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Chapter VIII

The New Era of Refractive Correction

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Abstract

During the last decade, advances in the knowledge and measurement of the eye's optical aberrations have moved the wave aberration theory from an obscure scientific concept to one that is central to efforts to improve vision. Nowadays, all the imperfections in the components and materials within the eye that cause light rays to deviate from the desired path are referred to as *optical aberrations*. Refractive surgery aims to minimize optical aberrations in the eye. Excimer laser surgery is the most performed surgical technique to improve unaided vision. The personalized correction of the eye's aberrations promises to be the next golden standard in laser refractive surgery. The technique necessitates an accurate determination of the wavefront error and a precise system of surgical correction. To date, although it has been demonstrated that image quality after customized procedures is improved over that of standard procedures, there are still significant aberrations induced after a wavefront-guided procedure that are neither expected nor predicted. The ability to anticipate confounding biophysical responses of the cornea at the level of the individual patient remains still limited and should be improved.

The development of innovative wavefront sensing and correcting methods and techniques is now opening new perspectives of high-precision refractive corrections. Data coming from the reliable measurements of the corneal and ocular wave aberration may be used to drive a more precise personalized correction of the eye's aberrations for eliminating low-order aberrations and further compensating high-order aberrations between cornea and lens to optimize the individual visual performance. Accordingly, identifying all the components of corneal biophysical response to develop therapeutic

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models for compensating for these factors will ultimately lead to increased predictability of visual outcomes.

Major advances in presbyopia correction are also expected in the near future, thanks to the application of innovative electro-optical technologies, such as liquid crystals, in vision science.

Expert Commentary

Causes and Sources of Vision Blurring

Vision begins with the formation of an optical image of the external world upon the retinal mosaic of light-sensitive photoreceptors. Because image formation is the very first step in the visual process, imperfections in the eye's optical apparatus have the potential for affecting every aspect of visual perception. The eye is an optical system having several optical elements for focusing light rays representing images onto the retina. Imperfections in the components and materials within the eye may cause light rays to deviate from the desired path. These deviations, referred to as *optical aberrations*, result in blurred images and decreased visual performance. Optical aberrations from the eye include low-order and high-order aberrations. Low-order aberrations, i.e., defocus and astigmatism, are the predominant optical aberrations in the human eye: they account for 90% to the overall wave aberration (WA) of the eye and are currently well corrected with spectacles, contact lenses or laser surgery. Although high-order aberrations (HOA) make a small contribution ($\leq 10\%$) to the total variance of the eye wave aberration, their correction improves visual performance substantially, as largely demonstrated with the use of Adaptive Optics techniques [1]. An increasing number of studies has shown the deleterious effect of HOA on image quality [2,3], especially for larger pupil sizes. On the other hand, HOA cannot be corrected adequately with current mainstream optical or surgical treatments. How HOA decrease the human visual performance is currently subject of debate [4]. The Rayleigh and Maréchal criterions [5] suggest that if the ocular WA exceeded a quarter-wavelength ($\lambda/4$: about 0.14 microns for green light) the image would be significantly degraded with respect to the diffraction-limited case [6]. Ocular and corneal wavefront sensors are capable of measuring with extreme precision sub-wavelength errors of the eye optics and we are already aware that the ocular wavefront typically exceeds this quarter-wave limit [7]. Hence, it is reasonable to expect that the full correction of the eye's WA will almost definitely lead to significant improvements in optical image quality. Authors reported that an aberration-minimizing procedure has to provide an ablation depth per pulse lower than 0.1 μm [8]. This calculation indicates that present day laser devices that work with an ablation rate of 0.25 μm per pulse may be improved; however, it is probable that wound healing and biomechanical effects may limit the precision of laser corneal reshaping [9,10].

Beyond optical aberrations, the human eye suffers also from *scattering*, *dispersion* of light and *diffraction*. *Scattering* occurs whenever light encounters refractive index discontinuities in its path. *Scatter* in the ocular media is mainly due to diffusion and the loss of transparency in the cornea, the lens, and the humours. The result of *dispersion* of the light in optical elements of the eye is the induction of chromatic aberrations. In other words, chromatic aberration is simply spherical refractive error that depends on wavelength. *Diffraction* is a fundamental property of the wave nature of light whenever it passes through the eye and the edge of the iris [11]. In theory, it is possible to improve image quality in the eye by reducing aberrations, but it is impossible to exceed the limits to image quality set by the unavoidable optical imperfections within the eye, such as scattering, dispersion or, most of all, diffraction. Ultimate optical quality is therefore referred to as "diffraction limited", that is, limited by diffraction only. Without aberrations, the perfect eye would convert incoming wavefronts into converging spherical waves. Thus, the effect of diffraction is to cause the image of a point to have a finite size: this point image resulting from diffraction is called the *Airy disk*.

During the past decade, there has been a remarkable expansion of the application of wavefront-related technologies to human eyes. Methods for measuring the optical aberrations of the individual eye have made possible large population ocular wavefront analysis. It is now well known that the form of the ocular WA varies substantially with the individual, presumably depending upon the surface asymmetries and surface tilts between the optical components of the particular eye and their relative locations with respect to the pupil. Various studies [3,7,12] have measured the distribution and contribution of each high-order aberration to the overall wavefront aberration of the eye, showing how there is a central tendency for human eyes to be free of higher-order aberrations, but with the individual aberration equally likely to have positive or negative value because of random biological variability. The one clear exception among the higher-order modes is spherical aberration which is systematically biased towards positive values. Also, there is no clear evidence that aberrations vary systematically with degree of ametropia [13]. The only distinction between eyes is that astigmatic eyes tend to have slightly larger total amount of higher-order aberrations than myopic, hyperopic or emmetropic eyes.

The optical performance of the normal eye is governed by the combination of aberrations in the corneal and intra-ocular optics and it has been shown that there is a significant correlation between these elements [14,15]. Different studies [16,17,18] have measured that the total amount of the WA for the whole eye is always less than values for either the anterior cornea or the internal optics. The results are explained by compensatory processing between the cornea and the lens. However, the compensation observed in young eyes is not present for older subjects and this has been related to a decrease in visual performance with aging [19,20].

Particular attention has also been devoted to the interocular balance of optical aberrations in order to better characterize binocular visual performance. Recent works [21,22,23,24,25,26] have demonstrated a mirror symmetry of the high-order WA maps of the cornea as well as the whole eye optics between eyes, especially for third and fourth order terms over a dilated pupil. It is also well known that the eye's wave aberration is not static but fluctuates over time. The largest source of temporal short-term instability (seconds and minutes) is micro-fluctuations in accommodation. Other possible causes for the fluctuations include local changes in tear film thickness over the cornea [27], perhaps caused by evaporation or blinking. On the other hand, the eye's WA has been demonstrated to be sufficiently stable over long periods of time (over the course of the day, and between successive days), indicating that a personalized aberration correction would be valuable.

Thanks to the increased longevity of people, the effect of aging on HOA of the human eye has also been largely investigated [28,29,30,31,32]. It has been reported that the amount of corneal and ocular HOA increases approximately linearly with age with a corresponding decline in visual performance [33,34]. The spherical aberration has been found on average to be slightly larger in older corneas, as also coma and other corneal HOA that showed to increase with aging. The increase in spherical aberration has been mainly related to a change in the asphericity of the cornea, which occurs from younger to older subjects. The overall shape of the cornea tends to become a sphere from an ellipsoid as age increases. As specified above, the net result of the decoupling of aberrations between the cornea and the internal eye optics is a decrease in visual performance. This is an important issue as it relates all the people that undergo to corneal laser ablation, where the decoupling of aberrations between eye optics is induced by the surgery itself [35].

Nowadays, presbyopia represents a major visual impairment of aging, due to the decline of lens ability to focus on near distance objects after age 45. The mechanism by which the eye can change focus on near and distant objects or *accommodation* has been debated for long centuries. The Helmholtz theory [36] indicates the impossibility of obtaining a variation in curvature of the crystalline lens following atrophy of the ciliary muscle. The Schachar theory [37] states that presbyopia is due to a decrease in the effective working distance of the ciliary muscle as a result of a normal increase in equatorial volume of the crystalline lens with aging.

The acquired knowledge of the aberration architecture of human eyes has generated an intensive effort to revise methods and techniques to correct vision. Novel technologies of measuring and correcting optical aberrations, have offered the promise of a new generation of vision correction methods that can correct HOA beyond defocus and astigmatism, enhancing visual performance beyond that provided by current treatments.

Wavefront Sensing and Correcting Techniques

The evolution of the field of wavefront sensing has proceeded at an extremely rapid pace since initially conceived. Nowadays, various wavefront sensing techniques have been developed for the measurement of the eye's WA. In general, all the apparatus include a source for generating the beam for producing the wavefront exiting the eye, a sensor element and an imaging device for receiving the wavefront to determine aberrations. Wavefront sensors measure the aberrations of the entire eye generated both by the corneal surface and the crystalline lens (*ocular aberrometer*), whereas corneal topographer can measure only the aberrations induced by the first corneal surface (*corneal aberrometer*).

The Shack-Hartmann (S-H) wavefront sensor [38] is the most employed technique for measuring the optical quality of the eye. The device was introduced in clinical use in the 1990s. This technique has been used in several areas of clinical research, e.g., studies of myopia, dry eye, keratoconus, cataract, refractive surgery, contact lenses and intraocular lenses [39,40,41,42], giving initial results on the wave aberration distribution in normal and diseased eye populations. On the other hand, the limited *dynamic range* and *measurement sensitivity* of this technique posed the basis for research efforts to design and develop alternative and innovative wavefront sensing techniques. Between these, curvature sensing [43], pyramidal sensing [44] and interferometry [45] are the most studied techniques to overcome the major disadvantages of the S-H sensor: they can achieve a larger dynamic range providing high accuracy measurements even in highly aberrated eyes. A more reliable estimation of the eye's optical aberrations will be valuable for different applications, such as the personalization of laser refractive surgery or the fabrication of personalized contact lenses and intra-ocular lenses. In addition, such an accurate wavefront sensor may represent a key element to develop a reliable and fast Adaptive Optics system for clinical purpose [46].

Adaptive Optics (AO) is a technique developed in astronomy to remove the effect of atmospheric turbulence from telescope image. The success of AO in astronomy and the declassification of the military's information in 1992, stimulated progress for other applications, including Ophthalmology.

AO can, in principle, correct for the total WA of the eye by altering the local optical path at each point in the pupil by an appropriate amount so that the overall paths for rays entering all points in the pupil are equal. Moreover, AO allows to perform experiments to better understand the impact of ocular optics on vision and in particular to explore the possible role of the neural system in sharpening the retinal images. Some experiments have indicated that not every aberration will have the same impact on vision [14] and how corneal and intraocular optics can interact to modulate visual performance in different light conditions [15,16]. Accordingly, an AO system can be used as a visual simulator to test in advance the effect of aberration correction produced by refractive surgery. Nowadays, deformable mirrors are the most popular devices for AO [46,47]. Former experiments revealed how this technology is effective in achieving a controllable and accurate measurement and correction of ocular aberrations [48,49]. On the other hand, there are many reasons to search for alternative solutions for application of AO in the clinical environment. The relative cost and dimension of this technology represent a major limitation for a wider use other than in laboratory. Therefore, many researchers in the world are studying and applying different AO methodologies to get this technology compact, relatively low-cost and effective for the every day clinical practice. To do this, different issues, as noise, speckle, error propagation and the dynamics of ocular aberrations, have to be studied and understood. The cumulative research work over the last few years is beginning to provide enough data to improve our understanding of most of these issues. Recently, new technologies for wavefront correction have been developed based on microelectromechanical mirrors (MEMM) [50,51,52] and liquid crystal spatial light modulators (LC-SLM) [53,54], which are both successful at reducing the WA of the eye and less expensive than conventional DM devices. The compactness of these new solutions and the continuous improvement in resolution and performance of these correcting elements justify the forecast of prospective clinical applications of AO technology.

The Present of Refractive Correction

Most of refractive surgery procedures involve altering the cornea; between these the excimer laser corneal surgery is the most commonly performed procedure for correcting myopia, hyperopia and astigmatism. Photorefractive keratectomy (PRK) [55] was the first technique performed; subsequently, laser in situ keratomileusis (LASIK) has become largely popular to correct the refractive defects of the eye. Other laser techniques include laser epithelial keratomileusis (LASEK) [56] and Epi-Lasik [57].

There are, however, various keratorefractive procedures to correct for refractive errors, such as the insertion of intrastromal corneal ring segments, the removal of clear crystalline lens, the implantation of phakic intraocular lens and conductive keratoplasty. These techniques are much less performed than excimer laser surgery, due to the less predictability of results; on the other hand, they may be preferred in particular cases. The intracorneal ring segment (ICRS) procedure involves placing plastic arcuate segments into channels created in the stroma of the midperipheral cornea. The central corneal shape is altered by the configuration of the segments and their location in the cornea. The application of this procedure is very limited due to its complications and lack of results. Currently, ICRS has been applied to reduce the irregular astigmatism of keratoconus [58]. Removal of the clear crystalline lens, with or without intra-ocular lens (IOL) implantation, has been performed to correct high hyperopic or myopic refractive errors for many years. Also, specially designed IOLs may be surgically placed in the anterior chamber, attached to the iris [59], or placed in the posterior chamber anterior to the crystalline lens [60] in the phakic eye to correct high myopic or hyperopic refractive errors. Conductive keratoplasty (CK) is performed to correct for hyperopia or presbyopia [61]; it uses a contact probe to deliver radio frequency energy by inserting the thin insulated tip sequentially in multiple locations of the peripheral cornea. The energy produces shrinkage of collagen lamellae that leads to steepening of the central cornea. The amount of change depends on a number of variables including the total amount of energy delivered, number of pulses, pulse energy, spot size, and clear zone, showing a moderate variability of refractive outcomes in the long term postoperative period [62].

Besides CK, the correction of presbyopia include other surgical methods or techniques, such as monovision, multifocal photoablation, anterior ciliary sclerotomy (ACS), scleral expansion bands, multifocal or accommodating IOLs, and intracorneal inlays. At present, the most widely used surgical approach to compensate for presbyopia is excimer laser photoablation to create monovision or inducing a different HOA architecture in the cornea by means of inferior off-center ablation or multifocal ablation [63, 64]. ACS [65] has been largely abandoned due to lack of efficacy and complications such as anterior segment ischemia, regression, and lack of effect. Scleral expansion bands [66] are currently being investigated as a means of increasing the distance between the ciliary muscle and lens.

Early results of accommodating and zonal-progressive multifocal [67,68] IOLs have been shown to reduce presbyopic symptoms. On the other hand, drawbacks included a progressive efficacy reduction in the years following surgery, increased glare and some reduction in low-contrast visual acuity.

The Future of Refractive Correction

During the last decade, photorefractive surgery has dramatically evolved with the simultaneous development of more precise laser platforms and systems for measuring the optical properties of the individual eye. The accurate analysis of new corneal topographer and ocular wavefront sensors has revealed that although standard laser refractive surgery eliminates conventional refractive errors, high-order errors are typically induced [35,40]. The dynamic evaluation of optical quality performed by AO systems has also revealed the effect of aberrations on visual performance [2].

The success of aberration-related techniques encourages the implementation of high-order correction in everyday vision through customized laser refractive surgery or also contact or intraocular lenses. The use of a reliable wavefront sensor capable to measure the whole eye optical aberrations, integrated with the data coming from videokeratoscopes [69], can refine algorithms of current excimer laser systems in order to achieve accurate ablation of the individual cornea. The personalization of the corneal ablation may be achieved transferring data output from the wavefront sensor and corneal topographer/aberrometer to the laser platform; the cornea will be accordingly remodeled for eliminating low-order aberrations and compensating high-order aberrations between the cornea and lens in order to optimize the visual performance for the individual. To reach the scope, future algorithms should take into account the predicted biomechanical response of the cornea based on individual geometrical features of the tissue.

Current excimer laser devices are capable to remove infinitesimally amount of corneal tissue (i.e., 0.25 μm), however, some inaccuracies, like the ablation profile and parameters as well as the biophysical response of the cornea, still limit the potential visual benefit one could achieve from reshaping the cornea [70]. Many authors are analyzing the possible predictors of individual responses [10,71,72] in order to develop accurate models for controlling or compensating for the biophysical responses of the corneal tissue to surgery [73]. The aim of research in this setting is, therefore, strictly linked to advancements in laser platform ablation parameters to improve visual outcomes of laser refractive surgery. Laser manufacturers are currently investigating ways to either minimize or compensate for the corneal biomechanical response as suggested by clinical researchers. The fundamental Munnerlyn theory [55] stating that the cornea is an homogeneous inert structure has been extensively demonstrated not to be adequate for modeling the behaviour of the corneal tissue. Since 1995, when a biomechanical response of the cornea after laser ablation has been first hypothesized [74], several models based on empirical analyses of postoperative data and on more complex assumptions on the corneal behaviour have been developed [75,76,77,78, 79]. The scope of these researches was to improve the predictability of results, further optimizing the postoperative optical quality of the cornea. The new question raising from recent studies is whether the biomechanical response can be manipulated to improve outcomes. For instance, clinical studies have demonstrated a mirror symmetric response of the anterior cornea to laser ablation, with the nasal peripheral region straining more than the temporal, and also a different response of the corneal periphery in relation to the amount of refractive correction [72,80]. The target of these studies was to drive the design of ablation profiles, by modifying the transition zone, in order to compensate for the invariable part of the corneal response. Further refinements in the ablation design should be then performed to optimize the procedure, depending on the geometrical and optical parameters of the individual cornea. These personalized improved algorithms can be, for instance, developed by analysing topographic and aberrometric data in a large population of eyes prior and after laser reshaping.

Moreover, wavefront sensing and correcting technologies can be further exploited to drive the fabrication of personalized contact lenses (CLs) or intraocular lenses (IOLs) by transferring the data output of the eye's WA to the manufacturing instruments. Recent advances in intraocular lens materials and manufacturing methods [81] make the customized correction of higher-order aberrations with CLs or IOLs to become standard practice in the next years [82].

In the context of customized refractive correction, new ideas for near-vision correction are expected. Considering that the replacement of cataractous crystalline lens with accommodating or pseudo-accommodating IOLs and other surgical solutions for the correction of presbyopia appear not to be effective in restoring adequate near vision performance, the research in this setting has not still shown significant advancements. Restoring accommodation represents the golden target of future refractive correction methods if considering that an incredible number of people worldwide need to wear spectacles for near vision.

The application of innovative technologies in Ophthalmology, such as liquid crystals, to replace common lenses to deviate light rays aims to solve and overcome limits of current methodologies for improving near vision in elderly population. During the last years, innovative researches are going to demonstrate the way to replace common lenses for vision correction with *variable lenses* exploiting the liquid crystal (LC) technology [83,84]. A research area is directed to develop a switchable, flat, liquid-crystal diffractive lens that can adaptively change its focusing power to correct for distance and near vision. A different area involves the development of an adaptive intraocular lens based on a modal liquid-crystal spatial phase modulator with wireless control. A prototype has been developed and experimentally evaluated [85]. The goal of these studies is to provide a controllable IOL with variable focusing power. Even if a not pure LC lens may be achieved but rather a sort of hybrid lens in which ordinary glass is used to correct the sphero-cylindrical refractive error and the liquid crystal display is used to correct the residual, higher order aberrations, we believe that both solutions have the potential of revolutionizing the field of presbyopia correction in the near future. Therefore, the LC technology appears to have the potential for providing an entirely new kind of electro-optical elements for 21st century spectacles or intra-ocular lenses.

Conclusion

In summary, we forecast major advances in vision correction treatments in the near future which will combine the power of wavefront-related technologies with the flexibility of electronics. The result will be a new generation of personalized laser treatment and variable spectacles or intra-ocular lenses capable of adapting to the specific requirements of individual eyes to produce customized optical correction of unprecedented quality. However, to make this prediction come true will require joint research efforts between the ophthalmic and engineering communities to apply these innovative technologies in the every day clinical practice.

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