Tobacco Smoking and Its Impact on Corneal Biomechanics

In their excellent study, Sahin et al.¹ investigated the effect of diabetes mellitus on various corneal biomechanical parameters, as measured by the Ocular Response Analyzer (ORA; Reichert, Inc., Depew, NY). The rationale of their study is very interesting. To my surprise, the authors showed a decrease in corneal hysteresis (CH) rather than the expected increase. Several factors suggest that diabetes mellitus would actually enhance corneal biomechanics by an increase in the cross-linking rate: First, an earlier retrospective study showed a lower incidence of keratoconus in diabetic patients, suggesting that corneal biomechanics are enhanced in diabetic corneas.² Second, the nonenzymatic glycosylation of proteins (Maillard reaction) that is prominent in diabetes mellitus, results in the formation of advanced glycosylation end products (AGEs). AGEs induce cross-links between connective tissue collagen and increase tissue rigidity, especially in the presence of glucose.³⁻⁴

Similar to diabetes, tobacco smoking represents a source of AGEs, and moreover, by-products of cigarette smoke, such as nitrogen oxides, nitrite, and formaldehyde, induce cross-links between collagen fibers.⁵⁻⁷ A recent epidemiologic study showed that the incidence of keratoconus in smokers is considerably lower than in the nonsmoking population,⁶ and we have recently performed a prospective comparative case series to investigate the effect of chronic tobacco smoking on corneal biomechanics using the ORA. Our results showed that chronic smoking increases corneal rigidity in a statistically significant manner.⁸

The study by Sahin et al.¹ shows the opposite and was performed in Turkey. From 1990 to 1999, Turkey had the second highest growth rate in cigarette consumption in the world, and in 1999, Turkey accounted for 2.2% of the total world cigarette consumption.⁹⁻¹⁰ Therefore, accounting for the smoking status of the participants in this study would be essential for the outcome and might have significantly altered the results. The authors could not be aware of the influence of chronic tobacco smoking might have on their results, because at the time of publication of their study our paper, now published, was in press.⁸

I therefore suggest that Sahin et al.¹ determine the smoking status of their patients and perform the statistical analysis in light of their findings.

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Citation: Invest Ophthalmol Vis Sci. 2010;51:6891–6892. doi:10.1167/iovs.10-5148

Lack of Statistical Power and Refractive Outcomes

We read with great interest the article by Raymond et al.¹ on a randomized controlled study comparing refractive outcomes after cataract surgery using applanation ultrasound (US) or partial coherence laser interferometry with the IOLMaster (Carl Zeiss Meditec, Dublin, CA). The purpose of the study was to assess whether these methods of measurement of axial length have a difference in precision of refractive outcomes. There are two aspects of the design of this study that compromise its conclusions.

The authors state that the trial was powered to detect a difference of 0.24 D in mean absolute error (MAE), without explaining the reasons or providing any evidence of why a difference of <0.24 D is not clinically significant. We can only assume that a level of 0.24 D was selected because of evidence supporting that a change of 0.25 D in spherical equivalent has an impact on unaided visual acuity.² A level of 0.24 D in MAE can actually have a big impact on refractive outcomes. For example, Olsen³ discovered a difference at 0.23 D in MAE between applanation US and IOLMaster biometry (0.65 D vs. 0.43 D). This result translated to improved refractive outcomes from 45.5% and 77.3% for applanation US to 62.5% and 92.4% for IOLMaster for deviations of ±0.5 and ±1.0 D from the expected outcome (P < 0.00001).³ According to the criteria set for the study by Raymond et al.,¹ this level of improvement in refractive outcomes is not clinically significant. There have been no clinical studies validating a specific level of clinical significance for MAE in the setting of refractive outcomes after cataract surgery.

MAE is a measure of the spread (precision) of a distribution assuming a mean numerical error (MNE) of 0. When the MNE is not 0, the MAE is increased, and it no longer quantifies spread (precision) alone but is also affected by inaccuracy. The authors’ decision not to use optimized IOL constants but to use those recommended by the manufacturer (118.9 for IOLMaster and 118.7 for applanation US) could have introduced systematic errors from high MNEs and further compromised the

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With great interest, I read the article by Artes and Chauhan in Signal/Noise Ratios to Compare Tests for Measuring Visual Field Progression. The authors proposed SNRs that assess a test’s sensitivity for measuring visual field loss and its progression. These SNRs are fundamentally different. It must be emphasized that the goal of measuring visual field progression (to discriminate or to evaluate patients) should be taken into account when choosing an SNR.

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Signal/Noise Ratios to Compare Tests for Measuring Visual Field Progression

With great interest, I read the article by Artes and Chauhan in the October 2009 issue. In this article, signal-to-noise ratios (SNRs) were used to quantify the variability of different metric techniques independent of their measurement scale. For each patient, signal and noise estimates were respectively derived from the mean and SD of superior–inferior differences in each sector of the Glaucoma Hemifield Test in six visual fields. The authors found larger SNRs for frequency-doubling technology (FDT2) perimetry than for standard automated perimetry (SAP). As an SNR expresses the test signal of interest in proportion to the measurement error, these results suggest that FDT2 is at least as efficient as SAP at detecting visual field loss. I support the use of SNRs because they give more information about the test’s potential than measures that include only the noise of a test, like SD values. Of note, the authors suggested that these SNRs could also be used in deciding whether tests are useful in measuring visual field progression.

Before SNRs are used for this purpose, one has to ask oneself what the necessary measurement properties are for tests to assess glaucomatous visual field progression. In clinical practice, the main purpose of assessing progression is to discriminate between patients who are at high risk for visual disability and therefore need a change in treatment, from patients who are optimally treated. Although no gold standard or optimal cutoff point is available, a useful method should anyway be able to show differences in visual field progression between patients. These differences can only be identified if the amount of measurement error is not too high. An SNR that is used to assess the instrument’s ability to measure visual field progression should therefore consist of a signal, expressing between-patient differences in visual field change, in proportion to the amount of measurement error (noise). Such a measure in fact shows the reliability of visual field change and focuses on the discrimination between patients who change a great deal and those who change little.

The authors proposed SNRs that assess a test’s sensitivity for cross-sectional spatial differences. These SNRs could be used as an approximation for a test’s sensitivity to visual field change over time. As the focus here is on detection of true change within patients over time, its purpose is evaluative instead of discriminative. Therefore, these SNRs used differences within patients as the signal of interest. An index of sensitivity to change could be used for assessing the ability of a test to detect even minimal visual field deterioration, but not to assess the ability to detect clinically relevant differences between patients. Although a smaller amount of measurement error (noise) results in both a higher sensitivity to change and a higher reliability of change, these SNRs are fundamentally different. It must be emphasized that the goal of measuring visual field progression (to discriminate or to evaluate patients) should be taken into account when choosing an SNR.

Author Response: Signal/Noise Ratios to Compare Tests for Measuring Visual Field Progression

We thank Dr. Ernest for his interest and his thoughtful comments on our article. We suggested that signal-to-noise ratios (SNRs) estimated from repeated visual field examinations provide initial guidance on whether a new test is likely be to useful in measuring visual field progression over time.

Dr. Ernest points out that the usefulness of a method for measuring progression lies in its ability to discriminate between patients who need a change of treatment and those who...