In-vivo digital wavefront sensing using swept source OCT

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Abstract: Sub-aperture based digital adaptive optics is demonstrated in a fiber based point scanning optical coherence tomography system using a 1060 nm swept source laser. To detect optical aberrations in-vivo, a small lateral field of view of ~150 x 150 μm² is scanned on the sample at a high volume rate of 17 Hz (~1.3 kHz B-scan rate) to avoid any significant lateral and axial motion of the sample, and is used as a “guide star” for the sub-aperture based DAO. The proof of principle is demonstrated using a micro-beads phantom sample, wherein a significant root mean square wavefront error (RMS WFE) of 1.48 waves (> 1 μm) is detected. In-vivo aberration measurement with a RMS WFE of 0.33 waves, which is ~5 times higher than the Marechal’s criterion of 1/14 waves for the diffraction limited performance, is shown for a human retinal OCT. Attempt has been made to validate the experimental results with the conventional Shack-Hartmann wavefront sensor within reasonable limitations.

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References and links
1. D. T. Miller, J. Qu, R. S. Jonnal, and K. E. Thorn, “Coherence gating and adaptive optics in the eye,” Proc. SPIE 4956, 65–72 (2003).
2. B. Herman, E. J. Fernández, A. Unterhuber, H. Sattmann, A. F. Fercher, W. Drexler, P. M. Prieto, and P. Artal, “Adaptive-optics ultrahigh-resolution optical coherence tomography,” Opt. Lett. 29(18), 2142–2144 (2004).
3. E. J. Fernández, B. Povazay, B. Hermann, A. Unterhuber, H. Sattmann, P. M. Prieto, R. Leitgeb, P. Ahnelt, P. Artal, and W. Drexler, “Three-dimensional adaptive optics ultrahigh-resolution optical coherence tomography using a liquid crystal spatial light modulator,” Vision Res. 45(28), 3432–3444 (2005).
4. R. J. Zawadzki, S. M. Jones, S. S. Olivier, M. Zhao, B. A. Bower, J. A. Izatt, S. Choi, S. Laut, and J. S. Werner, “Adaptive-optics optical coherence tomography for high-resolution and high-speed 3D retinal in vivo imaging,” Opt. Express 13(21), 8532–8546 (2005).
5. D. Merino, C. Dainty, A. Brud?, and A. G. Podoleanu, “Adaptive optics enhanced simultaneous en-face optical coherence tomography and scanning laser ophthalmoscopy,” Opt. Express 14(8), 3345–3353 (2006).
6. E. J. Fernández, B. Hermann, B. Povazay, A. Unterhuber, H. Sattmann, B. Hofer, P. K. Ahnelt, and W. Drexler, “Ultrahigh resolution optical coherence tomography and panceorrection for cellular imaging of the living human retina,” Opt. Express 16(15), 11083–11094 (2008).
7. F. A. Vera-Díaz, and N. Doble, The Human Eye and Adaptive optics (INTECH Open Access Publisher, 2012).
8. F. Felberer, J.-S. Kraisamer, B. Baumann, S. Zetter, U. Schmidt-Erfurth, C. K. Hitzenberger, and M. Pircher, “Adaptive optics SLO/OCT for 3D imaging of human photoreceptors in vivo,” Biomed. Opt. Express 5(2), 439–456 (2014).
9. D. T. Miller, O. P. Kocaoglu, Q. Wang, and S. Lee, “Adaptive optics and the eye (super resolution OCT),” Eye (Lond.) 25(3), 321–330 (2011).
10. R. J. Zawadzki, A. G. Capps, K. Dae Yu, A. Panorigas, S. B. Stevenson, B. Hamann, and J. S. Werner, “Progress on Developing Adaptive Optics–Optical Coherence Tomography for In Vivo Retinal Imaging: Monitoring and Correction of Eye Motion Arts,” IEEE J. Sel. Top. Quantum Electron. 20(2), 322–333 (2014).
11. Y. Zhang, J. Rha, R. Jonnal, and D. Miller, “Adaptive optics parallel spectral domain optical coherence tomography for imaging the living retina,” Opt. Express 13(12), 4792–4811 (2005).
12. Y. Zhang, B. Cense, J. Rha, R. S. Jonnal, W. Gao, R. J. Zawadzki, J. S. Werner, S. Jones, S. Olivier, and D. T. Miller, “High-speed volumetric imaging of cone photoreceptors with adaptive optics spectral-domain optical coherence tomography,” Opt. Express 14(10), 4380–4394 (2006).

13. R. K. Tyson, Principles of Adaptive Optics (CRC press, 2015).

14. W. Drexler, M. Liu, A. Kumar, T. Kamali, A. Unterhuber, and R. A. Leitgeb, “Optical coherence tomography today: speed, contrast, and multimodality,” J. Biomed. Opt. 19(7), 071412 (2014).

15. R. A. Leitgeb, A. Kumar, and W. Drexler, “Chapter 8 Frequency Domain Full-Field Optical Coherence Tomography,” in Handbook of Full-Field Optical Coherence Microscopy (Pan Stanford Publishing Pte. Ltd., 2016), pp. 303–322.

16. S. G. Adie, B. W. Graf, A. Ahmad, P. S. Carney, and S. A. Boppart, “Computational adaptive optics for broadband optical interferometric tomography of biological tissue,” Proceedings of the National Academy of Sciences (2012).

17. Y.-Z. Liu, N. D. Shemonski, S. G. Adie, A. Ahmad, A. J. Bower, P. S. Carney, and S. A. Boppart, “Computed optical interferometric tomography for high-speed volumetric cellular imaging,” Biomed. Opt. Express 5(9), 2988–3000 (2014).

18. N. D. Shemonski, F. A. South, Y.-Z. Liu, S. G. Adie, P. S. Carney, and S. A. Boppart, “Computational high-resolution optical imaging of the living human retina,” Nat. Photonics 9(7), 440–443 (2015).

19. D. Hillmann, H. Spahr, C. Hain, H. Sudkamp, G. Franke, C. Pfäffle, C. Winter, and G. Hüttmann, “Aberration-free volumetric high-speed imaging of in vivo retina,” arXiv preprint arXiv:1605.03747 (2016).

20. A. Kumar, W. Drexler, and R. A. Leitgeb, “Subaperture correlation based digital adaptive optics for full field optical coherence tomography,” Opt. Express 21(9), 10850–10866 (2013).

21. A. Kumar, A. R. Tumlinson, and R. Leitgeb, “Systems and methods for sub-aperture based aberration measurement and correction in interferometric imaging (US9247874 B2),” (Google Patents, 2014).

22. A. Kumar, T. Kamali, R. Platzer, A. Unterhuber, W. Drexler, and R. A. Leitgeb, “Anisotropic aberration correction using region of interest based digital adaptive optics in Fourier domain OCT,” Biomed. Opt. Express 6(4), 1124–1134 (2015).

23. A. Kumar, W. Drexler, and R. A. Leitgeb, “Numerical focusing methods for sub-aperture full field OCT: a comparison based on a common signal model,” Opt. Express 22(13), 16061–16078 (2014).

24. S. G. Adie, N. D. Shemonski, B. W. Graf, A. Ahmad, P. S. Carney, and S. A. Boppart, “Guide-star-based computational adaptive optics for broadband interferometric tomography,” Appl. Phys. Lett. 101(22), 221117 (2012).

25. J. R. Fienup and J. J. Miller, “Aberration correction by maximizing generalized sharpness metrics,” J. Opt. Soc. Am. A 20(4), 609–620 (2003).

26. S. T. Thurman and J. R. Fienup, “Phase-error correction in digital holography,” J. Opt. Soc. Am. A 25(4), 983–994 (2008).

27. N. D. Shemonski, S. G. Adie, Y.-Z. Liu, F. A. South, P. S. Carney, and S. A. Boppart, “A computational approach to high-resolution imaging of the living human retina without hardware adaptive optics,” Proc. SPIE 9307, 930710 (2015).

28. D. Hillmann, H. Spahr, C. Pfäffle, H. Sudkamp, G. Franke, and G. Hüttmann, “In vivo optical imaging of physiological responses to photostimulation in human photoreceptors,” arXiv preprint arXiv:1605.02959 (2016).

29. D. J. Fechtig, L. Ginner, A. Kumar, M. Pircher, T. Schmoll, L. M. Wurster, W. Drexler, and R. A. Leitgeb, “Retinal photoreceptor imaging with high-speed line-field parallel spectral domain OCT (Conference Presentation),” in SPIE BIOS (International Society for Optics and Photonics, 2016), pp. 969704–969704–969701.

30. N. D. Shemonski, S. S. Ahn, Y.-Z. Liu, F. A. South, P. S. Carney, and S. A. Boppart, “Three-dimensional motion correction using speckle and phase for in vivo computed optical interferometric tomography,” Biomed. Opt. Express 5(12), 4131–4143 (2014).

31. L. Ginner, C. Blatter, D. Fechtig, T. Schmoll, M. Gröschl, and R. Leitgeb, “Wide-Field OCT Angiography at 400 KHz Utilizing Spectral Splitting,” Photonics 1(4), 369–379 (2014).

32. D. Nankivil, A.-H. Dhalla, N. Gahm, K. Shia, S. Farsiu, and J. A. Izatt, “Coherence revival multiplexed, buffered swept source optical coherence tomography: 400 KHz imaging with a 100 kHz source,” Opt. Lett. 39(13), 3740–3743 (2014).

33. W. Choi, B. Potsaid, V. Jayaraman, B. Baumann, I. Grulkowski, J. J. Liu, C. D. Lu, A. E. Cable, D. Huang, J. S. Duker, and J. G. Fujimoto, “Phase-sensitive swept-source optical coherence tomography imaging of the human retina with a vertical cavity surface-emitting laser light source,” Opt. Lett. 38(3), 338–340 (2013).

34. R. Poddar, D. Y. Kim, J. S. Werner, and R. J. Zawadzki, “In vivo imaging of human vasculature in the chorioretinal complex using phase-variance contrast method with phase-stabilized 1-μm swept-source optical coherence tomography,” J. Biomed. Opt. 19(12), 126010 (2014).

35. B. Potsaid, B. Baumann, D. Huang, S. Barry, A. E. Cable, J. S. Schuman, J. S. Duker, and J. G. Fujimoto, “Ultrahigh speed 1050nm swept source/Fourier domain OCT retinal and anterior segment imaging at 100,000 to 400,000 axial scans per second,” Opt. Express 18(19), 20029–20048 (2010).

36. ANSI, “American National Standard for Safe Use of Lasers (ANSI Z136.1),” Laser Institute of America (2014).

37. A. Y. Van Heugten, and D. S. Durrie, “Integrated surgical microscope and wavefront sensor (US 20110267579 A1),” (Google Patents, 2011).
1. Introduction

Hardware based adaptive optics (AO) has been successfully combined with optical coherence tomography (OCT) to achieve high lateral resolution in combination with high axial resolution provided by OCT and to improve signal to noise ratio (SNR) [1–10]. Visualization of cone photoreceptors in 3-D has been successfully demonstrated using AO-OCT [4, 8, 11, 12]. AO commonly uses Shack-Hartmann wavefront sensor (SH-WFS) for wavefront aberration detection, deformable mirror or spatial light modulator (SLM) as wavefront corrector (WFC) to compensate for wavefront aberration, and a control system working in a feedback loop to set-up communication between WFS and WFC [13]. Successful implementation of AO in any optical system is always an engineering challenge, and often makes the overall system complex and economically expensive.

OCT being an interferometric imaging technique provides access to phase information. Especially OCT working in Fourier (spectral) domain inherently offers complex field information that encodes phase of the wavefront due to the involved data processing step of performing 1-D Fast Fourier transform (FFT) along the spectral dimension to get depth information [14, 15]. This phase information can be used in digital adaptive optics (DAO) techniques to correct optical aberration in the post processing step to obtain diffraction-limited space invariant lateral resolution throughout the image volume [16–24]. Thus, the need for hardware based AO can be eliminated, which in turn can reduce the system complexity and economical cost. Conventional DAO uses optimization based algorithms to assess and improve the image quality based on sharpness metric [16–18, 25, 26]. The coefficients of the phase correction function are varied in an iterative manner until image sharpness meets the desired criteria. A DAO approach using a sharpness maximization based on the use of a guide star has been shown to achieve more robust and superior performance in terms of image quality improvement [24]. Recently, this approach was used to computationally correct higher order ocular aberrations in en-face OCT image of living human retina in order to visualize photoreceptors [18, 27].

Kumar et al. demonstrated a sub-aperture correlation based DAO method, which is the digital equivalent of SH WFS, to achieve near diffraction-limited performance in full field swept source (FF SS) OCT [20]. The method is described in detail in the previous work [20] and it again briefly described in the method section. The advantage of this method is that, unlike other optimization based techniques, it is non-iterative in nature and it does not require a priori knowledge of any system parameters such as wavelength, focal length, numerical aperture (NA) or detector pixel size [20]. This method was also extended to region of interest (ROI) based aberration correction in order to achieve diffraction-limited lateral resolution beyond the iso-planatic patch in high resolution point scanning spectral domain (SD) OCT with a NA of 0.6 [22].

DAO correction has already been successfully demonstrated for ex-vivo and in-vivo biological tissue and human retina OCT images [18, 20, 22, 28]. However, a high volume rate of more than 10 Hz is required for in-vivo OCT imaging to avoid any significant sample motion and maintain the phase stability necessary for any successful implementation of DAO [18]. Hence, in-vivo implementation has been only shown using high speed en-face time domain (TD) OCT and full field (FF) SS OCT achieving a corresponding 10 Hz and 180 Hz volume rate respectively [18, 19, 28], or recently with line field (LF) OCT [29]. In the present
work, a fiber based point scanning SS OCT is used to scan a small lateral field of view (FOV) of ~150 × 150 μm² on the sample at an OCT volume rate of 17 Hz. It is shown that this small FOV can be used as a guide star to detect optical aberrations introduced by the system and the sample using the sub-aperture based DAO [20]. To our knowledge, this is the first DAO implementation in a point scanning SS OCT system. In-vivo aberration measurement is also shown for a human retinal OCT. Attempt has been made to validate the experimental results with the conventional SH-WFS within reasonable limitations. It is also shown that SH-WFS does not detect the same wavefront error as captured in OCT, which is due to the difference in detection path and method.

2. Methods

The experimental set-up consists of a fiber based point scanning OCT system, as shown in Fig. 1, using a swept source laser (SSL) (AXSUN Tech., λ₀ = 1060 nm, Δλ = 110 nm) with unidirectional wavelength sweep rate of 100 kHz with about 48 percent duty cycle. The measured axial resolution is ~5 μm in the tissue. The light from the SSL is split into the sample and the reference arm using a 50/50 coupler. The light reflected back from the sample is coupled back into the same coupler, whereas the light reflected from the retro-reflector in the reference arm is coupled into a 99/1 coupler. About 50 percent of the light from the sample and ~99 percent of the light from the reference arm is transferred to a 50/50 coupler just before the dual balance detector. The interference signal is detected by a dual balanced detector (DBD) (Thorlabs Inc., PDB430C) and digitized at a rate of 250 M samples/s using a 12 bit analogue to digital converter (Alazartech Inc., ATS9360). The sample arm of the OCT setup is equipped with a X-Y galvo-scanner (GS) (Cambridge Technology) to scan a lateral FOV. OCT data consisting of 400( )×400( ) lateral pixels and 1280 spectral (λ) pixels is acquired at a volume rate of ~0.6 Hz. By reducing the lateral FOV to 75( )×75( ) pixels, a volume rate of 17 Hz is achieved with the fast axis of the galvo-scanner in the sample arm running at 1.3 kHz. The waveform used for running the galvo-scanner is a linear ramp function (80 percent duty cycle) with an exponential decay. At this fast scanning speed, any significant lateral and axial motion of the sample, especially living human eye, can be avoided. Any phase instability due to residual axial motion can then be compensated numerically as described by Shemonski et al. [30], after which the acquired OCT data becomes phase stable for in-vivo DAO implementation. The use of two multiplexed lasers, coherence revival and optical buffering in combination with two spots illumination have been demonstrated to achieve 400 kHz sweep rate [31, 32]. At such high sweep rate, a B-scan rate of ~5.3 kHz and a volume rate of ~71 Hz can be achieved for lateral FOV of 75( )×75( ) pixels. This would require the use of high speed resonant scanner instead of galvo-scanners. Also, realization of high sweep rate of 400 kHz with the standard 100 kHz SSL often adds to the hardware complexity of the system and extra care needs to be taken to ensure that the system is phase stable [33–35]. However, the main aim of the presented research is to demonstrate that a simple standard phase stable SS OCT system can be used as a wavefront sensing instrument that utilizes the DAO approach. The current system using a standard SSL at 100 kHz sweep rate was sufficient to demonstrate the proof of principle.

The measured sensitivity of the system is 95 dB with 1.7 mW power on the sample. Note that this power is lower than the maximum permissible exposure (MPE) of 1.93 mW at 1060 nm wavelength [36]. The sample arm is also equipped with SH-WFS placed at the Fourier plane of the imaging system. For measurements using SH-WFS, a double path configuration with same 1060 nm SSL is used in case of microbeads phantom sample, whereas a configuration with different illumination and detection path using 840 nm SLD is used in case of living human eye for reasons described below. Measurements using SH-WFS were done immediately after OCT measurements with galvo-scanners fixed at the middle position of the
scanning pattern. SH-WFS measurements are used as reference to validate our experimental wavefront measurements obtained using sub-aperture based DAO, within some reasonable physical limitations.

First the proof of principle study was done for defocus correction using a phantom sample consisting of a single layer of micro beads with mean diameter of ~10 μm. The beam was focused on the sample using an objective lens (Thorlabs, LSM02-BB) with an effective numerical aperture (NA) of 0.13, placed after telescope T2 in Fig. 1. The resulting lateral resolution and depth of focus (DOF) in air are ~5 μm and 125 μm respectively. The light reflected back from the sample goes to the SH-WFS via a 50/50 beam splitter (BS), which results in a double path configuration for SH-WFS. For small scanned FOV in-vivo retinal OCT imaging the objective lens is removed, and the diameter of the beam at the cornea is 5.2 mm with the corresponding lateral resolution of ~4 μm in the retina. As mentioned above when imaging the human eye a configuration with different illumination and detection path is used for the wavefront sensing channel. This was done to avoid the problems of low power level of light reflected back from the retina, low sensitivity of silicon based CCD detector of the SH-WFS to 1060 nm wavelength and spurious back-reflections from the optics in the illumination path. Therefore, a collimated beam from a 840 nm SLD is used entering the eye directly via a 90/10 plate BS having a power of 0.6 mW, which is less than the allowed MPE of 0.73 mW at 840 nm wavelength for an exposure time of more than 10 seconds [36]. To direct the back reflected light to the SH-WFS a dichroic mirror is used this time instead of a 50/50 BS. To show the proof of principle using small scanned FOV OCT image for digital wavefront detection, microbeads sample was imaged with an objective lens placed after the 90/10 BS. Also the configuration with different illumination and detection path for SH-WFS was used as in the case of in-vivo measurements in the eye.

After the standard OCT data processing, which includes resampling and dispersion compensation, an en-face image of interest in the OCT volume is selected for analysis using the sub-aperture based DAO algorithm, which is the digital equivalent of SH WFS [20, 22]. In this method, first the 2-D FFT of the selected enface image field is calculated to get to the Fourier/pupil plane and then the aperture at the pupil plane or the spatial Fourier plane is digitally divided or segmented into smaller subapertures. The images of the sub-apertures, obtained by calculating inverse FFT of each subaperture, are then cross-correlated with the image of central reference sub-aperture to detect relative shifts in the presence of any wavefront aberration. Using relative shift information local slope of the wavefront error in each subaperture is calculated. The wavefront is assumed to be represented by a weighted sum of basis functions such as Zernike polynomials. Using derivatives of basis functions and local slope data put in a matrix formulation, least square solution is found to calculate the weightings or coefficients from which wavefront error is reconstructed [20,22].

In our experimental results, first the defocus estimation and correction is done using just two split apertures [23]. For higher order aberration estimation, a point like feature in the image is selected as guide star, windowed out and the pupil in the spatial Fourier domain after 2-D fast Fourier transformation (FFT) is segmented into 5x5 sub-apertures and Zernike terms of up to 6th order (first 25 terms) are fitted to estimate the wavefront error using DAO. The calculated pupil data is digitally phase conjugated with the estimated wavefront error, which upon 2D inverse FFT yields an image with reduced or no aberration [20, 22]. The pupil data is also digitally phase conjugated with wavefront error detected using SH-WFS and 2D inverse FFT is calculated to get a SH-WFS corrected reference image. The re-sampling and dispersion compensation was done using LabVIEW, whereas the DAO processing was done using MATLAB, both running on CPU (3.5 GHz, 64 GB RAM, 64 bit OS). The time for processing a data of size 75x75x2560 voxels (zero padded in spectral dimension) using LabVIEW is 4.4 seconds. The DAO processing of enface image of size 75x75 pixels takes only 1.8 seconds.
3. Experimental results

3.1 Proof of principle using a phantom sample

Figure 2(a) shows the en-face OCT image of microbeads (mean diameter ~10 µm) placed at 2 mm distance from the focal plane of the objective lens which corresponds to 16 times the DOF (32× Rayleigh’s range). Due to such large defocus, the image is heavily blurred and microbeads are not resolvable. Sub-aperture DAO using just two subapertures is used to estimate defocus phase error with peak to valley (P-V) value of 4.8 waves, shown in Fig. 2(d) [20, 23]. Figure 2(b) shows the image after applying the defocus correction, where individual microbeads can now be clearly resolved. This is also evident in the before and after profile plots, shown in Fig. 2(c), across the microbeads marked by the arrow in Fig. 2(b). The full width at half maximum (FWHM) of the profile plot after defocus correction is ~10.6 µm, which is close to the mean diameter of 10 µm of the microbeads.
The microbeads are imaged at different defocus distances and P-V defocus error in waves are calculated from the wavefront measurements done using DAO and the SH-WFS. Four measurements were taken at each defocus distance. The RMS errors of all the higher order aberrations were less than 0.07 waves and hence, defocus was the major source of aberration. Due to the difference in the imaging properties of a point scanning OCT system based on single mode fiber detection and a SH-WFS where a focused spot on the sample is imaged by a microlens on an area detector, the P-V defocus error for SH-WFS is 4 times higher than that for OCT for the same defocus distance. This is discussed in more detail in Appendix A. The mean of the deviation of P-V defocus errors from theoretical estimation is calculated for both DAO using OCT image and the SH-WFS, after taking into account the factor of 4, at each defocus distance and plotted as shown in Fig. 2(e). The error bar shows the standard deviation of the measurements. The difference for both DAO and the SH-WFS is less than 0.25 waves for all defocus distances up to 2 mm (32× Rayleigh’s range), which is the Rayleigh’s criterion for the diffraction limited performance, and hence the defocus estimations done by DAO and the SH-WFS are reasonably accurate. Also, from the plots it is clear that the defocus error estimated using DAO and the SH-WFS, after dividing the SH-WFS measured P-V defocus errors by the factor of 4, are very close to each other with maximum difference being only 0.04 waves at the defocus distance of 1.2 mm. Also, from the error bars in the plot of Fig. 2(e), it is clear that the measurements made by both SH-WFS and DAO are highly repeatable. The standard deviations (STD) of the P-V defocus error change for both DAO and SH-WFS are less than 0.03 waves. This is quite insignificant given the fact that defocus error needs to be at least 0.25 waves defined by Rayleigh’s criterion to observe any noticeable change.
To demonstrate the proof of principle that an OCT with small lateral FOV of 75(x)×75(y) pixels scanned at a high B-scan rate of ~1.3 kHz can be used to detect wavefront error using DAO, a microbeads sample placed at 250 µm (4× Rayleigh’s range) away from the focus of the objective lens is imaged. This time a configuration with different illumination and detection path using a SLD at 840 nm wavelength, as described in the section 2, is used for the SH-WFS. Figure 3(a) shows the original region of interest (ROI) with FOV of ~150×150 µm². The nature of blurring indicates the presence of defocus and also astigmatism, which may have occurred due to the use of 90/10 plate BS in the system for the SH-WFS channel as shown in Fig. 1. Figure 3(b) is the image after applying the wavefront correction, estimated using the SH-WFS, where reduction of smearing due to aberration is clearly evident and one starts to resolve two microbeads at the location marked by the arrow. However in the image obtained after DAO correction, as shown in Fig. 3(c), the smearing has been further reduced and two microbeads are clearly resolved. Before and after profile plots across the microbeads in Fig. 3(d) show two clearly resolved higher peaks after DAO correction, which also indicates the improvement in SNR. The plots are normalized to the highest peak value after DAO correction. The measured FWHM of one of the peaks is 8.5 µm after DAO correction, which is reasonable given that the mean diameter of the microbeads is ~10 µm. Figures 3(f) and 3(h) show the wavefront error, with significant RMSE value of 1.48 waves (> 1 µm), estimated by DAO and the corresponding Zernike coefficients plot respectively. They show major contribution of defocus and second order oblique and vertical astigmatism terms. The wavefront error and the corresponding Zernike coefficients plot for the SH-WFS are shown in Figs. 3(e) and 3(g). They show significant contribution of terms higher than second order. The wavefront error measurements were quite stable over the course of 4 repetitive measurements with STD of RMS error variation being less than 0.07 waves for both SH-WFS and DAO. Figure 3(i) displays the original enface OCT image with larger FOV (400(x)×400(y) pixels) scanned around the same location in the sample. Figures 3(j) and 3(k) are obtained after applying phase correction determined using the SH-WFS and DAO based on the small FOV OCT enface image respectively. The microbeads in the image after DAO correction appear more sharply focused and the calculated SNR is 35 dB as compared to the image after SH-WFS based correction having a SNR of 32 dB. The original image has a SNR of 29 dB, and thus an improvement of 6 dB is achieved after DAO correction. Based on the improvement in the image quality, the wavefront error estimated using DAO operating on a small scanned FOV OCT image seems to be closer to the ground truth.
Fig. 3. (a) Original small scanned FOV OCT enface image suffering from aberrations, (b) image after correction using wavefront error from SH-WFS, (c) image after correction using wavefront error from DAO, (d) before and after profile plots across the micro-beads marked by arrow in (c), (e) wavefront error detected using SH-WFS, (f) wavefront error detected using DAO, (g) plot of Zernike coefficients for SH-WFS, (h) plot of Zernike coefficients for DAO, (i) original large FOV scanned around the same location, (j) image after applying SH wavefront error in shown in (c), (k) image after applying DAO wavefront error shown in (f).

Even though DAO approach seems to give better results, care should be taken when drawing conclusion that wavefront estimation done by DAO is in general better than the SH-WFS. This is because the imaging properties of an OCT system are fundamentally different from those of SH-WFS, as explained in Appendix A. Also DAO operating on an OCT image
estimates the aberrations accumulated in the double path (illumination and detection), whereas the SH-WFS in the present case detects aberrations accumulated in different illumination and detection path. Although significant back-reflections are avoided by using the configuration with different illumination and detection path for the SH-WFS, remaining back-reflections from the back of the objective lens are hard to eliminate. This might have affected the accuracy of wavefront detection and caused the detection of higher order terms than actually present. Also, the SH-WFS could only be placed at the approximate Fourier plane relative to that of the OCT system, which can also cause some difference in the wavefront detection. Despite of all the above mentioned physical limitations, the improvement in the image quality shows that the SH-WFS detection is headed in a right direction. With additional hardware adaptive optics components such as a control system with iterative feedback loop in combination with a deformable mirror and pupil tracking, an optimal solution would have been achieved. However, based on these arguments we can say that DAO has provided the optimal solution in a single shot OCT image without requiring any elaborate adaptive optics hardware components. This leaves the optical system simple and compact in layout and design and also reduces the overall economic costs. Note that the comparison of complete hardware adaptive optics with DAO is out of the scope for the current paper and be will be dealt with in future work. We have used the SH-WFS detection as a reference to determine if the solution provided by DAO was appropriate, which based on the results seems to concur.

3.2 In-vivo measurements in a human eye

Figure 4(a) shows en-face OCT image of the photo-receptor layer of a human retina with lateral FOV of \(~800\times800\,\mu m^2\) and Fig. 4(b) shows the corresponding B-scan acquired at \(~6\) degrees from the fovea. A ROI with small lateral FOV of \(100\times100\,\mu m^2\) is imaged at the location marked by the yellow dotted box in Fig. 4(a). Figure 4(c) shows the original ROI, where it is hard to resolve individual photoreceptors due to smearing caused by aberration. In the image obtained after applying wavefront correction using the SH-WFS, the smearing has been reduced and one starts to resolve individual photoreceptors as shown in Fig. 4(d). Smearing is further reduced in the image after DAO correction, as shown in Fig. 4(e), where photoreceptors are more clearly resolvable, especially at the locations marked by arrows. Figure 4(f) shows the profile plots across the photoreceptors at the location marked by the dotted ellipse in Fig. 4(c), where the peaks are narrower after DAO correction. The FWHM of 4.8 \(\mu m\) for one of the peaks is quite reasonable for the size of photoreceptors at an eccentricity of \(~6\) degrees from the fovea. Figures 4(g) and 4(i) show the wavefront error and the corresponding Zernike coefficient plot for the SH-WFS. The total RMS WFE is 0.27 waves with significant second order astigmatism terms. In comparison, Figs. 4(h) and 4(j) show the wavefront error and the corresponding Zernike coefficient plot for DAO with the total RMS WFE of 0.33 waves, which about 5x higher than the Marechal’s criterion of 1/14 waves for the diffraction limited performance. DAO also detects significant second order astigmatism terms as the SH-WFS. Based on the improvement in the resolution of the photoreceptor image, the wavefront estimation done using DAO seems reasonably accurate and quite closer to the actual wavefront error.
Fig. 4. (a) Enface OCT image of the photo-receptor layer of human retina, (b) B-scan of human retina, (c) original small FOV scanned at the location shown by yellow dotted box in (a) and (b), (d) image after correction using wavefront error from SH-WFS, (e) image after correction using wavefront error from DAO, (f) before and after profile plots across the microbeads marked by dotted ellipse in (c), (g) wavefront error detected using SH-WFS, (h) wavefront error detected using DAO, (i) plot of Zernike coefficients in waves for SH-WFS, (j) plot of Zernike coefficients in waves for DAO.
4. Discussion

Sub-aperture based DAO is demonstrated for a point scanning SS OCT. A large defocus phase correction corresponding to 32x Rayleigh’s range was shown. The P-V defocus error measurements with DAO at different defocus distances match very well with the SH-WFS measurements. It is shown that a ROI with small FOV can be scanned at a high speed with SS OCT and used as a guide star for the DAO for the in-vivo wavefront error detection. A B-scan rate of ~1.3 kHz is achieved for a lateral FOV of 75(y) × 75(y) pixels for the laser sweep rate of 100 kHz. This speed was sufficient to do the in-vivo wavefront measurement applying DAO to data from a human volunteer. However, a higher B-scan rate of more than 1.5 kHz may be required for a wide range of patients with larger eye motion [18, 30]. This would require SSL with higher sweep rate and also high speed X-Y scanners which can provide a B-scan rate of > 1.5 kHz. Also at higher speed a large FOV can be covered, which would lead to wavefront corrected images with more details that can be analyzed in a comprehensive way. However, the SNR of the OCT signal is reduced at higher sweep or A-scan rate. Hence, successful implementation of DAO under such conditions also needs to be investigated in the future. Nevertheless, the proof of principle demonstrated in this paper shows a way to detect the wavefront error using a simple SS OCT system. The above mentioned issues are technological challenges which can be overcome with the development of high speed SSL and scanners. With the real time implementation of the method using GPU or FPGA based processing, it may be possible in the future to do dynamic wavefront error measurements, which could be quite helpful in intraoperative wavefront sensing during refractive and cataract surgery [37, 38]. Also, when combined with a wavefront correction device such as a deformable mirror, it may also provide dynamic aberration correction of images with improved SNR.

Appendix A

In case of a fiber based point scanning OCT system, the detected image field $E_i$ of a single sample layer is given by [39]

$$E_i(x, y) = r_i(x, y; z) \otimes \left[ h_{ill}(x, y; z) \otimes \phi(x, y) \right] \left[ h_{det}(x, y; z) \otimes \phi'(x, y) \right]$$

(1)

where $r_i$ is the sample reflectivity which is assumed to be at distance $z$ from the focus of objective lens, $h_{ill}$ is the illumination point spread function (PSF), $h_{det}$ is the detection PSF, $\phi$ is the fiber mode, which is a real Gaussian function, and $\otimes$ denotes convolution. For a double pass OCT system as in case of our experimental setup, we have $h_{ill} = h_{det}$ and $\phi = \phi'$. This reduces Eq. (1) to

$$E_i(x, y) = r_i(x, y; z) \otimes \left[ h_{ill}(x, y; z) \otimes \phi(x, y) \right]^2$$

(2)

where the effective PSF is given by $\left[ h_{ill}(x, y; z) \otimes \phi(x, y) \right]^2$ which takes into account the aberrations introduced by telescopes T1 and T2 and the optics of the eye or objective lens in a double pass, as shown in Fig. 1.

In contrast, the signal field $E_w$ at the SH-WFS plane with co-ordinate $(\tilde{x}, \tilde{y})$ is given by

$$E_w(\tilde{x}, \tilde{y}) = FT_{2D}[E_i(x, y)]$$

(3)

where $FT_{2D}$ is the two-dimensional Fourier transform of the intermediate image field $E_i$, which is given by
where \( h_o \) is the PSF due to the illumination optics which includes optics of the eye or the objective lens, and \( h_i \) is the PSF for imaging the object plane to the intermediate virtual image plane that has a Fourier transform relationship with the SH-WFS plane. The PSF \( h_o \) captures the aberration caused by the optics in the illumination path, and \( h_i \) captures the aberration in the path of the SH-WFS detection channel, which includes optics of the eye or the objective lens. The effective PSF for the field \( E' \) is the convolution of illumination PSF \( h_o \) and imaging PSF \( h_i \), which is due to the fact that in case of SH-WFS there is no scanning involved and an area detection instead of point or confocal detection is used [40]. Thus we can see from Eqs. (2) and (4) that the aberrations detected in the OCT and the SH-WFS can be different, based on the difference in the imaging properties of the two. Even if both OCT and SH-WFS share same illumination path aberrations, the difference in wavefront error detection may arise due to difference in detection path and method.

In case where defocus is the main aberration caused by displacement of the sample by distance \( z \) from the focal plane of the objective lens, we can write \( h_{\text{ill}} \) for an OCT system as [41]

\[
h_{\text{ill}}(x, y; z) = A_i(x, y) \exp(-ikz) \exp\left(-\frac{ik}{2z} (x^2 + y^2)\right)
\]

where \( A_i \) is the amplitude with real Gaussian function and \( k = 2\pi/\lambda \) is the wavenumber. Assuming point object with \( r_i(x, y; z) = \delta(x, y) \) and confocal detection due to the use of single mode fiber with \( \phi(x, y) = \delta(x, y) \) for simplicity, the defocused PSF of the OCT system, based on Eq. (2), is given by

\[
PSF_{\text{oct}} = A^2_i(x, y) \exp(-i2kz) \exp\left[-\frac{ik}{z} (x^2 + y^2)\right]
\]

The corresponding defocus phase at the Fourier plane is given by

\[
\arg[FT_{2D}(PSF_{\text{oct}})] \approx \arg\left\{ \exp\left[\frac{-i\pi\lambda z}{2} (f_x^2 + f_y^2)\right]\right\} = -\frac{i\pi\lambda z}{2} (f_x^2 + f_y^2)
\]

For the same defocus in case of SH-WFS, we have

\[
h_o(x, y; z) = h_{\text{ill}}(x, y; z) \approx \exp\left[-\frac{ik}{2z} (x^2 + y^2)\right]
\]

and

\[
h_i(x, y; z) \approx FT_{2D}\left[\exp\left[-i\pi\lambda z (f_x^2 + f_y^2)\right]\right]
\]

where the amplitude of the field has been neglected for simplicity as we are only interested in phase. Also, the imaging magnification for \( h_i \) is assumed to be unity. This is valid if the pupil is imaged on the SH-WFS with unity magnification, as in case of our experimental setup [23]. Assuming a point object \( r_i(x, y) = \delta(x, y) \) the signal field \( E_o \) at the SH-WFS plane, applying the convolution theorem for Fourier transformation, is given by
\[ E_w \propto FT_{2D} \left[ h_w(x, y; z) \right] FT_{2D} \left[ h_i(x, y; z) \right] \]
\[ \propto \exp \left[ -i2\pi \lambda z \left( f_x^2 + f_y^2 \right) \right] \]  \hspace{1cm} \text{(10)}

Thus, from Eq. (7) and Eq. (10), for the same pupil size with diameter \( D = \sqrt{f_x^2 + f_y^2} \), SH-WFS detects a P-V defocus error, which is 4 times higher than that detected by OCT.

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**Disclosures**

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