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The Effect of Aberrations and Scatter on Image Resolution Assessed by Adaptive Optics Retinal Section Imaging

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Abstract

The effect of increased high order wavefront aberrations on image resolution was investigated and the performance of adaptive optics (AO) for correcting wavefront error in the presence of increased light scatter was assessed in a model eye. An AO section imaging system provided an oblique view of a simulated model eye retina and incorporated a wavefront sensor and deformable mirror for measurement and compensation of wavefront aberrations. Image resolution was quantified by the width of a Lorentzian curve fitted to a laser line image. Wavefront aberrations were significantly reduced with AO resulting in improvement of image resolution. Increased coma and spherical aberrations adversely affected image resolution. In the presence of increased light scatter, correction of wavefront error and improvement in image resolution were achieved with AO. The findings of the current study suggest that AO imaging systems can potentially improve image resolution in aging and/or diseased eyes with increased aberrations and scatter.

Keywords

Adaptive Optics; Retinal Imaging; Aberrations; Scatter

Introduction

Retinal image resolution is affected by wavefront aberrations and intraocular light scatter that may be present in the optics of the eye. Improvement in retinal image resolution has been demonstrated by recently developed wavefront sensing technologies and adaptive optics (AO) in the form of a deformable mirror (DM) that measure and compensate for wavefront aberrations. Employment of these technologies to extend capabilities of retinal imaging systems can significantly impact the diagnosis and understanding of the pathophysiology of retinal diseases. In older and/or retinal-diseased subjects, wavefront aberrations^{1–6} and intraocular light scatter^{7–12} are elevated as compared to young healthy subjects.^{4, 5, 10–12} Therefore, it is important to know the effect of high levels of wavefront aberrations on retinal image resolution and evaluate the performance of AO to compensate for wavefront aberrations in the presence of increased light scatter.

Several retinal imaging techniques that incorporate AO have been recently developed. An AO ophthalmoscope has improved the resolution of retinal imaging by compensating for high order wavefront aberrations of the eye^{13–16} and allowed functional studies of photoreceptor cells in living human eyes.^{17–22} However, the AO ophthalmoscope has limited depth discrimination. The AO scanning laser ophthalmoscope (SLO) provides optical sectioning of the retina with

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improved depth resolution.²³⁻²⁸ Optical coherence tomography (OCT) has the highest depth resolution compared to all retinal imaging systems and with the addition of AO, improved lateral resolution has been demonstrated.²⁹ Currently, due to long image acquisition time, en face retinal imaging by OCT is prohibited, though research instruments are overcoming this limitation.^{30, 31} We have developed an optical section retinal imaging technique³² with high spatial resolution and depth resolution intermediate between that of SLO and OCT. Though our technique has lower depth resolution than OCT, it offers the advantages of higher image acquisition rate, better coverage for retinal thickness mapping, and flexibility in varying the incident laser wavelength to image fluorescence as well as reflectance. In the current study, AO was incorporated in our retinal section imaging system to determine the effect of increased high order wavefront aberrations and light scatter on image resolution.

Methods

Imaging Principle

The principle of retinal section imaging is similar to slitlamp biomicroscopy. A laser beam is projected at an oblique angle to provide an angled view through the depth of the retina (Fig 1). An optical section image of the retina is generated from reflection and/or scattering of the laser light from the retinal surfaces. Since the incident laser beam is not coaxial with the viewing axis, structures at various depths appear laterally displaced on the optical section image according to their depth location. Due to the line focus of the laser beam on the retina, the optical section image is bounded by 2 laterally displaced vertical lines, corresponding to the anterior and posterior retinal surfaces. In human eyes, the anterior and posterior surfaces correspond to the vitreoretinal interface (inner limiting membrane) and chorioretinal interface (retinal pigment epithelium-choroid complex), respectively.^{33, 34} According to Rayleigh's criterion,³⁵ two peaks that are separated by the diameter of a diffraction limited spot can be resolved. Accordingly, image resolution, or the ability to distinguish structures that are laterally displaced, is determined by the width of the laser line. The longitudinal resolution of our technique is determined by the ratio of the width of the laser line and the angle between the incident laser and viewing axis.

Instrumentation

A bench-top version of our previously established prototype retinal section imaging system¹² was developed that incorporated AO to compensate for measured wavefront aberrations. The schematic diagram of the AO section imaging system is shown in Fig 2. The optical imaging system consisted of four main components: laser delivery, wavefront sensing, wavefront error correction, and retinal section imaging. A spatially-filtered collimated diode laser beam (LaserMate Group, Pomona, California) at a wavelength of 532 nm was projected at a 7° oblique angle and focused on the model retina by the optics of the model eye. Light reflected/scattered from the model retina produced a distorted wavefront at the pupil. For wavefront sensing, the wavefront was sampled using a lenslet array (AOA Inc, Cambridge, Massachusetts) placed at a plane conjugate with the pupil of the model eye. The lenslet consisted of a 65×65 array of lenses each with a diameter of 400 microns and a focal length of 24 mm. The resulting Shack-Hartmann (SH) image of a two-dimensional array of spots was acquired by a charge-coupled device (CCD) camera (Sony, Japan). For wavefront error correction, a microelectromechanical system (MEMS) DM (Boston Micromachines Inc, Boston, Massachusetts) was placed at a plane conjugate with the pupil of the model eye. The DM was 3.3×3.3 mm² and consisted of a 12×12 array of elements with 0.3 mm spacing and a stroke of ±1 micron. For section imaging, a cylindrical lens was placed in the laser delivery path to focus a laser line on the model retina. A section image was captured by a second CCD camera (Texas Instruments, Dallas, Texas).

Model Eye

The AO section imaging system was tested using a previously developed model eye, with dimensions similar to the human eye.³⁶ A schematic diagram of the model eye is shown in Fig 3. The model eye was fitted with a simulated cornea with a radius of curvature of 7.9 mm and pupil of 6 mm diameter. The lens of the model eye consisted of a small transparent hollow glass cuvette with a path length of 2.5 mm that could be filled with water, independently from the simulated vitreous cavity also filled with water. The walls of the cuvette-lens were made of flat pieces of glass with a thickness of 0.25 mm and an index of refraction of approximately 1.5. The model retina was simulated by a transparent plastic ruler with a thickness of 500 microns. Filling the cuvette-lens with water represented a no scatter condition, while increased light scatter was simulated by filling the cuvette-lens with water solutions containing various concentrations of 1 micron diameter polystyrene microbeads (Polyscience, Inc., Warrington, Pennsylvania). For imaging, the model eye was positioned in front of the instrument. An aerial lens placed in front of the eye allowed imaging of the model retina without use of a contact lens. Only defocus (not astigmatism) was corrected by adjustment of the aerial lens. The aerial lens was positioned to produce the sharpest image, intermediate between the best focus of the anterior and posterior lines. Since the focus was evaluated subjectively by viewing the section image on a video monitor, low order wavefront aberrations including residual defocus were likely present.

Wavefront Error Measurement and Correction

Software was developed to reconstruct the wavefront aberration function by computing the difference between the centroid positions of SH spots (Fig 4A) and a uniform spot pattern representing a non-distorted plane wave. The centroid detection algorithm consisted of first centering a bounding box (15×15 pixels) on the maximum pixel intensity of each SH spot. The minimum pixel intensity within each box was then subtracted from each pixel intensity to ensure the centroid calculation was not biased by non-zero intensity values outside of the SH spot boundary. The x and y coordinates of SH spot centroids were determined using a center of mass calculation. The difference between centroid positions of the SH spots and the uniform spot pattern was calculated, corresponding to the local gradients of the wavefront at each sampling spot. The wavefront aberration function was determined as the sum of 2nd to 7th order Zernike polynomials using a least-squares method, as previously described.¹² As illustrated in Fig 4B, wavefront error was measured for a 6 mm pupil by the root mean square (RMS) of the Zernike coefficients (2nd to 7th), separately for each Zernike order, following published standards for reporting optical aberrations of the eye.³⁷

To correct wavefront error, software was developed to automate a calibration procedure to determine the positions of the DM's elements in the pupil plane and a closed loop control procedure was used to minimize the RMS wavefront error. During the calibration procedure, a fixed deflection level was applied to a DM's actuator and the resulting radial movement of the neighboring SH spots towards the active actuator was recorded. The projected intersection of the linear paths of the SH spots was used to estimate the position of the active actuator. This procedure was repeated for each actuator of the DM until all positions were known. Control of the DM was based on a previously described technique.¹³ Wavefront correction was attained with closed feedback control. During each loop, the wavefront aberration function for a 6 mm pupil was determined from a SH image. The mirror shape was then conformed to correct 15% of the wavefront error by mapping the wavefront aberration onto the DM actuator array, resulting in a smooth and gradual decrease of wavefront error. This procedure was repeated 30 times to ensure the RMS wavefront error was minimized and reached convergence. The correction rate of the AO system was approximately 21 Hz and typically it took approximately 10 iterations (476 msec) to minimize the wavefront error. Improvement was assessed by comparing the RMS wavefront error before and after AO correction.

Image Resolution

A representative AO corrected section image of the model retina is shown in Fig 5A. The image is composed of laterally displaced vertical lines corresponding to light reflected/scattered from the anterior and posterior surfaces of the model retina. Reflected light from the anterior surface originated predominately from the front transparent surface of the model retina. On the posterior surface, light was reflected and scattered from the non-transparent surface to which the transparent plastic (model retina) was attached. Due to reflection and scattering from the non-transparent surface, the width and intensity of the posterior line appeared larger than the anterior line. Image resolution was determined based on the width of the anterior line. To isolate the anterior surface, intensity profiles were derived from a region on the model retina that was devoid of light returned from the posterior surface due to a black tic mark on the plastic ruler. This region was divided into 4 equal areas, each area 10×80 pixels in the vertical and horizontal dimension, respectively (Fig 5A). In each area, an intensity profile was derived by vertical averaging and then normalized by subtracting the minimum pixel intensity and dividing by the difference between the maximum and minimum pixel intensities of the profile. The normalized intensity profile was fitted with a Lorentzian curve (Fig 5B) and the full width at half maximum (FWHM) of the curve was calculated. Image resolution was estimated by the mean FWHM of the 4 intensity profiles. The FWHM measured in pixels units was multiplied by the ratio of the CCD camera pixel size and imaging magnification factor to provide image resolution in units of microns on the model retina image plane.

Aberrations and Image Resolution

Image resolution was assessed while systematically varying the level and type of aberrations with AO. After first correcting wavefront aberrations with the DM, 10 levels of aberrations (-0.5 to 0.5 microns at 0.1 micron intervals) for 3 high order Zernike modes (C7, C8, C12) corresponding to vertical coma, horizontal coma, and spherical aberrations were introduced onto the DM. The effect of increased coma and spherical aberrations on image resolution was studied since these high order aberrations can be moderately increased in young healthy subjects³⁸⁻⁴¹ and are significantly increased in subjects with age- and/or disease-related cataracts.^{4, 5, 10} Three section images were captured for each aberration level added to each Zernike mode. The mean and standard deviation (SD) of the FWHM of the anterior Lorentzian fitted curve were calculated.

Scatter and Image Resolution

Image resolution was assessed while incrementally increasing the number of light scattering particles in the model eye. Five polystyrene dilutions were made with particle concentrations ranging between 0% (water) and 0.01% (weight/volume). For each dilution, solutions were well mixed and then sequentially injected into the cuvette-lens of the model eye to vary the light scatter. Transmission of laser light at the wavelength of 532 nm through the cuvette-lens was measured using an optical power meter (ThorLabs, Newton, New Jersey). The light transmission results obtained with each dilution are shown in Table 1. Transmissions ranged between 78% and 25%, corresponding to scattering particle concentrations between 0% and 0.01%, respectively. The measured light transmission of the cuvette-lens, in the absence of scattering particles, is accounted for by an approximate 10% light loss at each glass surface. This range of scattering particle concentration was selected to represent the transmission of the crystalline lens of human eyes which varies between approximately 85% and 30% for people in the age range of 20 and 90 years.^{42, 43} Three section images were captured with the cuvette-lens filled with each dilution, before and after wavefront error correction with AO. The mean and SD of the FWHM of the anterior Lorentzian fitted curve were determined for each level of scatter.

Results

The mean and SD of the RMS wavefront error for each Zernike order, measured in the model eye, before and after wavefront error correction with AO are shown in Fig 6. Before AO correction, the RMS wavefront error for 2nd, 3rd, and 4th orders were 0.34 ± 0.01 , 0.23 ± 0.02 , and 0.09 ± 0.02 microns (N = 11), respectively. Since only the defocus term was subjectively (and not optimally) corrected before AO, astigmatism and residual defocus contributed to the measured 2nd order wavefront error. Similar levels of low order aberrations have been reported in human eyes, despite standard refractive error correction.¹³ For Zernike orders 5 and above, the RMS wavefront error was below 0.07 microns. After AO correction, a reduction in RMS wavefront error was observed for all Zernike orders up to 7th order to values less than 0.04 microns. The total RMS wavefront error measured before and after AO correction were 0.44 ± 0.02 and 0.07 ± 0.01 microns (N = 11), respectively. The section image acquired before wavefront error correction (Fig 7A) had lower resolution as compared to the AO corrected image (Fig 7B). The FWHM of the Lorentzian fitted curves before and after AO correction were 49.3 ± 2.7 and 21.2 ± 2.4 microns (N = 11), respectively.

The relationship between image resolution (FWHM) and induced levels of high order aberrations is shown in Fig 8. An increase in the AO corrected FWHM was observed as spherical and horizontal coma aberrations were individually and incrementally increased to ± 0.5 microns. The FWHM remained relatively constant with increased vertical coma aberration. The increase in the FWHM was slightly larger for horizontal coma aberration of positive sign as compared to aberrations of the same magnitude and of opposite sign. The FWHM displayed a greater increase with addition of negative spherical aberrations than positive spherical aberration of the same magnitude. Approximately a 5-fold increase in the FWHM was observed with the addition of -0.5 microns of spherical aberration.

Typical SH images obtained under a no scatter condition and 0.01% scattering particle concentration are shown in Fig 9A and Fig 9B, respectively. A decrease in image contrast and intensity was observed for 0.01% scattering particle concentration as compared to the image acquired under a no scatter condition. The relationship between RMS wavefront error measurement and scattering particle concentration (or equivalently, light scatter level) is shown in Fig 9C. The measured RMS wavefront error before AO correction remained relatively constant at all light scatter levels and was minimally affected by the scattering particle concentration. The variabilities of the wavefront error measurement under a no scatter condition and increased scatter conditions were similar. After AO correction, RMS wavefront error was consistently reduced, indicating that wavefront error correction was not affected by the presence of scattered light at the levels introduced in this study.

Typical section images acquired before and after AO correction with 0.01% scatter particle concentration are shown in Fig 7C and Fig 7D, respectively. Image contrast and intensity were reduced under increased light scatter conditions as compared to images acquired under a no scatter condition (Fig 7A and Fig 7B). The relationship between the FWHM and scattering particle concentrations is shown in Fig 10. Before AO correction, the FWHM was relatively constant for all scattering particle concentrations and similar to the FWHM obtained under a no scatter condition. After AO correction, the FWHM was reduced under all light scatter levels to a similar FWHM value attained under a no scatter condition, indicating improvement in image resolution was minimally affected by the presence of increased light scatter.

Discussion

Image resolution can be adversely affected by the presence of increased wavefront aberrations and light scatter. In young healthy subjects, compensation for high order wavefront aberrations

(3rd and above) with the use of AO has been demonstrated, resulting in imaging of retinal tissue at the cellular level.^{13, 14} Since older and/or retinal-diseased subjects have increased high order wavefront aberrations and intraocular light scatter as compared to young healthy subjects,^{4, 5, 10, 11} we investigated the performance of AO to improve image resolution by compensating for wavefront aberrations in the presence of different levels of light scatter in a model eye. By using AO, wavefront aberrations of the model eye were significantly reduced and image resolution was improved, as observed by a more than 2-fold reduction in the FWHM of the Lorentzian fitted curve. In the model eye, image resolution was degraded with increased high order wavefront aberrations (horizontal coma and spherical) and improved with AO correction of the wavefront error in the presence of increased light scatter.

Increased high order wavefront aberrations had a considerable affect on image resolution. Nearly a 5-fold decrease in image resolution was observed with the addition of -0.5 microns of spherical aberration for a 6 mm pupil. Reduction in image resolution was related to the magnitude of horizontal coma and spherical aberrations. This finding is attributed to the fact that horizontal coma and spherical aberrations contain large gradients in the horizontal direction which tend to spread light away from the vertical line shape of the section image, thus increasing the FWHM. Increased vertical coma aberrations affected the FWHM measurements to a lesser degree, because of the small horizontal gradient across the pupil. Spherical aberrations of negative sign were observed to influence image resolution to a greater degree, as compared to aberrations of the same magnitude and opposite sign. According to a previously published study,⁴⁴ combined defocus and spherical aberration of positive sign produce better image quality as compared to combined defocus and spherical aberration of opposite sign due to the strong interaction of Zernike modes. The observed lower image resolution by addition of negative spherical aberration may be partially due to the presence of residual defocus in our system. Additionally, increased spherical aberration by the DM may have introduced changes in other Zernike modes. This possibility is supported by the fact that experimentally measured Zernike modes after superposition of spherical aberration on the wavefront corrected DM shape displayed higher astigmatism and coma aberrations with negative spherical aberration as compared to positive spherical aberration of the same magnitude. Further studies in human eyes are beneficial to establish the source of the observed asymmetry.

The presence of light scatter did not influence wavefront aberration measurements, nor did it limit the capability of AO to correct wavefront error and improve image resolution. The finding that wavefront aberration measurements did not change with increasing scattering particle concentrations is consistent with a previous study that reported aberration measurements were independent of light scatter.⁴⁵ In the current study, scattering particle concentrations in the range of 0% - 0.01% (transmission of 78 -25%) were studied, corresponding to lens transmission of people between approximately 20 and 90 years of age.^{42, 43} Although increased scattering particle concentrations reduced light transmission through the cuvette-lens, the scattering process of the microbead solution may be more homogeneous than the scattering process that occurs in a real human lens. Therefore, further studies are needed to evaluate the performance of the system in aging and cataractous human eyes.

Since increased light scatter reduces the contrast and signal to noise (SNR) ratio of the SH image, it can adversely affect the accuracy of the wavefront error measurements. To investigate the affect of increased light scatter on wavefront error measurement, the low SNR condition created by the highest light scatter level (scattering particle concentration of 0.01%) was simulated by placing a neutral density filter in front of the SH imaging optics. A high SNR condition was replicated by removing the filter. RMS wavefront error measurements obtained under the simulated low and high SNR conditions were similar. The robustness of the centroid detection algorithm under a low SNR condition was examined. The average variability

(standard deviation) of the x and y coordinates of the centroid positions at low SNR (highest light scatter level condition) were 0.14 and 0.10 pixels ($N = 136$), respectively. The average variability of the x and y coordinates of the centroid positions at high SNR (similar to no scatter condition) were 0.13 and 0.09 pixels ($N = 136$), respectively. The similarity between the two variabilities suggests that the centroid detection algorithm was minimally influenced by the range of light scatter levels introduced in the study. Under a low SNR condition, the FWHM of the Lorentzian fitted curve was effectively reduced to the same FWHM value obtained under a high SNR condition, indicating the AO performance for correcting wavefront error was not limited due to increased noise.

In older people, both wavefront aberrations and light scatter in the eye are known to be increased. In the current study, under increased light scatter conditions, high order wavefront aberrations were effectively minimized with AO and image resolution was improved in the model eye, suggesting that AO systems can potentially improve image resolution in aging eyes.

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Figure 1.

Principle of the retinal section imaging technique. An optical section image is generated by projecting a laser line onto the retina at an oblique angle and viewing the reflection and/or scattering of the laser light from the anterior and posterior retinal surfaces. Due to the angle between the incident laser and viewing axis, structures at various depths appear laterally displaced.

Figure 2.

Schematic diagram of the adaptive optics retinal section imaging system. An optical section image is acquired while wavefront aberrations are measured by a Shack-Hartmann wavefront sensor. Wavefront error is corrected with the use of a deformable mirror (DM).

Figure 3. Schematic diagram of the model eye. The model eye contained a cornea, lens consisting of a transparent glass cuvette, vitreous cavity, and a transparent retina.

Figure 4.

(A) A typical Shack-Hartmann image for a 6 mm pupil obtained in a model eye; (B) Root mean square (RMS) wavefront error for each Zernike order.

Figure 5.

(A) A typical AO corrected section image acquired in a model eye. Light reflected/scattered from the anterior (left) and posterior (right) surfaces are depicted by vertical lines. In the upper right portion of the section image, light returned from the posterior surface is obscured (black notch) due to the tick mark on the model retina. Intensity profiles across the anterior line were derived from 4 areas identified by white rectangles. B) A typical intensity profile derived from one area in (A) was fitted with a Lorentzian curve.

Figure 6.

The root mean square (RMS) wavefront error for each Zernike order before (triangle) and after (rectangle) AO correction for a 6 mm pupil. The total RMS wavefront error before and after correction were 0.44 ± 0.02 and 0.07 ± 0.01 ($N = 11$) microns, respectively.

Figure 7.

Section images acquired under no scatter condition (A) before and (B) after AO correction. Section images acquired with a scattering particle concentration of 0.01% in the cuvette-lens (C) before and (D) after AO correction. The left and right vertical lines on each section image correspond to light returned from the anterior and posterior surfaces, respectively.

Figure 8.

The relationship between the full width at half maximum (FWHM) of the Lorentzian fitted curve and the level of high order aberrations: vertical coma (triangle), horizontal coma (circle), spherical (rectangle).

Figure 9.

Typical Shack-Hartmann (SH) images acquired in a model eye with 6 mm pupil (A) under no scatter condition and (B) with scattering particle concentration of 0.01% in the cuvette-lens. (C) The relationship between the total root mean square (RMS) and scattering particle concentration before (triangle) and after (rectangle) AO correction.

Figure 10. The relationship between the full width at half maximum (FWHM) of the Lorentzian fitted curve and scattering particle concentration before (triangle) and after (rectangle) AO correction.

Table 1

Scattering particle concentrations (weight/volume) and the corresponding percent light transmission at a wavelength of 532 nm.

Particle Concentration (%)	Transmission (%)
0.0000	78
0.0025	58
0.0050	39
0.0075	30
0.0100	25