EDITORIAL

Wavefront Guided Ablation

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ADAPTIVE OPTICS WAS FIRST SUGGESTED IN 1953 BY astronomer Horace Babcock to remove the blurring effects of turbulence in the atmosphere on telescopic images of stars.[1] The U.S. Defense Department later invested heavily in the development of adaptive optics technology to improve the effectiveness of laser weapons as part of its Star Wars Program. This information would eventually allow vision scientists to apply this technology to better understand the eye's optic and retinal image quality. In 1994, Liang and associates used a Shack–Hartmann wavefront sensor to describe higher order aberrations in the human eye.[2] In 1997, Liang, Williams, and Miller used the Shack–Hartmann wavefront sensor to detect the eye's aberrations and then applied an adaptive optics deformable mirror to correct the eye's lower and higher order aberrations.[3] With this system, they noted that adaptive optics provided a sixfold increase in contrast sensitivity to high spatial frequencies when the pupil was large. This study was the first to demonstrate that the correction of higher-order aberrations can lead to supernormal visual performance in normal eyes. The Liang, Williams, and Miller study used monochromatic light.[4] Normal viewing conditions usually involve broadband light, and retinal images formed in broadband (white) light are blurred by chromatic aberration, as well as the monochromatic aberrations that adaptive optics can correct. Yoon and Williams showed that, in broadband light which characterizes normal viewing conditions, adaptive optics still provides a twofold increase in contrast sensitivity at high spatial frequencies in typical eyes, even when chromatic aberration is present.[5]

These findings spurred a ground swell of interest in wavefront sensing and the possibility of coupling it with wavefront correction in the form of customized corneal ablation. In this editorial, we will look at the visual benefit of correcting higher-order aberrations, the limits of the human visual system, and some of the future challenges of the ambitious and sometimes misunderstood world of customized corneal ablation.

The wavefront sensor allows the clinician not only to measure the defocus and astigmatism that are the most important determinants of refractive error, but also "higher-order aberrations" as well. Defocus and astigmatism are referred to as second-order aberrations. Higher-order aberrations, such as coma and spherical aberration, refer to aberrations other than defocus and astigmatism. The wavefront sensor, such as that constructed by Liang and Williams,[3] can reliably detect as many as 64 higher-order aberrations. Some of these higher-order aberrations had not been previously measured in human eyes and all were usually lumped by clinicians into a single category misleadingly called "irregular astigmatism." They are better referred to as higher-order aberrations since most have nothing to do with astigmatism.

The spectacle correction that provides the best subjective refraction depends not only on defocus and astigmatism but also, to a lesser extent, on higher-order aberrations.[6] For this reason, the description of the eye's wave aberration provided by a wave-front sensor, when properly processed, can provide an especially accurate objective estimate of subjective refraction.

The Limitations of Higher-Order Aberration Correction

IN THE AVERAGE, NONSURGICAL EYE, THE BLURRING caused by higher-order aberrations is not particularly large. It is equivalent to only about 0.3 diopter of defocus.[6] Moreover, as recent articles have pointed out,[7,8] there are a number of factors that limit how much we can optimize human vision. These include:

1. Pupil diameter;
2. Chromatic aberrations;
3. Dependence of higher-order aberrations on accommodative state;
4. Accommodative lag;
5. Rapid changes in wave aberration over time;
6. Changes in wave aberrations with aging;
7. Depth of field;

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8. Photoreceptor sampling and neural factors;
9. Biomechanical effects in the cornea;
10. Accuracy of centration of correction.

• **1. PUPIL DIAMETER:** The benefit of correcting higher-order aberrations is limited to viewing conditions when the pupil is large.[9–12] When the pupil diameter is about 3 mm or smaller, as it is in bright light conditions, higher-order aberrations are greatly reduced and the optical quality of the eye is determined mainly by blurring due to the diffraction of light at the pupil. Clearly, customized correction cannot undo the blur caused by diffraction. However, in young eyes, which tend to have large pupils, dim conditions such as night driving, and eyes with especially large amounts of higher-order aberrations, customized correction of these aberrations may be valuable.

• **2. CHROMATIC ABERRATIONS:** There is no particularly effective method to correct axial and transverse chromatic aberrations in everyday vision. These aberrations will blur the retinal image even if the monochromatic aberrations are corrected perfectly with a customized procedure.

• **3. DEPENDENCE OF HIGHER-ORDER ABERRATIONS ON ACCOMMODATIVE STATE:** Hofer and associates have demonstrated that the pattern of higher-order aberrations in an individual depends on accommodation.[8] This means that the ideal correction for distance vision may be ineffective or even make vision worse when viewing near objects. For most individuals, we believe that higher-order aberration correction for distance vision would be optimal, since most people when viewing near targets can control distance, as when reading a book. Also, the pupil constricts with accommodation, which lessens the effects of higher order aberrations. More research needs to be done to understand how this factor can be taken into account to optimize vision based on the needs of specific patients.

• **4. ACCOMMODATIVE LAG:** The failure to focus correctly on the target, or accommodative lag, will also diminish the visual benefit of higher-order aberration correction.

• **5. RAPID CHANGES IN THE WAVE ABERRATION OVER TIME:** There are relatively rapid temporal fluctuations in the wave aberrations, such as microfluctuations of accommodation, which reduce the value or visual benefit of a static correcting procedure such as customized corneal ablation.

• **6. CHANGES WAVE ABERRATIONS WITH AGE:** Another important consideration is how stable wave aberrations are in adults as they age. Although we believe the wave aberration to be fairly stable over periods of months to perhaps even a few years, there is a significant steady increase in ocular aberrations with age.[13,14] Both changes in the crystalline lens and changes in the cornea are responsible. Investigators noted that in younger individuals, the cornea and lens higher-order aberrations tend to compensate for each other, but this compensation diminishes with aging, which may partially account for vision reduction with aging.[13] These factors ultimately limit the longevity of an effective customized ablation and argue for the need of a procedure that allows retreatments with time.

• **7. DEPTH OF FIELD:** Removing the eye's higher-order aberrations increases optical quality for objects that lie at the best focus. However, it reduces optical quality for objects that are far out of best focus. Exactly how this benefit and cost tradeoff functions in everyday vision has not yet been carefully studied.

• **8. PHOTORECEPTOR SAMPLING AND NEURAL FACTORS:** The cone mosaic spacing limits human vision much as the pixel frequency limits the fidelity of a TV image. This limit is often quantified by the Nyquist limit, which is a spatial frequency equal to the reciprocal of the retinal cone spacing divided by two. In the human fovea, the Nyquist limit is about 60 cycles/degree. There is no simple transformation from grating acuity (expressed in cycles/degree) to the Snellen acuity more familiar to clinicians. However, the three horizontal line strokes in a 20/10 Snellen "E" have a periodicity corresponding to 60 cycles/degree. The Nyquist limit indicates roughly the finest grating patterns that human foveal vision can reasonably expect to resolve, in the sense of being able to see the regular stripes of a contrast sensitivity grating imaged on the retina. At spatial frequencies above the Nyquist limit, gratings appear more like wavy zebra stripes and appear coarser than the actual gratings on the retina, a phenomenon called "aliasing".[15] For aliasing to disrupt vision in ordinary scenes, the optical quality of the eye would need to be considerably better than it is. Neural factors beyond the cone mosaic also play a role here, and no amount of customized correction of the optics can overcome the limits set by the retina and brain.

• **9. BIOMECHANICAL EFFECTS IN THE CORNEA:** Also, as Roberts has persuasively argued, the cornea changes its shape in response to ablation and this change, along with wound healing effects, must be taken into account before customized correction can null higher-order aberrations.[16] Spherical aberration is increased after LASIK.[16–19] This higher-order aberration creates a large halo when viewing small, bright objects such as car headlights when driving at night, and is probably the source of many of the night vision complaints reported from LASIK patients.[19] Studies by Roberts and coworkers suggest that the increase in spherical aberration following LASIK may be caused by a biomechanically induced steepening and thickening that may occur in the midperiphery of the cornea.[16] Such a response may not be easily resolved by removing more tissue in the midperiphery to simply flatten the midperipheral cornea more. This biomechanical response may limit the amount of myopia surgeons can correct without inducing unwanted spherical aberration.

• **10. ACCURACY OF CENTRATION OF CORRECTION**: In practice, the effectiveness of customized correction cannot be any better than the care with which the cornea is sculpted. Decentration of the customized correction will degrade its effectiveness.[20] Studies done by Guirao and associates indicate that a decentration of 0.25 mm (250/ μm) reduces the benefit of correcting higher-order aberrations by 50%.[21]

The Benefits of Correcting Higher-Order Aberrations

DOES THIS MEAN THE QUEST TO TREAT HIGHER-order aberrations is misguided? We believe it is not. The visual benefit in some eyes in the normal population is considerable. These eyes have large amounts of higher-order aberrations just as some normal eyes have a large amount of astigmatism.[22] In these patients we have found wavefront sensing to be a powerful tool in characterizing their specific optical abnormality, which was previously difficult to describe.

One way that we can define the visual benefit of correcting higher-order aberration is by comparing the modulation transfer function with correction of higher-order aberrations to the modulation transfer function without correction of higher-order aberration. (The modulation transfer function is a way to describe the fidelity of an optical system, whether it is a camera or the human eye.) Researchers noted, in a population study, that a small visual benefit of 1.3× may be obtained for a 3 mm pupil under normal light conditions, but the benefit increases substantially to 2.5×'s when the pupil dilates to 5.7 mm.[23]

It is noteworthy that visual acuity is a far less sensitive measure of the benefits of correcting higher-order aberrations than contrast sensitivity. This is because the contrast sensitivity function decreases quickly at the acuity limit and a large increase in contrast sensitivity increases visual acuity only minimally. Thus the greatest gains in correcting higher-order aberration are noted in improved contrast particularly under low light conditions.[8]

Clinicians may also benefit by using wavefront sensors to diagnose and possibly treat a variety of conditions including corneas with "irregular astigmatism" from corneal transplantation and radial keratotomy, decentered or irregular ablations, and central islands.

In the past, corneal transplant surgeons occasionally have seen postoperative corneal transplant corneal topographies with three-steep lobes instead of two (as seen in "regular" astigmatism), which may perplex them, since it had never been commonly described nor was there a term to describe it. With wavefront sensing, surgeons can now not only describe this as being excessive trefoil but could also quantify it in exact mathematical terms to determine whether it is visually disabling. Likewise, patients complaining of double- or one-sided blurred vision may have coma, which creates a cometlike image when looking at a point light source such as a star. Clinicians can now explain why their patients are seeing the flares and halos they sometimes report, and we may soon be capable of eliminating them.[19]

• **THE WEAKNESSES OF WAVEFRONT SENSING**: Wavefront sensors also have their weaknesses. Many Shack–Hartmann wavefront sensors have a limited dynamic range, making them less useful in eyes with severe amounts of higher-order aberrations such as those with advanced keratoconus. This will no doubt be improved with the next generation of systems. The wavefront sensors also only give us information about the optics of the eye over the pupil diameter. However, in laser refractive surgery, we are not only interested in the optical changes over the pupil but also the curvature changes that occur outside the pupil diameter. Experience has taught us that transition zones outside the pupil diameter may profoundly influence the quality of the optics inside the pupil diameter.[16,24] In response to this, several companies are attempting to couple their wavefront sensors with corneal topographers, which can provide information on corneal curvature and shape changes beyond the pupil.

Another disadvantage of wavefront sensing is that it does not inform us about the optical blur caused by light scatter within the eye. While it is exquisitively sensitive to gradual changes in the wavefront across the pupil, it does not measure variations at a scale smaller than a few hundred microns typically. Therefore, scattering effects that might be caused by corneal edema or a cataract go undetected. It is possible to extract information about scattered light from the wavefront sensor image, and work is under way to incorporate this feature.

• **WAVEFRONT CORRECTION VIA LASER REFRACTIVE SURGERY**: Virtually all of the excimer laser companies are developing wavefront sensing driven customized ablation in an attempt to try to minimize or reduce higher-order aberrations. The first groups of wavefront guided customized ablation clinical trials are now starting to report preliminary data that are encouraging but still tentative.[25–27] Investigators are first trying to minimize the increase in higher-order aberrations induced by conventional LASIK and then reduce higher order aberrations below preoperative levels especially in highly aberrated eyes. Several of the excimer laser manufacturers are already planning to change their ablation profiles from spherical to aspheric profiles to correct for spherical aberrations. The eyes that potentially could gain the most are those with large amounts of higher-order aberration such as postoperative corneal transplant eyes or postoperative LASIK eyes with decentrations, central islands, or asymmetric ablations. If this latter group of difficult cases can be successfully treated with wavefront driven ablation, we will have taken a vital step in improving the safety and efficacy of excimer laser visual correction.

A small number of early studies doing customized ablation using PRK suggest greater improvements in the prevention and treatment of higher-order aberrations when compared to LASIK.[28,29] This observation raises the question of whether higher-order aberrations can be predictably corrected under a microkeratome flap that may act as a low-pass filter (in LASIK), which blurs the higher-order aberration correction. Another possibility is that the flap actually increases the higher-order aberrations in an unpredictable fashion, which would make the treatment of higher-order aberrations difficult at best. We have recently noted that simply creating a LASIK flap (without laser treatment) increases higher-order aberration in an unpredictable fashion.[18] This finding supports the concept that customized ablation may be best performed using a surface ablation such as PRK or LASEK, or by doing a two-stage LASIK, with the second stage adjusting for increased higher-order aberration created by the flap and the initial ablation (stage one).

Where Do We Go From Here?

THERE ARE MANY CHALLENGES AND UNANSWERED questions in the burgeoning field of higher-order aberration correction. This area may give us an opportunity to assist patients who suffer from abnormal amounts of higher-order aberrations that we can now characterize, quantify, and hopefully diminish. It has been 150 years since clinicians began treating astigmatism at the time of Helmholtz.[30] We are on the verge of correcting more complex higher-order aberrations with strategies that are now being implemented. No doubt there are even better strategies that have not yet been thought of. Our optimism about correcting higher-order aberrations is tempered by our understanding of the fundamental limits of the human vision and the accuracy with which we can expect to sculpt biological structures like the cornea. Nonetheless, there is no doubt that the recent improvements in wavefront sensing that now make it accessible in the clinic will lead to improvements in the outcome of laser refractive surgery. In revealing the iatragenic aberrations produced by the procedure itself, wavefront sensing also creates a path toward reducing, if not eliminating, these aberrations. Moreover, eyes that naturally have large amounts of higher-order aberrations as well as a conventional refractive error will no doubt benefit from correction with customized procedures. The focus should be on attacking these problems and not on providing people who already have excellent vision with "super vision."

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