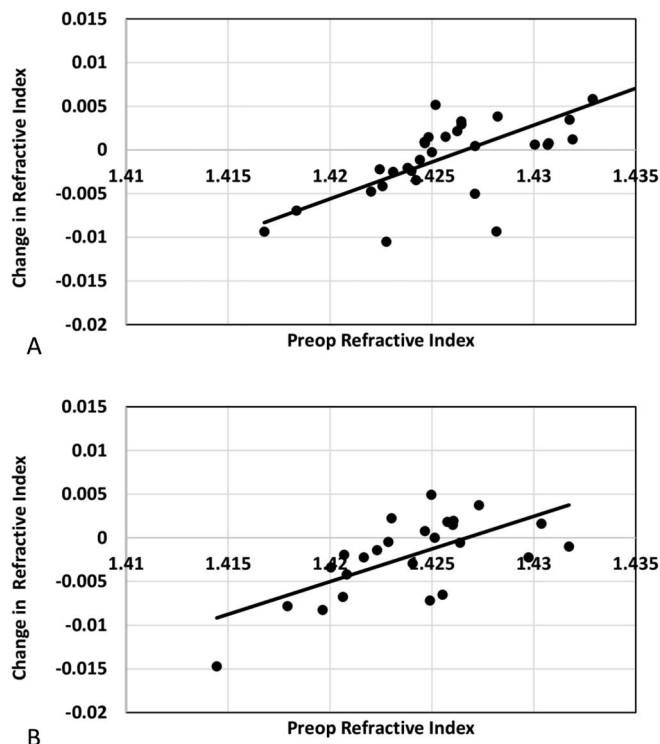


FIGURE 4. A and B, Relationship between preoperative RI (x axis) and the change in the RI after surgery (y axis) according to observers 1 (6a) and 2 (6b). The association between the 2 parameters is represented by $y = 0.844x - 1.203$ ($r = 0.694$, $n = 31$, $P \leq 0.001$, observer 1) and $y = 0.755x - 1.108$ ($r = 0.681$, $n = 31$, $P \leq 0.001$, observer 2).

by the invasive techniques used by the respective investigators. The noninvasive technique produces an averaged value over the depth of the cornea and not just individual compartments. The average RI in the living human cornea could be higher than the value currently accepted without question.

According to the results obtained by observer 2, there was a statistically significant increase in the mean RI after phacoemulsification. The increase was small and neither clinically meaningful nor supported by the results according to observer 1. A decrease in the RI would be expected if, on average, corneal hydration tended to increase after phacoemulsification. Conversely, a moderate increase in the RI would result from depreciation of corneal hydration. Thinning of the cornea, indicating some dehydration, after phacoemulsification has been reported,³⁰ and this would substantiate the finding. In general, thickness changes tend to regress to preoperative levels after a month,^{31–33} and some report no significant change in endothelial cell density after cataract surgery.³⁴ The implication is that corneal hydration is not overtly affected; hence, the average corneal RI should not change. This would substantiate the results according to observer 1. Nevertheless, there is strong interobserver agreement when, for each individual case, the change in the RI is compared with the preoperative RI value. As shown in Figures 4A, B, the RI changes encountered ranged from -0.015 to $+0.005$. Standard models^{16,17} predict that the dioptric power of the eye increases by 0.50 diopter sphere (DS) when the average value of the RI over the depth of the cornea decreases by 0.015. Therefore, unexpected variable refractive errors after phacoemulsification could be due to changes in the average value of the RI.

When the preoperative value exceeded 1.425, the postoperative RI value tended to decrease after phacoemulsification. This is in keeping with our initial expectation following on from a possible decrease in endothelial efficacy and a subsequent increase in corneal hydration. However, when the preoperative RI value fell below 1.425, there was a tendency for the postoperative RI value to increase after phacoemulsification. This contradicts the noted expectation. There is no clear logical explanation accounting for this paradox.

In conclusion, we believe that this is the first report of empirically derived estimates for the RI of the human cornea obtained in vivo by noninvasive means. The estimates abrogate the more traditional values reported in the literature. Furthermore, phacoemulsification did not substantially affect the average corneal RI of our subjects; however, meaningful changes were encountered in some individual cases. A totally objective, noninvasive technique for estimating the corneal RI could provide even more useful information that may, in turn, lead to better outcomes after corneal or cataract surgery.

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