Applications of an adaptive optics visual simulation system

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ABSTRACT: The purpose of this paper is to carry out a scientific literature review of the basic principles used by an adaptive optics (AO) visual simulator system and its main applications in optometry and ophthalmology. AO systems are used to measure, correct, and simulate wavefront aberrations. They all share three basic components: a wavefront sensor, a wavefront corrector, and a control computer. The visual simulator uses a Hartmann-Shack aberrometer with a square array of 1024 lenslets to measure the wavefront at 850 nm, while the AO system uses a deformable mirror with 52 independent electromagnetic actuators under a membrane as a correcting element. A commercially available software allows control of the deformable mirror surface. The technique has many applications, such as optimization of instrument optical quality to improve visualization of the retina, study of vision quality, and the development of new optical designs for intraocular lenses, customized contact lenses or wavefront-guided refractive surgery. Thus, AO could be useful for choosing the best surgical technique without having to perform surgery.

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The human eye suffers from higher-order monochromatic aberrations besides defocus and astigmatism that contribute to degradation of the retinal image and therefore limit the visual performance[1].

Among the many different methods to correct ocular wavefront aberrations, adaptive optics (AO) by means of a deformable mirror is probably the most popular[2]. AO aims to control and correct wavefront aberrations or any other optical artefacts introduced by the media between the object and the image[3-6], thereby improving the quality of an optical system by reducing the induced aberrations to obtain a closer-to-perfect point spread function. AO was originally developed for astronomy around 60 years ago to compensate for atmospheric disturbances affecting the imaging of astronomical bodies in outer space[4,7]. However, the first on-sky partial experiments were not conducted until the late 1970s and the first full operating system did not appear until the late 1980s[3]. The technique was then exported to biomedicine, particularly to the field of visual optics[3,4]. The first complete AO system that successfully corrected the most significant higher-order aberrations (HOAs) of the eye was built in the mid-1990s by Liang and colleagues[4].

The aim of this paper is to explain the principles of an AO system, and to describe the main applications of this technique in visual optics.

1. The AO system

1.1 Wavefront aberrations

Wavefront aberrations and diffraction limit visual acuity (VA) below the spatial bandwidth imposed by the neural visual system[4]. In order to understand AO, wavefront aberrations must be first explained. Ocular wavefront aberrations are distortions in the wavefront passing through the pupil of the eye, decreasing the quality of the image formed on the retina[8]. They are defined as the difference between the aberration-free wavefront (perfect wavefront) and the real wavefront for every point over the pupil of the eye. Every optical system has wavefront aberrations to a greater or lesser extent[4].

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A wavefront can be described as a summation of polynomials. In vision science, these are usually Zernike polynomials, which have several advantages over other mathematical descriptors. When using Zernike polynomials, each coefficient represents one aberration type, and has a certain weight depending on the contribution of that aberration to the global wavefront[9]. Wavefront aberrations may be classified as lower-order aberrations (LOAs) (up to second order) and HOAs (third order and above). The lower order aberrations are piston (n = 0), two tilts that represent translations and rotations of the reference system (n = 1), and the blur and astigmatism at 0°/90° and at 45°/135° (n = 2); the main HOAs are vertical and horizontal coma, triangular astigmatism (or trefoil), and spherical aberration[4,10].

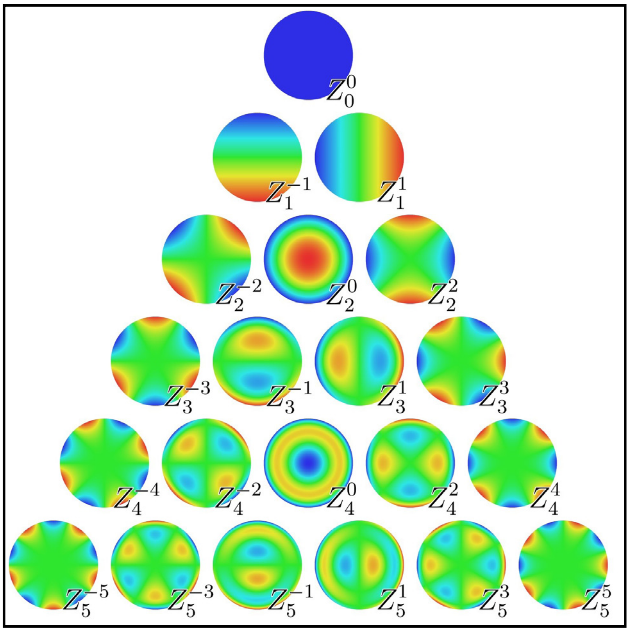

Figure 1. Zernike polynomials Z_n^m up to order five made into pyramid shape, as a function of radial degree or order n, and azimuthal frequency m (attribution: Zom-B at en.wikipedia; CC BY 3.0).

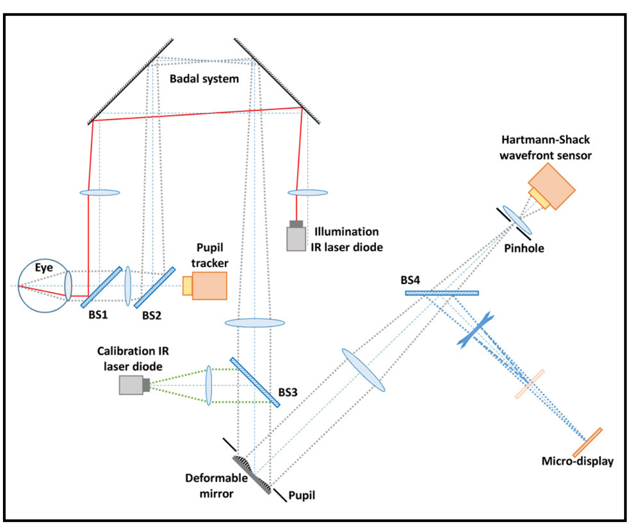

Figure 2. Schematic layout of the optical simulator setup (drawing is not to scale). Illumination beam is depicted in red color. Calibration and micro-display optical paths are shown in green and blue dotted-lines, respectively, while wavefront measurement optical path is shown in grey dotted-line. BS stands for beam-splitter, while IR stands for infra-red.

The different Zernike components can be displayed in the form of a pyramid, known as the Zernike pyramid (see Figure 1). Within this pyramid, the vertex represents order 0, increasing one order per line towards the base. Usually, the lower the order, the greater the contribution to the total wavefront; there is generally no benefit in studying aberrations above the fifth order for most vision science applications[9].

Aberrations depend on factors such as pupil size, age, accommodation, and refractive state[4]. The aberrations associated with the anterior surface of the cornea can be computed from its shape as measured with corneal topography instruments, and the aberrations of the complete eye can be measured using an aberrometer[9].

1.2 The visual simulator

AO allows ocular aberrations to be corrected. It can be also used to induce controlled wave aberration patterns in the eye to better understand the impact of the ocular optics on vision[4,11,12]. The key element of an AO system is a deformable mirror that can be controlled to compensate the aberrations[3]. This section will explain how it works and how it generates visual simulations.

Only one AO visual simulator will be described here, since most AO systems use a similar procedure. The AO visual simulator is used to measure, correct and simulate optical aberrations[4,13]. It allows ocular wavefront measurement, AO custom-wavefront correction, user-defined AO wavefront generation, visual performance assessment through user-defined wavefront aberrations, and wavefront assessment of accommodation[4]. It contains three basic components: a wavefront sensor, a wavefront corrector, and a control computer. The instrument also allows the assessment of visual function through a microdisplay[4,5,11,13-27]. Figure 2 shows a diagram of the visual simulator optical setup.

a) <u>The wavefront sensor</u>

The visual simulator uses a Hartmann-Shack (HS) wavefront sensor to measure the wavefront, and consists of a square array of 1024 lenslets[4,5,13-19,22-29]. Each lenslet samples a local portion of the incident wavefront and focuses this light on a charge-coupled device (CCD) sensor, corresponding to a square area of 230 × 230 μm^2 at the pupil plane. The displacement of any given spot from its intended position is directly related to the slopes of the wavefront in that portion of the pupil[4,28,29,30].

The HS image quality is assessed based on HS image spot areas[31].

b) The wavefront corrector

The AO system uses a deformable mirror with 52 independent electromagnetic actuators under a membrane as a correcting element[4,5,13-19,22-28]. There are many types of deformable mirrors in use in AO retinal imaging systems[30]. In the deformable mirror inside the AO system, each actuator exerts a force on a miniature magnet when supplied with an electrical current, somewhat similar to the principle followed by a conventional loudspeaker[23]. The inter-actuator spacing within the deformable mirror is 840 μm in the pupil plane, so the resolution of the measurement is larger than the resolution of correction[4,28,29]. Currently available deformable mirrors have a limited capacity for correcting ocular wavefront aberrations, being limited by the number of actuators and the physical response of the membrane, in terms of the amplitude range that can be induced[6].

Wavefront aberrations may be corrected in two ways: by changing the light path, or by modifying the refraction index. The AO system explained herein uses the first approach. In liquid crystal spatial light modulators, the phase modulation is induced by the change in the refractive index, consequently affecting the optical path through the nematic liquid crystal in response to changes in the applied electrical field. The latest devices present several advantages for use in the human eye, such as relatively user-friendly practical implementation and calibration, and a high density of independent pixels to generate the required phase profiles; however, they are limited by their relatively slow temporal response, and the need to use polarized light[6].

Deformable mirrors essentially consist of a mirrored surface whose shape can be modified by different actuators. This surface can be composed of either independent mirrors, known therefore as segmented mirrors, or can be continuous. Segmented mirrors present the drawbacks of energy loss due to the spacing between segments and diffraction effects from each segment, but also have some advantages, such as their relatively low cost and easy replacement. However, for ophthalmic applications, continuous mirrored membranes are the preferred option[6].

Some of the limitations encountered with previous AO systems using electrostatic deformable mirrors and liquid crystal spatial light modulators were recently overcome by electromagnetic technology[23].

Deformable mirrors using electroceramic cylindrical actuators have been extensively used in the eye[6,32], but these actuators cannot be densely packed and therefore require relatively wide diameters[33].

Electrostatic deformable mirrors have been also used for applications in the human eye[6,34], being one of the most cost-effective approaches so far. In this case, the actuators are electrodes exerting an electrostatic force over the deformable membrane due to the interaction between two elements loaded with adjustable static electrical charges. Microelectromechanical deformable mirrors —also used in systems applied to human eye examination[6,35] — use electrical forces to shape the mirrored surface, as in the previous case, but mechanically displace the actuators instead.

c) The control computer

The deformable mirror surface is controlled by a commercially available software package, allowing the reshaping of the deformable mirror from its normally flat surface to a shape that corrects HOAs and/or adds different aberration values[4,5,14-19,22-29].

Other components of the device are a Badal system based on a trombone optical configuration that allows the visual target to be presented at different distances, which can be used to minimize the subject's spherical error, while the cylindrical error can be corrected with a trial lens placed near the pupil plane[31]. Additionally, the observer looks at visual tests generated on a microdisplay through the AO system and an artificial pupil, and the impact of the corrected and/or modified aberrations on vision can thus be analysed.

There are three different procedures in which an AO system may be used for application in human eyes[17,23,26]:

- Wavefront measurement: ocular wavefront aberrations are recorded while the deformable mirror is set to an aberration-free shape.
- Dynamic wavefront correction/generation: user-defined aberrations are applied using a closed-loop configuration that comprises a double-pass of light through the eye, so that the total aberrations (eye+device) encountered along the line of sight remains constant. These dynamically-adjusting wavefronts enable compensation of small eye decentrations and aberration variations due to the tear film or accommodation[4,18,23,24,29].
- Static wavefront correction/generation: user-defined aberrations are applied and maintained constant, independently of wavefront fluctuations that may occur in the eye during the measurement. There is a practical advantage when carrying out experiments with static wavefronts, namely, eliminating the need for illuminating the retina with infrared light and therefore not disturbing visual simulation, as opposed to dynamic adjustment of wavefronts. However, the AO system must be accurately aligned with the pupil. To

correct the static wavefront, the visual simulator reshapes the deformable mirror to generate the opposite wavefront of the patient's eye, and thereby compensates the wavefront aberrations of the eye. Additionally, when generating a static wavefront, the operator defines a simulated wavefront that is then introduced by the device using an internal closed-loop system that sets the mirror surface to the desired shape and keeps it constant. Ideally, the AO simulator software continuously displays the residual wavefront value of the wavefront generated by the deformable mirror, compared with the wavefront defined by the operator, to control the reliability of the system during measurements. The device software calculates the difference between the wavefront measured by the HS sensor and the expected wavefront outcome; it then displays the residual wavefront correction as the root mean square (RMS) error at the level of the deformable mirror[4,14-16,18,23,24,29]. In other words, the system generates a static wavefront error that is added to the subject's ocular aberration.

1.3 Measurement process

The ocular wavefront is measured and the deformable mirror is set to an aberration-free shape. Thus, the system performs the function of a wavefront aberrometer that measures ocular aberrations following a Zernike polynomial expansion. The deformable mirror can then change its shape to correct or induce any aberration pattern expressed in terms of its Zernike coefficients[4,5,13-17,22-26].

The device also has an internal aperture optically conjugated with the eye-pupil plane, which allows the pupil size to be adjusted artificially. The AO system requires precise alignment of the individual's pupil with the optical axis setup. Throughout the visual simulation process, an eye-tracking system monitors the relative positions of the instrument's optical axis and the subject's pupil. In other words, the visual simulator uses a CCD camera integrated into the AO and real-time display of the pupil to enable alignment of the eye. The hand wheel of pupils of the AO system enables the pupil position to be maintained, providing quick, smooth, and fine adjustment[11,14,16,18,22-26].

The eye-tracker data are continuously displayed as two circular targets in a software window; these graphic circles help maintain the best possible alignment during testing[4,5,13,14,17].

The subject's head position is important, and the device uses a standard chin-and-forehead rest and a biter to ensure optimum alignment of the pupil and apparatus while reducing head movement[4,11,16,17,22,23,28,29]. The subject looks at a microdisplay through the deformable mirror, Badal system, and pupil conjugation lenses of the simulator. These elements are coaxially aligned within the optical system. Additionally, images and patterns are generated by a laptop personal computer connected to the microdisplay through a standard super video graphics array cable[4,29].

1.4 Other simulators

- AOVS: an AO visual simulator using a HS wavefront sensor with a hexagonal array of 97 lenslets, a 37-actuator piezo deformable mirror, a control system integrated into a personal computer, and a visual stimulus device. An infrared beam from a 905-nm laser diode is collimated into the observer's retina[12,36].
- Liquid crystal AOVS (LC-AOVS): this simulator has a liquid crystal programmable phase modulator as an active optical medium for wavefront manipulation. This active element has the advantages of high accuracy, allowing single step phase manipulation, and high spatial resolution, overcoming the continuous limitations of most deformable mirrors[7].

Most AO systems have two limitations that prevent them from being used in clinical practice[23], namely their relatively large size and limited range of correction.

2. Applications of AO

The AO has many applications such as improvement of *in vivo* retinal imaging resolution[4], or compensation of HOAs to improve better visual function, particularly in highly distorted corneas that present a large amount of HOAs[4,11].

An increase in the total amount of spherical aberration (SA) of the eye results in an increase in the total amount of HOAs, therefore decreasing visual function. However, SA induces multiple focal points that may contribute to increase the depth of focus[11,37,38]. Thus, another application could be study of the impact of the correction of certain aberrations in vision.

Visual simulation enables experiments to be conducted to better understand the process of vision. Many studies have been carried out inducing controlled wave aberration patterns in the eye, and evaluating the changes in visual performance by means of VA and contrast sensitivity[4].

The main application of AO is therefore to predict the visual benefits of invasive surgical procedures without the need to perform surgery, such as in customized visual correction[4,5,7,12].

In this section, the main applications of the AO referred to in the literature will be described.

2.1 Retinal imaging

Optical imaging systems aim to provide as crisp and detailed view of ocular structures as possible. The anterior optics of the eye permit such non-invasive visualization of the retina and associated pathology, although imaging resolution is limited by HOAs introduced by the eye and the imaging system itself[3,30,39-41]. The AO system can control and correct these aberrations, thus enabling imaging systems to reach their nominal power[3].

The first AO fundus camera was developed in David William's laboratory at the University of Rochester around 20 years ago[30,41]. This system has already been applied to multiple forms of microscopy, like confocal microscopy, two-photon microscopy, coherence-gated microscopy or wide-field microscopy[3]. AO has been applied to different technologies for retinal imaging, such as scanning laser ophthalmoscopy (SLO), optical coherence tomography (OCT) or flood illumination imaging[30,40,41]. Many studies have confirmed the usefulness of AO systems in enabling *in vivo* visualization in the human eye of individual photoreceptors, retinal pigment epithelium, and white blood cells[4,8,30,31,39-43], providing the opportunity for noninvasively monitoring retinal function, following the progression of retinal disease and assessing the efficacy of therapies at microscopic level[4].

The AO scanning laser ophthalmoscope (AOSLO) measures ocular aberrations using a wavefront sensor, most commonly a HS. A deformable mirror then compensates the wavefront aberrations, while image-based eye-tracking provides image stabilization, allowing resolution of small structures like photoreceptors[8]. Confocallity is a major advantage of AOSLO; light not originating from the focal plane of the retina is excluded through the use of a pinhole conjugated to the retinal focal plane, thus increasing the contrast of the final image. Lateral and axial resolution of the AOSLO can be modified by changing the pinhole size of the system[30]. While a confocal SLO device can have a lateral resolution of 5-10µm and an axial resolution of 20-50µm, AOSLO can reach a lateral resolution of 1.5-3 µm, depending on motion stabilization (less than cone-to-cone spacing)[8]. The applications of this device are numerous, and include high-resolution imaging, eye tracking, laser modulation for stimulus delivery, multichannel imaging, and stabilized stimulus delivery for psychophysics and electrophysiology[30,41].

AO can be used to compensate the monochromatic aberrations of the eye in OCT too. While OCT provides subcellular resolution in the axial direction, its transverse resolution is still limited by the ocular aberrations of the eye. Thus, AO, in combination with OCT, allows subcellular resolution in all three spatial directions[39]. Three-dimensional visualization of the nerve fibre layer, individual cone and rod photoreceptors, retinal vasculature, ganglion cells, and lamina cribrosa, as well as the retinal pigment epithelium mosaic and choriocapillaris, have been achieved using high speed AOOCT[4,30,39].

Recent developments in AOSLOs have enabled *in vivo* assessment of retinal microvasculature without the need for exogenous contrast agents, using motion contrast image processing[43,44]. The technique involves displacement of a larger confocal pinhole, located at the retinal plane conjugate in front of the detector. Retinal microvasculature contrast is maximised by manually displacing the confocal pinhole along the horizontal direction only. Chui et al.[43] concluded that AOSLO provides direct and non-invasive visualisation of the retinal microvasculature of healthy and pathological retinas. This technique might facilitate identification of more sensitive indicators of diabetic retinopathy progression, for instance, based on features of the microvasculature. Furthermore, ocular HOAs and light scatter have also been shown to be increased in diabetic subjects, which may further contribute to visual impairment[45].

These studies confirm that AO imaging has changed the way in which vision scientists and ophthalmologists see the retina, helping clarify our understanding of the retinal structure and function, and the aetiology of various retinal diseases[30].

2.2 Study of vision

In recent years, the use of AO in research has significantly increased our understanding of the relationship between wavefront aberrations and visual performance[46].

AO can be used to induce or correct aberrations and analyse the vision changes, allowing the study of some visual parameters that can be applied in future optical developments. The visual impact of aberrations may also help to understand and predict the visual outcomes of wavefront-guided procedures[4,23,24].

It might be expected that correcting aberrations will interact with variables such as pupil size and letter characteristics. For example, the advantages and disadvantages of removing aberrations may be more obvious for larger rather than smaller pupil sizes[47]. Bernal-Molina et al.[13] studied experimental values of the depth-of-field of the human eye for different accommodative states. They measured the wavefront as a function of the accommodative stimulus by varying the object's vergence from 1 D to 6 D in steps of 1 D. The accommodation of the eye was then paralyzed by instilling one drop of cyclopentolate 1%, and a single wavefront measurement was recorded. For each accommodative stimulus, the authors modified the deformable mirror to add the aberration pattern measured, before finally measuring the depth-of-field. They found that the difference between the ideal and real accommodation response (LAG) is mainly attributed to the presence of the depth-of-field.

Rocha et al.[22] evaluated the impact of HOAs on depth of focus using an AO visual simulator. The wavefront pattern of the eye was measured, and after mydriasis and cycloplegia had been confirmed, the subject's through-focus response was also determined while different ocular aberrations were optically introduced. They concluded that systematic induction of targeted amounts of spherical aberration (positive and negative) can improve depth of focus, which is a useful finding for the development of presbyopic corneal or lenticular treatments and future aspheric intraocular lens (IOL) design.

Using an AO system, Chen et al.[48] found that depth of focus is larger when HOAs are present in the eye, and the correction of HOAs improves image quality at the best focus but reduces image quality for defocus values away from the maximum, thereby reducing the depth of focus of the eye. Their results suggest that at least some subjects can use monochromatic HOA aberrations to guide accommodation.

Piers et al.[46] analysed the impact of SA on contrast sensitivity (CS) using an AO visual simulator to determine the optimal amount of SA to include in customized corrections of wavefront aberrations. They found that in-focus contrast performance peaks when all SAs are corrected, even when all HOAs are corrected.

Atchinson et al.[47] investigated the limits at which induced blur of letter targets becomes noticeable, troublesome and objectionable, by varying spherical defocus through an AO system. They found that both pupil and letter size had a highly significant effect on blur limits, while these decreased as pupil size increased.

Additionally, Baskaran et al.[49] found that the correction of all aberrations using AO improved both high and low contrast resolution acuity in a single low-vision subject with a long-standing central scotoma. Li et al.[12] found that best VA was achieved when both the lower and higher order monochromatic aberrations were fully corrected, suggesting that correction of third order aberrations and SA alone produces most of the improvement in visual performance.

Rocha et al.[29] evaluated the changes in VA and visual perception generated by correcting HOAs in keratoconic eyes and in symptomatic postoperative refractive surgery (LASIK) eyes using an AO visual simulator. They concluded that the improvement in VA was significantly correlated with a predefined amount of the eye wavefront aberration.

AO technology may be of clinical benefit when advising patients with highly aberrated eyes regarding their maximum potential for vision correction. AO can therefore be used in a clinical practice for customized refractive surgery, customized contact lens corrections, and wavefront-customized IOL implantation.

Rouger et al.[24] used an AO system to dynamically correct patients' aberrations up to the 5th order, and to induce various amounts of single Zernike modes while measuring visual performance by means of CS and VA tests. Whereas the introduction of Zernike aberrations resulted in larger interindividual variability when measuring CS loss, no major differences in VA loss were observed among individuals. Image quality metrics based on wavefront aberration measurement were able to predict the impact of individual Zernike aberrations on CS and VA. These findings could be useful for designers of contact lenses or IOLs.

Applegate et al.[50] observed that aberrations near the centre of the Zernike pyramid (defocus, coma and spherical aberration) were more detrimental in VA than aberrations at the periphery of the pyramid. Yoon et al.[10] showed reliable improvements in CS and VA when HOAs were corrected.

However, Legras et al.[5] concluded that metrics based on wavefront aberration measurements are able to predict the impact of these aberrations on CS and should be able to predict its effects on VA with the use of categorized neural CS functions. These simulations are a useful tool for optical designers, since they allow the effect of optics on visual performance to be predicted without needing to manufacture prototypes, hence saving time and money. Additionally, some eyes showed no benefit whereas others obtained a CS benefit when the aberrations were corrected. This variability may be explained by the hypothesis of a cortical adaptation to blur, by which the neural visual system is adapted to the eye's particular aberrations. In other words, possible reasons for this reduced correlation between the amount of corrected ocular aberrations and the improvement in visual function could be attributed to neuroadaptation, and also residual HOAs that remained uncorrected by the mirror[4,5,23,24].

Although recent studies have suggested that we might be adapted to our retinal image, which would have an impact on the visual benefit of correcting the aberrations of the eye[51,52], this question requires further investigation[5].

AO may be also useful to study the mechanisms and optical signals that the visual system uses to respond to myopic and hyperopic defocus, and to characterize the stimuli that guide the dynamic response of accommodation. Previous research has suggested that the visual system, in its accommodative response, is able to determine the signs of blur. Therefore, the response to a given stimulus focused in front of or behind the retina might not follow a negative feedback response based on a trial and error system with the sole objective of maximizing the contrast of the retinal image. Analyses with AO systems could provide results that will allow us to determine, for example, if the accommodative signal is a response to certain monocular cues present in the aberrated wavefront in the retina. AO and aberrometry thus provide a new method to examine the stimulus for accommodation in the absence of defocus, astigmatism and HOAs, with and without feedback from defocus and HOAs (ERC-2012-StG 309416-SACCO Project).

2.3 Customized contact lenses

Contact lenses are potential means of correcting HOAs[4], although there are some limitations, such as the flexure, rotation, translation, and tear film effects that may introduce additional aberrations.

With visual simulators, the patient's vision can be simulated without having to fit contact lenses. If we know the aberration pattern of a contact lens, the visual performance can be assessed after fitting that lens design, also allowing comparisons[4].

Rigid gas permeable (RGP) contact lenses improve visual performance by significantly reducing the ocular aberrations, including both LOAs and HOAs[53]. Yang et al.[36] used a customized AO system to correct residual aberrations in myopic and keratoconic patients who were prescribed RGP contact lenses, and measured and compared their CS function before and after AO correction. For the myopic group, CS after AO correction of residual aberrations did not improve significantly, whereas for the keratoconic group, CS for all spatial frequencies with AO correction were higher than without, showing that the correction of residual aberrations improves CS in these patients.

AO can be applied to evaluate the residual aberrations of the contact lenses and how they affect visual function, and develop customized contact lenses. Therefore, although customization is easy to support in theory, it is still challenging to implement in the clinic[36]. Porter et al.[54] suggested than an appropriate aspheric correction surface would reduce the SA of the eye, and therefore the development of customized contact lenses for correcting the HOAs of the eye would have an important impact.

Montés-Micó et al.[55] used AO to compensate ocular aberrations and analyse how the wavefront aberration pattern is affected over time by the use of soft contact lenses. They concluded that the AO system allows the optical quality of a contact lens to be accurately analysed *in vivo* and, moreover, diurnal variations across contact lenses may result in differences in visual performance. This comparison could not have been made without AO.

2.4 IOLs and refractive surgery

AO can be used to generate wavefront aberrations of IOLs or wavefront patterns after refractive surgery, to study how they affect vision through visual simulations. Furthermore, new surgical techniques and lens designs are becoming increasingly sophisticated, not only providing the appropriate power and astigmatism correction, but also compensating the mean induced SA[56]; visual simulation could therefore allow the visual impact of these surgically-induced changes in optical quality to be determined prior to the procedure.

From a technical and ethical point of view, different surgical procedures cannot be performed on a subject to determine the optimal treatment[16,28]. Thus, AO allows the better surgical intervention to be chosen without requiring surgery. In cataract surgery, the patient can assess his visual performance with different types of IOLs before surgery, allowing the surgeon to decide what type of IOL is best depending on the patient's characteristics. However, these studies have some limitations: the effect of the surgery, postoperative changes, IOL tilt or other postoperative complications, the subject's age, the effect of the surgery or lens decentrations[4,14,16-19,26].

If the individual eye wavefront aberrations are measured and compensated, wavefront patterns from different situations such as new lens designs or surgical procedures may be induced to simulate their effects on vision. There is substantial evidence of these advantages in the scientific literature. Pérez-Vives et al.[14] compared the visual and optical quality of the accommodative IOL Crystalens HD with a monofocal IOL. The AO system compensated the wavefront error of the eye, and then the measured IOL aberrations and representative corneal aberrations were added to the optical wavefront, forming the image in each subject's eye. They concluded that the optical and visual quality with both IOLs were comparable for distance vision. Similarly[19], they compared the visual quality of implantable collamer lens (ICL) with and without a central hole at different degrees of decentring. They concluded that both ICLs provide good and comparable visual performance for all powers and pupil sizes evaluated. Moreover, ICL decentring affects both ICL models evaluated in the same way.

Madrid-Costa et al.[16] analysed visual quality differences between IOLs (two aspheric and two spherical), and assessed the impact of IOL decentration and tilt on visual quality. The AO system was used to apply the wavefront pattern of each IOL in each situation and the HOAs of the cornea. They found that the aspheric aberration-correcting IOLs and spherical IOLs studied provided comparable visual quality when they were centred. However, tilt and decentration of the

IOL had an effect on the visual quality of the subjects that was greater with the aberration-correcting IOLs than with the spherical IOLs. Furthermore, residual spherical aberration slightly improved the depth of focus and the tolerance to defocus.

Tabernero et al.[57] compared two IOLs (one spherical and other aspheric) under different tilts and decentrations with an AO system. They found that this model is useful to predict IOL performance.

Furthermore, combinations between IOLs and corneal ablations have been made with AO systems. Ruiz-Alcocer et al.[28] studied the visual quality of an aspheric aberration-correcting IOL combined with normal corneas, with low and high myopic corneal ablations, and with low and high hyperopic corneal ablations. The AO system was used to apply the wavefront patterns of the IOL and the cornea in each of these simulations. They found that the aspheric aberration-correcting IOL provides comparable results when it is combined with normal corneas and with corneas with simulated low myopic ablations.

Madrid-Costa et al.[20] evaluated the visual performance of an aberration-free IOL in patients with virgin corneas, and with low and high myopic and hyperopic ablations. They used an AO system to eliminate intersubject variability and physiological variables that can confound measurements *in vivo*. They concluded that the IOL design gives an excellent visual performance for a range of SA from 0.027 to 0.277 μm.

Ruiz-Alcocer et al.[11] evaluated the depth of focus with three monofocal IOLs (two aspheric and one spherical) in patients with different corneal profiles (normal corneas and corneas with high and low myopic and hyperopic ablations) using an AO visual simulator. The AO system added the wavefront pattern of the IOLs, and they measured the defocus curves and VA. They found that for patients with prior myopic corneal refractive surgeries, the aspheric designs seem to provide the better compromise between distance VA and depth of focus. They also studied visual quality differences among IOLs (two spherical and one aspheric) in patients with previous hyperopic laser ablations, and assessed the impact of IOL decentration and tilt on visual quality[21]. They concluded that in patients with a negative increment of corneal SA due to hyperopic LASIK, all simulated IOLs provided good visual quality when they were centred, with better results for lower increments of negative SA. However, tilt and decentration of monofocal IOLs had a negative impact on visual function in patients with hyperopic ablations.

Pérez-Vives et al.[25] evaluated the visual quality achieved in patients undergoing implantation of standard or modified ICLs to correct residual myopic error after LASIK surgery. They measured the ICL wavefront patterns and the AO system simulated LASIK surgery of moderate and high myopia with a myopic regression. They found that ICLs could be a favourable alternative for correcting myopic residual refractive errors after LASIK. Moreover, when the SA of the ICL was modified, the post-LASIK eyes with high myopia were those that most benefited, as these eyes were more aberrated than after moderate myopic LASIK.

Some studies have also compared different surgical techniques. Pérez-Vives et al.[18] compared optical and visual quality of ICL implantation and femtosecond LASIK (F-LASIK) for myopia. They used an AO visual simulator to simulate ICL and F-LASIK aberration patterns. As expected, the SA was more positive in F-LASIK than in ICL wavefront patterns. Thus, ICLs produced lower aberrations and offered better retinal image quality. Nevertheless, both surgical techniques provided good optical and visual quality, although ICL provided better outcomes. The same authors[26] compared optical and visual quality of the ICL and LASIK for myopia. They concluded that the use of an AO visual optics simulator allowed the impact of different surgical techniques on the visual performance of a patient to be compared before the surgical procedure. Although both myopic ICL and LASIK procedures provided good optical and visual quality, ICL potentially provided better outcomes than LASIK surgery, especially for higher refractive errors and pupil sizes, because LASIK induced higher HOAs than ICL implantation. Pérez-Vives et al.[17] also compared the optical and visual quality of a simulated toric ICL and a bioptics technique to treat high myopic astigmatism. They used an AO system because it allows two procedures in the same eye to be directly compared in the same patient. They concluded that simulations of both the toric ICL and bioptics treatment provided good optical and visual quality in the correction of moderate and high myopic astigmatism, although ICL implantation provided better outcomes than the bioptics procedure, particularly when the pupil diameter increased from 3 to 5 mm, because the bioptics procedure induced more HOAs than ICLs.

CONCLUSIONS

This manuscript explains AO visual simulators and their main applications. AO allows the measurement, correction, and simulation of wavefront aberrations to increase image quality or to study how aberrations affect vision quality. AO could also have a relevant role in the near future to study the retina, significantly increasing the resolution of diagnostic techniques like OCT or SLO to observe retinal structures.

This technology can also provide very useful information for future IOL development, wavefront-guided refractive surgery, customised ophthalmic lenses or customised contact lenses. IOL and contact lenses should ideally be designed with an aberration profile matching that of the cornea or the lens to increase their optical quality.

Finally, AO technology may also serve as a tool to optimize the choice of surgical technique that will provide the best visual outcomes prior to performing any surgery.

AO visual simulators could significantly improve the visual satisfaction of our patients.

REFERENCES

1. Liang J, Williams DR. Aberrations and retinal image quality of the normal human eye. J Opt Soc Am A. 1997; 14:2873-83.
2. López-Gil N, Castejón-Mochón JF, Fernández-Sánchez V. Limitations of the ocular wavefront correction with contact lenses. Vis Res. 2009; 49:1729-37.
3. Duchêne G. Review of "Adaptive Optics for Biological Imaging" edited by Joel A. Kubby. Biomed Eng Online. 2014:1-4.
4. Pérez-Vives C, Belda-Salmerón L, García-Lázaro S, Madrid-Costa D, Ferrer-Blasco T. Adaptive optics, wavefront aberrations and visual simulation. J Emmetropia. 2011; 2: 103-9.
5. Legras R, Rouger H. Calculations and measurements of the visual benefit of correcting the higher-order aberrations using adaptive optics technology. J Optom. 2008; 1:22-9.
6. Fernández EJ, Vabre L, Hermann B, Unterhuber A, Považay B, Drexler W. Adaptive optics with a magnetic deformable mirror: Applications in the human eye. Opt Express. 2006; 14:8900-17.
7. Manzanera S, Prieto PM, Ayala DB, Lindacher JM, Artal P. Liquid crystal adaptive optics visual simulator: Application to testing and design of ophthalmic optical elements. Opt Express. 2007; 15:16177-88.
8. Gramatikov BI. Modern technologies for retinal scanning and imaging: An introduction for the biomedical engineer. BiomedEng Online. 2014; 13.
9. López-Gil N. ¿Cómo se miden, en clínica, las aberraciones y que fiabilidad tienen en la medición? In: Gispets-i-Parcerisas J, González-Anera R, López-Gil N, Merayo-Lloves J, Rodríguez-Zarzuelo G, Villa-Collar C. Aberraciones oculares aspectos clínicos. Madrid: Colegio Nacional de Ópticos-Optometristas de España; 2005. p. 27-42.
10. Yoon G-, Williams DR. Visual performance after correcting the monochromatic and chromatic aberrations of the eye. J Opt Soc Am A. 2002; 19:266-75.
11. Ruiz-Alcocer J, Pérez-Vives C, Madrid-Costa D, Garcí-Lázaro S, Montés-Micó R. Depth of focus through different intraocular lenses in patients with different corneal profiles using adaptive optics visual simulation. J Refractive Surg. 2012; 28:406-12.
12. Li S, Xiong Y, Li J, et al. Effects of monochromatic aberration on visual acuity using adaptive optics. Optom Vis Sci. 2009; 86:868-74.
13. Bernal-Molina P, Montés-Micó R, Legras R, López-Gil N. Depth-of-field of the accommodating eye. Optom Vis Sci. 2014; 91:1208-14.
14. Pérez-Vives C, Montés-Micó R, López-Gil N, Ferrer-Blasco T, García-Lázaro S. Crystalens HD intraocular lens analysis using an adaptive optics visual simulator. Optom Vis Sci. 2013; 90:1413-23.
15. Madrid-Costa D, Pérez-Vives C, Ruiz-Alcocer J, Albarrán-Diego C, Montés-Micó R. Visual simulation through different intraocular lenses in patients with previous myopic corneal ablation using adaptive optics: Effect of tilt and decentration. J Cataract Refractive Surg. 2012; 38:774-86.
16. Madrid-Costa D, Ruiz-Alcocer J, Pérez-Vives C, Ferrer-Blasco T, López-Gil N, Montés-Micó R. Visual simulation through different intraocular lenses using adaptive optics: Effect of tilt and decentration. J Cataract Refractive Surg. 2012; 38:947-58.
17. Pérez-Vives C, Domínguez-Vicent A, Madrid-Costa D, Ferrer-Blasco T, Montés-Micó R. Myopic astigmatism correction: Comparison of a Toric Implantable Collamer Lens and a bioptics technique by an adaptive optics visual simulator. Ophthalmic Physiol Opt. 2013; 33:114-22.
18. Pérez-Vives C, Albarrán-Diego C, García-Lázaro S, Ferrer-Blasco T, Montés-Micó R. Implantable collamer lens and femtosecond laser for myopia: Comparison using an adaptive optics visual simulator. Arq Bras Oftalmol. 2014; 77:103-9.
19. Pérez-Vives C, Ferrer-Blasco T, Madrid-Costa D, García-Lázaro S, Montés-Micó R. Visual quality comparison of conventional and Hole-Visian implantable collamer lens at different degrees of decentering. Br J Ophthalmol. 2014; 98:59-64.
20. Madrid-Costa D, Ruiz-Alcocer J, García-Lázaro S, Albarrán-Diego C, Montés-Micó R. Visual performance of the Akreos Adapt AO intraocular lens in patients with different corneal profiles measured with an adaptive optics visual simulator. Br J Ophthalmol. 2012; 96:1099-103.
21. Ruiz-Alcocer J, Pérez-Vives C, Madrid-Costa D, López-Gil N, Montés-Micó R. Effect of simulated IOL tilt and decentration on spherical aberration after hyperopic LASIK for different intraocular lenses. J Refractive Surg. 2012; 28:327-34.
22. Rocha KM, Vabre L, Chateau N, Krueger RR. Expanding depth of focus by modifying higher-order aberrations induced by an adaptive optics visual simulator. J Cataract Refractive Surg. 2009; 35:1885-92.
23. Rocha KM, Vabre L, Harms F, Chateau N, Krueger RR. Effects of Zernike wavefront aberrations on visual acuity measured using electromagnetic adaptive optics technology. J Refractive Surg. 2007; 23:953-9.
24. Rouger H, Benard Y, Legras R. Effect of monochromatic induced aberrations on visual performance measured by adaptive optics technology. J Refractive Surg. 2010; 26:578-87.
25. Pérez-Vives C, Belda-Salmerón L, García-Lázaro S, Ferrer-Blasco T, Montés-Micó R. Optical and visual simulation of standard and modified spherical aberration implantable collamer lens post myopic LASIK surgery. Eur J Ophthalmol. 2014; 24:330-7.

26. Pérez-Vives C, Dominguez-Vicent A, García-Lázaro S, Ferrer-Blasco T, Montés-Micó R. Optical and visual quality comparison of implantable collamer lens and laser in situ keratomileusis for myopia using an adaptive optics visual simulator. Eur J Ophthalmol. 2013; 23:39-46.
27. Porter J, Queener H, Lin J, Thorn K, Awwal A, eds. Adaptive Optics for Vision Science: Principles, Practices, Design, and Applications. Hoboken,NJ:WileyInterscience; 2006.
28. Ruiz-Alcócer J, Madrid-Costa D, García-Lázaro S, Albarrán-Diego C, Ferrer-Blasco T. Visual simulation through an aspheric aberration-correcting intraocular lens in subjects with different corneal profiles using adaptive optics.ClinExpOptom. 2013; 96:379-84.
29. Rocha KM, Vabre L, Chateau N, Krueger RR. Enhanced visual acuity and image perception following correction of highly aberrated eyes using an adaptive optics visual simulator. J Refractive Surg. 2010; 26:52-6.
30. Godara P, Dubis AM, Roorda A, Duncan JL, Carroll J. Adaptive optics retinal imaging: Emerging clinical applications. Optom Vis Sci. 2010; 87:930-41.
31. Valeshabad AK, Wanek J, Grant P, et al. Wavefront error correction with adaptive optics in diabetic retinopathy. Optom Vis Sci. 2014; 91:1238-43.
32. Hofer H, Chen L, Yoon GY, Singer B, Yamauchi Y, Williams DR. Improvement in retinal image quality with dynamic correction of the eye's aberrations. Opt Express. 2001; 8:631-43.
33. Zawadzki RJ, Jones SM, Olivier SS, et al. Adaptive-optics optical coherence tomography for high-resolution and high-speed 3D retinal in vivo imaging. Opt Express. 2005; 13.
34. Fernández EJ, Manzanera S, Piers P, Artal P. Adaptive optics visual simulator. J Refractive Surg. 2002; 18:S634-8.
35. Doble N, Yoon G, Chen L, et al. Use of a microelectromechanical mirror for adaptive optics in the human eye. Opt Lett. 2002; 27:1537-9.
36. Yang B, Liang B, Liu L, et al. Contrast sensitivity function after correcting residual wavefront aberrations during RGP lens wear. Optom Vis Sci. 2014; 91:1271-7.
37. Li J, Xiong Y, Wang N, et al. Effects of spherical aberration on visual acuity at different contrasts. J Cataract Refractive Surg. 2009; 35:1389-95.
38. Rocha KM, Soriano ES, Chamon W, Chalita MR, Nosé W. Spherical Aberration and Depth of Focus in Eyes Implanted with Aspheric and Spherical Intraocular Lenses. A Prospective Randomized Study. Ophthalmology. 2007; 114:2050-4.
39. Morgan JIW. The fundus photo has met its match: Optical coherence tomography and adaptive optics ophthalmoscopy are here to stay. Ophthalmic Physiol Opt. 2016; 36:218-39.
40. Ramaswamy G, Devaney N. Pre-processing, registration and selection of adaptive optics corrected retinal images. Ophthalmic Physiol Opt. 2013; 33:527-39.
41. Roorda A. Applications of adaptive optics scanning laser ophthalmoscopy. Optom Vis Sci. 2010; 87:260-8.
42. Huang G, Qi X, Chui TYP, Zhong Z, Burns SA. A clinical planning module for adaptive optics SLO imaging. Optom Vis Sci. 2012; 89:593-01.
43. Chui TYP, Pinhas A, Gan A, et al. Longitudinal imaging of microvascular remodelling in proliferative diabetic retinopathy using adaptive optics scanning light ophthalmoscopy. Ophthalmic Physiol Opt. 2016; 36:290-302.
44. Chui TYP, VanNasdale DA, Burns SA. The use of forward scatter to improve retinal vascular imaging with an adaptive optics scanning laser ophthalmoscope. Biomed Opt Express. 2012; 3:2537-49.
45. Shahidi M, Blair NP, Mori M, Zelkha R. Optical section retinal imaging and wavefront sensing in diabetes.Optom Vis Sci. 2004; 81:778-84.
46. Piers PA, Manzanera S, Prieto PM, Gorceix N, Artal P. Use of adaptive optics to determine the optimal ocular spherical aberration. J Cataract Refractive Surg. 2007; 33:1721-6.
47. Atchison DA, Guo H, Fisher SW. Limits of spherical blur determined with an adaptive optics mirror. Ophthalmic Physiol Opt. 2009; 29:300-11.
48. Chen L, Kruger PB, Hofer H, Singer B, Williams DR. Accommodation with higher-order monochromatic aberrations corrected with adaptive optics. J Opt Soc Am A. 2006; 23:1-8.
49. Baskaran K, Rosén R, Lewis P, Unsbo P, Gustafsson J. Benefit of adaptive optics aberration correction at preferred retinal locus. Optom Vis Sci. 2012; 89:1417-23.
50. Applegate RA, Sarver EJ, Khemsara V. Are all aberrations equal? J RefractSurg. 2002; 18:S556-62.
51. Artal P, Chen L, Fernández EJ, Singer B, Manzanera S, Williams DR. Neural compensation for the eye's optical aberrations. J Vis. 2004; 4:281-7.
52. Chen L, Artal P, Gutierrez D, Williams DR. Neural compensation for the best aberration correction. J Vis. 2007; 7.
53. Lu F, Mao X, Qu J, Xu D, He JC. Monochromatic wavefront aberrations in the human eye with contact lenses. Optom Vis Sci. 2003; 80:135-41.
54. Porter J, Guirao A, Cox IG, Williams DR. Monochromatic aberrations of the human eye in a large population. J Opt Soc Am A. 2001; 18:1793-803.
55. Montés-Micó R, Belda-Salmerón L, Ferrer-Blasco T, Albarrán-Diego C, García-Lázaro S. On-eye optical quality of daily disposable contact lenses for different wearing times. Ophthalmic Physiol Opt. 2013; 33:581-91.
56. Guo H, Fallah HR, Dainty C, Goncharov AV. Subjective evaluation of intraocular lenses by visual acuity measurement using adaptive optics. Opt Lett. 2012; 37:2226-8.
57. Tabernero J, Piers P, Benito A, Redondo M, Artal P. Predicting the optical performance of eyes implanted with IOLs to correct spherical aberration. Invest Ophthalmol Vis Sci. 2006; 47:4651-8.

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