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Clinical Applications of Wavefront Refraction

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ABSTRACT

Purpose. To determine normative reference ranges for higher-order wavefront error (HO-WFE), compare these values with those in common ocular pathologies, and evaluate treatments.

Methods. A review of 17 major studies on HO-WFE was made, involving data for a total of 31,605 subjects. The upper limit of the 95% confidence interval (CI) for HO-WFE was calculated from the most comprehensive of these studies using normal healthy patients aged 20 to 80 years. There were no studies identified using the natural pupil size for subjects, and for this reason, the HO-WFE was tabulated for pupil diameters of 3 to 7 mm. Effects of keratoconus, pterygium, cataract, and dry eye on HO-WFE were reviewed and treatment efficacy was considered.

Results. The calculated upper limit of the 95% CI for HO-WFE in a healthy normal 35-year-old patient with a mesopic pupil diameter of 6 mm would be 0.471 μm (471 nm) root-mean-square or less. Although the normal HO-WFE increases with age for a given pupil size, it is not yet completely clear how the concurrent influence of age-related pupillary miosis affects these findings. Abnormal ocular conditions such as keratoconus can induce a large HO-WFE, often in excess of 3.0 μm, particularly attributed to coma. For pterygium or cortical cataract, a combination of coma and trefoil was more commonly induced. Nuclear cataract can induce a negative spherical HO-WFE, usually in excess of 1.0 μm.

Conclusions. The upper limit of the 95% CI for HO-WFE root-mean-square is about 0.5 μm with normal physiological pupil sizes. With ocular pathologies, HO-WFE can be in excess of 1.0 μm, although many devices and therapeutic and surgical treatments are reported to be highly effective at minimizing HO-WFE. More accurate normative reference ranges for HO-WFE will require future studies using the subjects' natural pupil size.

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Key Words: wavefront refraction, cataract, keratoconus, higher-order aberrations of the eye, normal populations

Dr. Irvin Borish and his classic textbook *Clinical Refraction* helped teach many of us the art of refraction. He also taught us in his later years the use of new and evolving science and technologies to make clinical refraction more accurate and more efficient.[1] The first significant implementation of wavefront science in vision care emerged in wavefront-guided corneal refractive laser surgery in the late 1990s.[2] In the past 10 years, the increasing use of wavefront refraction has guided us toward a more accurate and efficient clinical refraction that Dr. Borish envisioned.

Wavefront refraction has been recognized as an optical science by Scheiner's and Newton's observations of aberrated light in the 17th and 18th centuries.[3] The modern wavefront aberrometer applies a form of high-resolution autorefraction across the entire area of the patient's pupil, giving the wavefront error (WFE) in terms of micrometers of deviation (root-mean-square [RMS]) from the ideal wavefront plane.[4] The irregular portion of the WFE is termed *higher-order wavefront error* (HO-WFE), that is, not correctable with traditional sphero-cylindrical spectacles.

Visual acuity remains the most common method by which eye care professionals assess patients' optical image quality. However, this technique does little to assess retinal image quality (blur, halos, poor edge discrimination, glare, and reduced contrast sensitivity) related to HO-WFE.[5] Eye care professionals and researchers have described quality of vision issues in refraction for many years.[6,7]

In both the refraction and correction of lower-order WFE and HO-WFE, the pupil size is one of the most critical considerations.[8,9] In wavefront refraction, the pupil size is an integral part of the specification of the WFE.[10] Changes in the pupil size may cause subjective differences in the clinical refraction, that is, "day versus night" considerations. Mild pharmacological miosis may assist with subjective night vision symptoms like halos, glare, and reduced contrast sensitivity from aggregate spherical aberrations (SAs).[10]

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New optical wavefront technologies have also been applied into visual correction. Such applications include, but are not limited to, optical devices such as "HO-WFE correcting" spectacles, contact lenses, intraocular lenses (IOLs), and diagnostic instruments and are applied in custom wavefront corneal laser surgery. These corrective applications have experienced mixed success owing to an array of dynamic pupillary, optical, physiological, immunological, and environmental variables and challenges, which are all difficult to control.[11]

This article reviews the major studies of HO-WFE in normal healthy patients and compiles normative data for a wide range of ages and pupil diameters. Also considered are possible future advances in the normal reference ranges for HO-WFE. The effects of common ocular pathologies on the HO-WFE are reviewed, and corrective procedures and devices are considered.

NORMAL HO-WFE

Many studies have been conducted to measure HO-WFE in normal healthy eyes; however, even in 2014, new studies continue to be published, in part because of the perception that there is a "paucity of data on the normal reference ranges."[12] Studies with different populations and methodologies are summarized in Table 1.[4,13–28] The studies are tabulated by age group and ordered by pupil diameter, because these two factors account for most of the variance in HO-WFE in normal healthy eyes.[14]

Studies with a 4- or 5-mm optical zone found the average HO-WFE to be less than 0.30 μm, often lower in the younger age groups (Table 1). There was more variability in the average HO-WFE for studies using a 6-mm optical zone, with the average HO-WFE being up to 0.518 μm. There were no studies that used the natural pupil size for subjects, not even the studies that concern age, where pupil size is known to be a variable.

It is difficult to define the normal HO-WFE in a population without studies that use the subjects' natural pupil size. However, the normal HO-WFE can be estimated by using separate studies of the natural pupil size with age. Winn et al.[29] reported that average pupil size decreases linearly as a function of age, for all luminance levels. On this basis, Applegate et al.[14] estimated that the average HO-WFE at low-luminance levels would slightly reduce with age, whereas at high luminance levels, it may slightly increase with age.

The study by Applegate et al.[14] gives the most comprehensive HO-WFE data set for subjects aged 20 to 80 years. Data sets such as this enable the upper limit of the 95% confidence interval (CI) for a normal population to be calculated.[30–32] Table 2 shows the upper limit of the 95% CI for HO-WFE, as a function of age and pupil size, calculated from the study by Applegate et al.[14] For example, an average 35-year-old patient would be expected to have a mesopic pupil size of about 6 mm[33]; the expected HO-WFE for such a patient would be 0.471 μm (471 nm) or less (Table 2). A measurement greater than this level (for this age and pupil diameter) would be suspicious for abnormality, at the 95% level.

Table 2 also presents the upper limit of the 95% CI of the Applegate et al.[14] data, for several other HO-WFE individual terms—coma, spherical, and trefoil. These terms describe distinctive wavefront shapes. Although the terms are less widely used than, for example, astigmatism, the effect on vision for each may be no less profound.

Refracting clinicians are familiar with the clinical experience that some patients can detect blur before acuity is lost,[34] for example, where the patient may say: "I can read it, but it's not clear." Patients will be able to identify their HO-WFE at an RMS level of 0.43 μm or greater,[35] and experienced observers under laboratory conditions may detect HO-WFE blur at even lower levels.[34] The linear equation, M_e (defocus) = $4\pi\sqrt{3}$ RMS error/area of pupil, may be used to convert RMS values to dioptric power.[9] Therefore, an RMS value of greater than or equal to 0.43 μm is equivalent, for a 5-mm pupil aperture, to about greater than or equal to 0.50 diopters. A qualitative illustration of what the patient sees is the point spread function, which can reveal unique refractive information.[9,36]

The cortical interpretation of human vision means that WFE measurements require confirmation through the "gold standard" of subjective refraction.[36,37] However, the RMS data provide insight into the classic refractive question: "Which is better, one or two, or no difference?," or simply "Which is better?"[3] The "just noticeable difference" (*jnd*) for experienced subjects may be as small as 0.04 μm of RMS aberration.[38] In terms of visual acuity, 0.25 μm of RMS defocus error over a 6-mm pupil results in a loss of an average of eight letters (1.6 lines).[39]

In summary, normative data such as those presented in Table 2 may be applied to help in the diagnosis of abnormal conditions. The next advance in normal reference ranges for HO-WFE may use the subjects' natural physiological pupil diameter, because the pupil diameter is an integral part of the WFE.

WAVEFRONT REFRACTION IN COMMON CLINICAL CONDITIONS

In clinical vision care, refraction is directly affected by numerous conditions of the eyelids, ocular surface, tear film, cornea, crystalline lens, and beyond. These effects on vision produce varying degrees of lower-order WFE and HO-WFE. Irrespective of their etiology, the wavefront refraction can provide an accurate means of measuring the effects of such conditions. Some of the more common diseases and their effects include, but are not limited to, the following examples.

Keratoconus

Keratoconus can have a devastating effect on vision. The impact is so large because keratoconus has a central effect on the corneal front surface, the most important refractive element of the eye. No condition probably has the potential to cause greater HO-WFE, that is, irregular astigmatism not correctable with spectacles. Indeed, severe keratoconus can cause extreme WFEs, beyond the range of measurement for standard instruments.[40,41]

Characteristically, keratoconus causes a significant coma WFE, owing to the cone being displaced from the center of the cornea (Fig. 1). Jafri et al.[42] found for early keratoconus that the mean coma was 2.034 μm RMS (±1.532 SD), with a 6.5-mm pupil. Gobbe and Guillon[43] assessed 45 patients with keratoconus, ranging from early keratoconus to very advanced cases, and measured total HO-WFE for a 6-mm pupil to be 3.744 μm (±3.086). Pantanelli et al.[41] concluded that coma accounted for 62 ± 30% of the higher-order variance in their sample of 19 patients with keratoconus. A high correlation has been found between the abnormal corneal

TABLE 1.

Wavefront refraction: Larger population studies, ordered by pupil size

Study	Study design	Instrument	Sample (N)	Age range (mean ± SD), y	Mydriatic	Pupil, mm	Total HO WFE (mean ± SD), μm
Hartwig and Atchison 2012[13]	Multisite study of refractive error and right vs. left eyes	i.Profiler (Carl Zeiss Vision)	24,604	Not available	No	4.5	0.18 ± 0.08 myopia group
Applegate et al. 2007[14]	Quantified the influence of age and pupil diameter	Custom Shack-Hartmann sensor	146	20–80	Yes	5.0	0.174 ± 0.062 age group, 30–39 y
Atchison and Markwell 2008[15]	Assessed emmetropic subjects for age and peripheral refraction	COAS (Wavefront Sciences)	106	19–70	Yes	5.0	(0.20 ± 0.09 estimated from figure)
Brunette et al. 2003[16]	Compared age groups: 0–20, 21–40, 41–60, and 61–82 y	Custom Shack-Hartmann sensor	114	6–82 (43.2 ± 24.5)	Yes	5.0	0.27 ± 0.30 age group, 21–40 y
Salmon and van de Pol 2006[17]	Meta-analysis of data collected from 10 laboratories	Wavescan, COAS, Topcon, Zywave	1433	18–71 (35 ± 10)	Yes	5.0	0.186 ± 0.078 whole group
Wan et al. 2014[18]	Assess a rural Chinese population	i-Trace aberrometer (Tracey Technologies)	404	31–86 (49.9 ± 10.5)	No	5.0	0.296 ± 0.147 whole group
Porter et al. 2001[19]	Normative study in healthy subjects and right vs. left eyes	Custom Hartmann-Shack sensor	109	21–65 mean, 41	No	5.7	(0.138 ± 0.103 spherical aberration)
Lyall et al. 2013[20]	Prospective case series to compare age groups 40–89 y	i-Trace aberrometer (Tracey Technologies)	167	19–91 mean, 64	Yes	6.0	0.518 ± 0.164 age group, 40–49 y
Athaide et al. 2009[21]	Evaluate contribution of cornea and lens to the effect of age	LadarWave (Alcon Laboratories)	315	5–64 (31 ± 16)	Yes	6.5	0.32 ± 0.48 whole group
Wavefront refraction: Larger refractive surgery and younger age group studies, ordered by pupil size							
Yamane et al. 2004[22]	Study of refractive surgery candidates	KR-9000PW (Topcon)	110	33 ± 8	No	4.0	0.118 ± 0.044 preoperative
Thibos et al. 2002[4]	Population study using university staff and students	Custom Shack-Hartmann sensor	100	18–50 most 22–35	Yes	5.0	0.163 ± 0.067 from Salmon 2006
Philip et al. 2012[23]	Study of refractive error in adolescents	COAS (Wavefront Sciences)	675	16–19 (16.9 ± 0.7)	Yes	5.0	0.171 ± 0.05 emmetropia sample
Hashemian et al. 2012[24]	Study of refractive surgery candidates	Zywave (Bausch + Lomb)	1350	18–56 (28.3 ± 7.32)	Yes	6.0	0.369 ± 0.233 myopia group
Kingston and Cox 2013[25]	Study of spherical aberration in refractive surgery candidates	Zywave II (Bausch + Lomb)	1124	19–45 mean, 32	Yes	6.0	(0.25 ± 0.12 spherical aberration)
Nakano et al. 2006[26]	Assessed Asian and non-Asian refractive surgery patients	OPD-Scan (NIDEK Co Ltd)	324	32 ± 8	Yes	6.0	0.514 ± 0.711 Asian subjects N = 192
Plainis and Pallikaris 2008[27]	Normative study of a group of near-emmetropic subjects	Allegreto (Wavelight Laser Technologies)	218	21–43 (33 ± 5)	No	6.0	0.26 ± 0.10 emmetropia sample
Wang and Koch 2003[28]	Study of refractive surgery candidates	Wavescan (Visx, Inc)	306	20–71 (41 ± 10)	Yes	6.0	0.305 ± 0.095 whole group

curvature and the total WFE and hence the HO-WFE can be useful in diagnosis.[40,42]

Wavefront Correction

Higher-order wavefront error in keratoconus is correctable, giving the patient good vision, as has been demonstrated using adaptive optics.[44] Gas permeable corneal lenses and scleral contact lenses typically correct visual acuity in keratoconus more effectively than soft lenses or spectacles.[31] However, even with gas permeable lenses, there may be a residual uncorrected HO-WFE, in part owing to irregularity in the posterior corneal surface.[31,45]

Wavefront-corrected contact lenses for keratoconus have been described, in custom hydrogel or rigid scleral lens designs. The visual acuity is typically improved by 1 to 2 lines of acuity over the standard contact lenses, reaching 20/20 to 20/30.[30,46] Because static rotation or lateral displacements represent a significant

TABLE 2.

What is normal? The upper limit of the 95% CI for WFE as a function of age and pupil size

Pupil size	20–29 y	30–39 y	40–49 y	50–59 y	60–69 y	70–79 y
Higher-order WFE, μm						
3 mm	0.095	0.096	0.112	0.144	0.127	0.162
4 mm	0.177	0.184	0.209	0.266	0.245	0.319
5 mm	0.298	0.298	0.351	0.429	0.438	0.570
6 mm	0.484	0.471	0.594	0.691	0.737	1.054
7 mm	0.697	0.789	0.994	0.960	1.110	1.566
Coma WFE, μm						
3 mm	0.066	0.075	0.076	0.104	0.099	0.107
4 mm	0.117	0.141	0.139	0.189	0.183	0.195
5 mm	0.185	0.214	0.222	0.309	0.315	0.343
6 mm	0.289	0.310	0.347	0.488	0.506	0.679
7 mm	0.451	0.483	0.527	0.517	0.724	0.931
Spherical WFE, μm						
3 mm	0.039	0.034	0.038	0.036	0.053	0.074
4 mm	0.088	0.068	0.095	0.093	0.128	0.167
5 mm	0.179	0.146	0.211	0.207	0.269	0.317
6 mm	0.348	0.310	0.413	0.427	0.517	0.617
7 mm	0.529	0.621	0.783	0.755	0.880	1.065
Trefoil WFE, μm						
3 mm	0.065	0.061	0.084	0.097	0.083	0.121
4 mm	0.122	0.119	0.157	0.171	0.172	0.225
5 mm	0.209	0.201	0.238	0.255	0.283	0.382
6 mm	0.319	0.317	0.353	0.383	0.426	0.642
7 mm	0.425	0.509	0.528	0.614	0.595	1.006

Wavefront error is specified as RMS (in micrometers). Data are mean + 2 × SD, from Applegate et al. 2007.[14]

limitation to the efficacy of a wavefront contact lens correction,[47] it seems likely that further advances in contact lens correction for keratoconus will be made with the most stable fitting lenses in modern lens materials, which are scleral designs in either a rigid or a silicone-hydrogel material.

Corneal surgery for keratoconus, such as penetrating keratoplasty or intracorneal ring segments, usually improves the unaided visual acuity and reduces the regular refractive error (sphere and astigmatism), but the procedures often still result in a significant HO-WFE.[41,48] Deep anterior lamellar keratoplasty is also

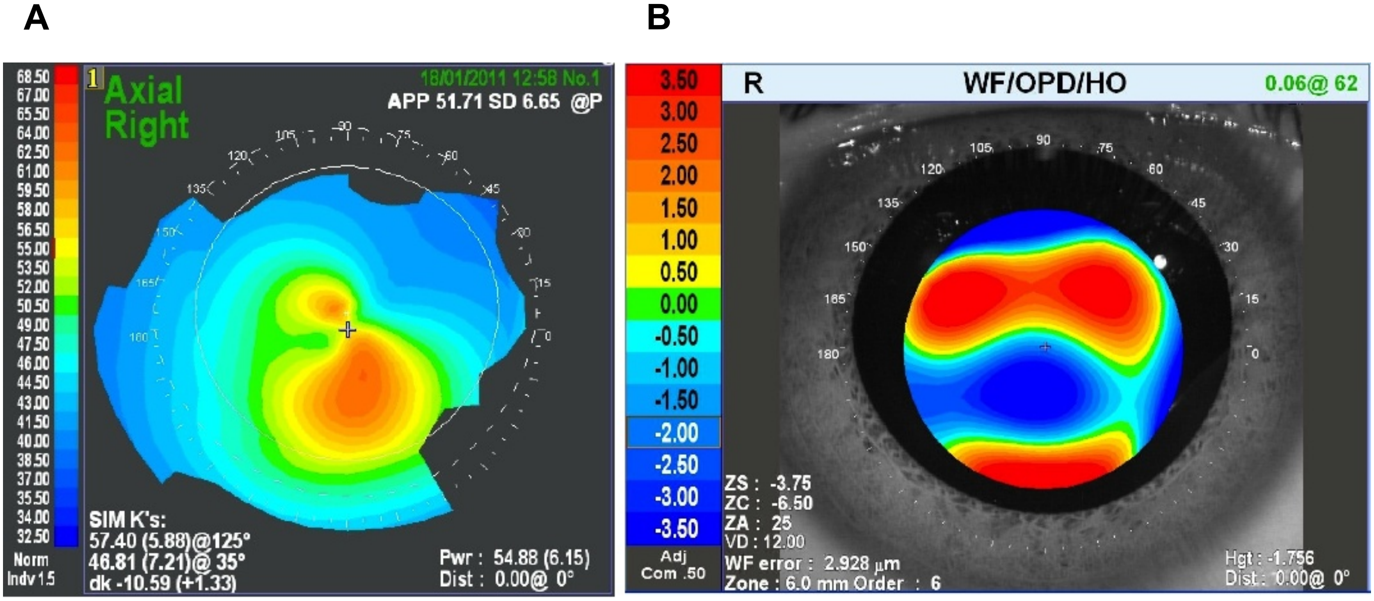

FIGURE 1.

Keratoconus in the right eye of a 20-year-old man. (A) Corneal topography map showing an apical power of 65 diopters. (B) HO-WFE map for a 6-mm pupil, with total higher order, 2.928 μm; total coma, 2.087 μm; total spherical, 0.870 μm; and total trefoil, 1.744 μm. The HO-WFE is significantly abnormal in relation to the keratoconus.

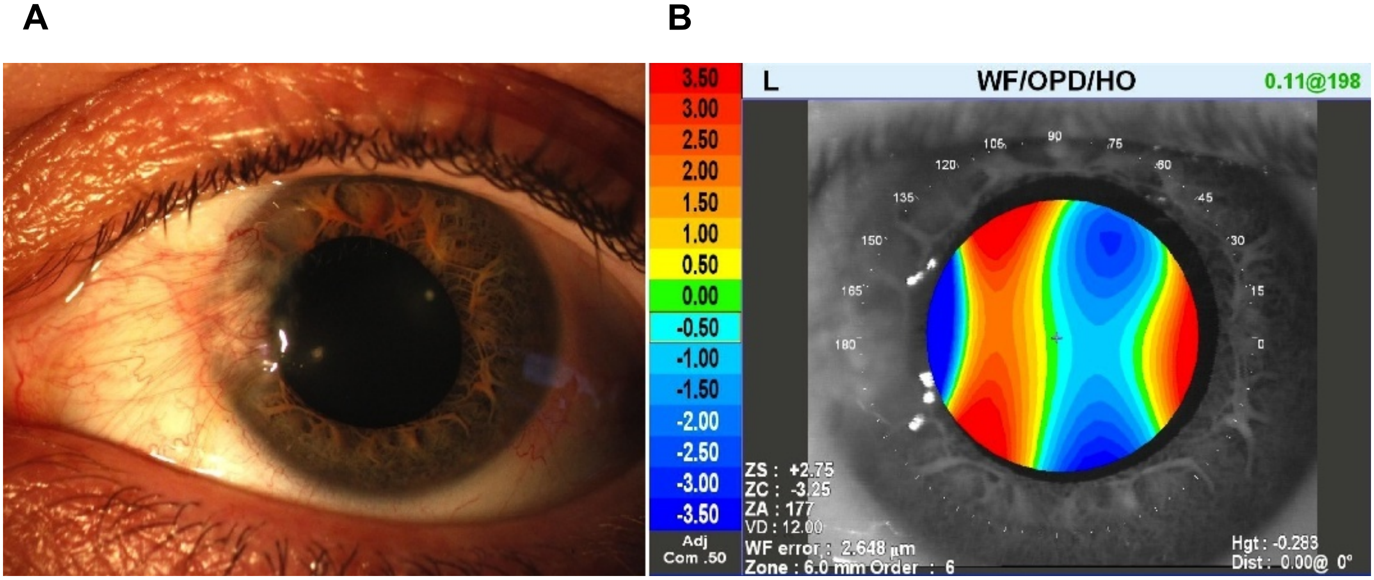

FIGURE 2.

Pterygium in the left eye of a 42-year-old woman. (A) Anterior eye image. (B) HO-WFE map for a 6-mm pupil, with total higher order, 2.648 µm; total coma, 1.202 µm; total spherical, 0.223 µm; and total trefoil, 2.149 µm. The HO-WFE is significantly abnormal owing to the pterygium.

associated with a significant postoperative HO-WFE,[49] although it does have the advantage of improved endothelial integrity. Collagen cross-linking is a treatment for progression in keratoconus, which may also slightly reduce HO-WFE, although the visual acuity may not improve.[50,51]

Pterygium

A pterygium can cause an asymmetric distortion of the cornea, because the lesion typically extends radially from the corneal periphery (Fig. 2). The disruption to the corneal surface topography induces both coma and trefoil WFEs.[52,53] There is commonly an increase in corneal and refractive astigmatism with pterygium, as well as an increase in HO-WFE, with an effect proportional to the extent of the lesion.[54,55] Because the condition approaches lateral to the visual axis, a change in SA is not usually a feature of the condition.[56] Higher-order wavefront error is associated with corresponding reductions in visual acuity and contrast sensitivity.[52]

Zare et al.[56] specified the pterygium in terms of the uninvolved optical zone of the cornea, measured from the slit lamp view, contending that this approach removed the influence of corneal size from the visual impact of the pterygia. Despite measuring only within a 5-mm-diameter optical zone, they found that the patient group with an uninvolved optical zone of 7 to 9 mm was associated with a total HO-WFE averaging 2.58 µm, and for patients grouped into the uninvolved optical zone of 5 to 7 mm, the total HO-WFE averaged 3.35 µm.

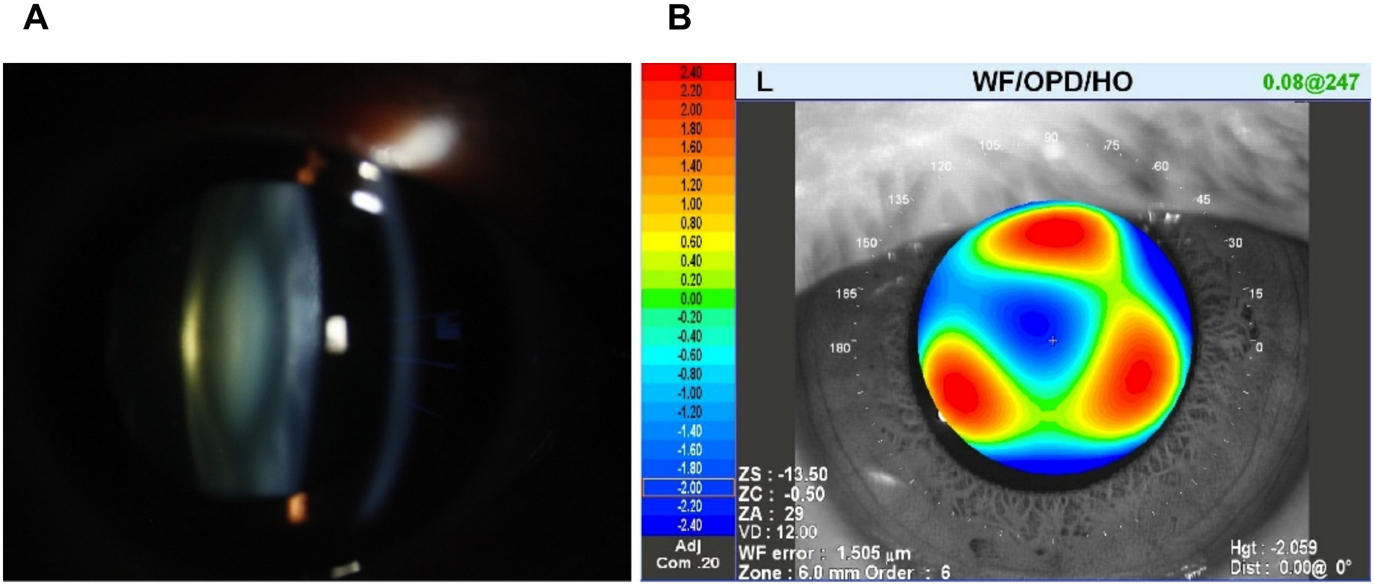

FIGURE 3.

Moderate nuclear sclerosis cataract in the left eye of a 45-year-old woman. The patient had experienced a −8.00-diopter myopic shift in 2 years, with best-corrected acuity of 20/70 (pinhole 20/40). (A) Anterior eye image. (B) HO-WFE map for a 6-mm pupil, with total higher order, 1.505 µm; total coma, 0.521 µm; total spherical, −0.893 µm; and total trefoil, 1.059 µm. The WFE is significantly abnormal owing to the cataract.

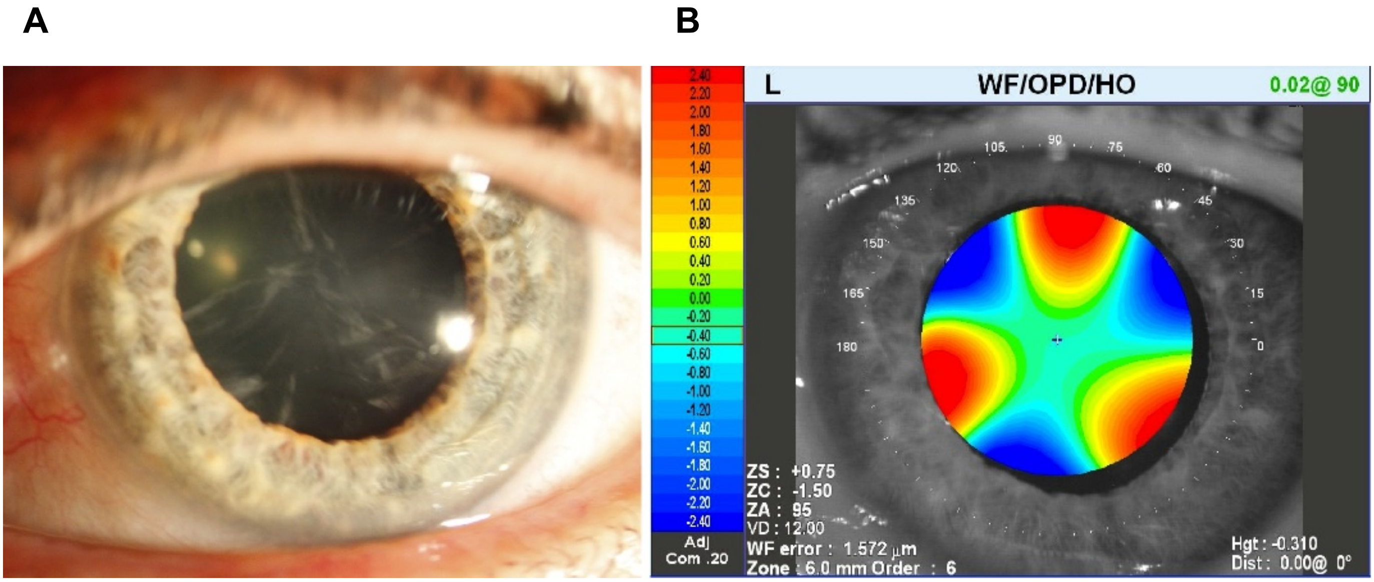

FIGURE 4.

Anterior cortical cataract in the left eye of a 72-year-old female patient, with best-corrected acuity of 20/70. (A) Anterior eye image. (B) HO-WFE map for a 6-mm pupil, with total higher order, 1.572 μm; total coma, 0.099 μm; total spherical, 0.121 μm; and total trefoil, 1.528 μm. The WFE is significantly abnormal, mainly attributed to trefoil.

Wavefront Correction

Kwon et al.[55] found a more effective reduction in WFE and astigmatism if there was surgical intervention in eyes with pterygia sized less than 3.0 mm. Although surgical excision of larger pterygia greater than 3 mm provided a significant benefit, reducing the total mean higher-order error with a 6.5-mm pupil from 3.73 μm preoperatively to 1.92 μm at 3 months postop did not result in the irregular WFE fully returning to the reference range. Surgical intervention in eyes with pterygia sized less than 3.0 mm reduced the total mean HO-WFE with a 6.5-mm pupil from 2.21 μm preoperatively to 1.18 μm at 3 months postop. Similarly, Gumus et al.[57] showed that pterygium excision with conjunctival autograft plus corneal polishing significantly reduced most of the pterygium-induced HO-WFE, with improvements continuing into the 1-year postoperative period.

Cataract

Initial reports of the wavefront analysis of cataract were provided by Kuroda et al.[58] in 2002. Nuclear sclerosis was associated with negative SA of -1.274 ± 0.733 μm for a 6-mm pupil in four patients.[58] This finding was significant because the SA in normal healthy eyes is usually positive in sign.[19,28] The negative SA appears because of the increased refractive index in the nuclear cataract, causing an increased refractive power in central lens compared with the periphery (Fig. 3).[58] Other studies have since confirmed increased negative SA in nuclear cataract.[5]

Clinically, the visual effect of nuclear cataract depends on the pupil size. If the pupil is small, such as for patients older than 70 years, then a nuclear cataract may manifest as a myopic shift because of the increased central refractive power.[59] However, visible crystalline lens changes may commence as early as the age of 40 owing to factors including high ambient temperature or medications.[60,61] Nuclear cataract in middle-aged patients, or those with a larger pupil, may cause monocular triplopia, attributed to a combination of SA and trefoil.[62]

Cortical cataract tends to not affect SA, but to increase other WFEs, particularly coma (Fig. 4).[63] Rocha et al.[5] found increased coma and trefoil associated with cortical cataract, compared with nuclear cataract or control patients. This is consistent with the observation that cortical cataract tends to cause changes in astigmatism, rather than a myopic shift.[59] Monocular diplopia can be associated with cortical cataract or the water cleft subtype of cataract, which may be attributed to the increased trefoil WFE.[64,65]

Posterior subcapsular cataract is not well characterized in terms of the wavefront effects, because it can be quite dense, causing missing data points in the central area of the scan and a lack of reproducibility.[5] It may be that the visual effects of posterior subcapsular cataract are not so much refractive, but more related to light absorption and scatter.

Wavefront Correction

Cataract surgery is a frequently performed procedure in many countries, and numerous studies evaluate the IOL implants and surgical techniques. An aspheric IOL may reduce postoperative SA and improve contrast sensitivity under mesopic and scotopic light conditions.[66,67] The amount of negative SA in an aspheric IOL is reported as either zero (Akreos AO, Bausch & Lomb, Rochester, NY), −0.20 μm (SN60WF, Alcon Labs, Fort Worth, TX), or −0.27 μm (Tecnis ZA9003, Advanced Medical Optics, Santa Ana, CA) for a 6-mm optical zone.[66–68] However, an aspheric IOL requires more accurate positioning in the eye, in terms of displacement or tilt, to minimize the HO-WFE.[67,69]

The corneal incision associated with cataract surgery can also impact the final HO-WFE, inducing spherical, trefoil, or tetrafoil HO-WFE for a 5.0- or 6.0-mm optical zone, although the effect may not be significant for a 3.5-mm pupil size.[70] Posterior capsular opacification of the IOL can increase the HO-WFE, particularly trefoil, but this can be remediated with Nd:YAG laser posterior capsulotomy.[71]

Multifocal IOLs can provide targeted amounts of negative SA to increase a patient's depth of focus and assist the patient's near vision.[72] Conversely, Santhiago et al.[67] contend that the positive SA associated with spherical and a zero SA IOL may be helpful in terms of maintaining depth of focus for the patient, although they suggest that further studies are needed using the patients' natural physiological pupil size.

Dry Eye

When the tear film breaks up in the normal healthy eye, there can be a huge dynamic effect on HO-WFE compared with the relatively small effect of the normal cornea and crystalline lens. Thibos et al.[73,74] were among the first to demonstrate that wavefront refraction was influenced by tear film stability. They also documented microscopic change in the tear film, with distortion of the individual dots in the Shack-Hartmann instrument matrix array.

The effect of tear film breakup on HO-WFE appears to be related to local thinning of the tear film, as well as refractive effects at the edges of the areas of tear film breakup and changes in the tear meniscus.[4,74] Tear film instability causes not only "macroscopic" WFEs but also microscopic changes to the WFE, which Himebaugh et al.[75] termed *very high order aberrations* or *microaberrations.*

Koh et al.[76] showed an increase in HO-WFE associated with tear film breakup. They compared higher-order errors immediately after blinking and 15 seconds later in 20 normal subjects. Regardless of the pupil size, all higher-order errors including spherical and coma were significantly increased. Higher-order wavefront error was increased 44% in the central 4-mm zone after tear film breakup and increased 23% in the central 6-mm zone.

More rapid changes in HO-WFE were demonstrated for dry eye patients by Montés-Micó et al.[77] They measured soon after tear film breakup, 5 to 10 seconds after the blink. Higher-order wavefront error was increased 158% in the central 4-mm zone after tear film breakup and increased 129% in the central 6-mm zone. Again, the results were relatively independent of pupil size and both spherical and coma errors were affected. The authors used the term *tear film irregularity* to describe the effect of dry eye on higher-order aberrations. Similar results were demonstrated by Denoyer et al.[78] who used serial wavefront measures in the first 10 seconds after the blink in mild-moderate dry eye patients. Higher-order wavefront error increased from 0.095 ± 0.015 μm immediately after blinking to 0.23 ± 0.06 μm within 10 seconds.

Wavefront Correction

Improvement in tear film regularity with lubricant treatment was demonstrated by Montés-Micó et al.[79] They instilled 0.18% sodium hyaluronate into the eyes of 15 patients with mild-moderate dry eye. The initial total HO-WFE of 0.81 ± 0.1 μm was improved to 0.40 ± 0.12 μm at 10 minutes. More viscous eyedrops, such as 0.3% sodium hyaluronate or 0.5% carboxymethylcellulose sodium/0.9% glycerin may cause an initial brief increase in HO-WFE at instillation,[80,81] although with prolonged use, this effect may diminish.

A further issue in dry eye is the effect of superficial punctate keratopathy, which exacerbates HO-WFE.[82] Lekhanont et al.[83] assessed the effect of 0.18% sodium hyaluronate in a group of 50 moderate to severe dry eye patients. There was a significant improvement in patient symptoms with the test drop for the 2-hour duration of the study, but the HO-WFE of 1.78 ± 0.54 μm at baseline was not changed by the treatment, an effect attributed in part to the presence of punctate epithelial keratopathy.

CONCLUSIONS

The wavefront refraction combines the critical refractive metrics of lower-order refraction, HO-WFE, pupillometry, point spread function, *jnd*, and beyond. The technique is designed to improve the accuracy and efficiency of refraction in clinical practice. Population studies of wavefront refraction for normal healthy eyes have shown that the upper limit of the 95% CI for HO-WFE RMS is about 0.5 μm with normal physiological pupil sizes. Other clinical studies have established that the threshold of awareness for a HO-WFE error is also about 0.5 μm, providing some concordance and giving an important baseline with which to evaluate clinical disorders. More accurate normal reference ranges for HO-WFE may require studies using the subjects' natural physiological pupil sizes across the age groups. Wavefront refractive studies have shown a HO-WFE in excess of 1.0 μm for a range of abnormal and irregular conditions, including keratoconus, pterygium, cataract, and dry eye. Wavefront corrections are increasingly being used with contact lenses, therapeutic and surgical treatments, retinal imaging, and other methodologies. Dr. Borish would be pleased with the advances in refraction. Today's eye care practitioners should be as well.

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