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High resolution imaging of the inner retina

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Since the introduction of adaptive optics (AO) technology to ophthalmic imaging [1], the cone photoreceptor and retinal pigment epithelial cell mosaics have been routinely imaged to study the healthy and diseased retina [2-15]. Resolving inner retinal cells, however, has been more elusive, due to its transparency. AO optical coherence tomography has the required axial resolution and contrast to visualize the inner retina at the cellular level, but it has been limited by image speckle, acquisition speed and eye motion [11-13]. Non-interferometric AO phase imaging techniques that fraction the entrance and/or exit pupils have failed to provide the necessary axial resolution and contrast [16]. Recent advances in the optical design of AO scanning ophthalmoscopes (AOSOs) have allowed us to significantly improve the lateral resolution of our instruments, allowing, for example, visualizing the full and contiguous cone and rod photoreceptor mosaics in vivo. This increase in resolution has allowed us to resolve sub-cellular features in the retinal nerve fiber layer in reflectance that are consistent with the retinal ganglion cell (RGC) axonal varicosities, and cellular structures consistent with astrocytes and pericytes. These varicosities are approximately 3 μ m in diameter in the healthy retina, and their size does not significantly vary across the retina, consistent with our findings. RGC axonal varicosities contain high concentrations of mitochondria, and therefore their visualization in vivo opens a new avenue for studying mechanisms of eye diseases such as glaucoma and Leber's hereditary optic neuropathy, as well as neurological conditions such as multiple sclerosis and Parkinson's disease.

References

1. J. Liang, D.R. Williams and D.T. Miller, "Supernormal vision and high-resolution retinal imaging through adaptive optics," *J. Opt. Soc. Am. A* 14, 2884-2892 (1997).
2. A. Roorda and D.R. Williams, "The arrangement of the three cone classes in the living human eye," *Nature* 397, 520-522 (1999).
3. J. Carroll, M. Neitz, H. Hofer, J. Neitz and D.R. Williams, "Functional photoreceptor loss revealed with adaptive optics: An alternate cause of color blindness," *PNAS* 101 (22) 8461-8466 (2004).
4. J.I. Wolfing, M. Chung, J. Carroll, A. Roorda and D.R. Williams, "High-resolution retinal imaging of cone-rod dystrophy," *Ophthalmology* 113 (6), 1014-1019.e1 (2006).
5. S.S. Choi, N. Doble, J.L. Hardy, S.M. Jones, J.L. Keltner, S.S. Olivier and J.S. Werner, "In vivo imaging of the photoreceptor mosaic in retinal dystrophies and correlations with visual function," *Invest. Ophthalmol. Vis. Sci.* May 47 (5) 2080-2092 (2006).
6. J.L. Duncan, Y. Zhang, J. Gandhi, C. Nakanishi, M. Othman, K.E. H. Branham, A. Swaroop and A. Roorda, "High-resolution imaging with adaptive optics in patients with inherited retinal degeneration," *Invest. Ophthalmol. Vis. Sci.* 48 (7) 3283-3291 (2007).
7. A. Roorda, Y. Zhang and J.L. Duncan, "High-resolution in vivo imaging of the RPE mosaic in eyes with retinal disease," *Invest. Ophthalmol. Vis. Sci.* 48 (5) 2297-2303 (2007).
8. R.C. Baraas, J. Carroll, K.L. Gunther, M. Chung, D.R. Williams, D.H. Foster and M. Neitz, "Adaptive optics retinal imaging reveals S-cone dystrophy in tritan color-vision deficiency," *J. Opt. Soc. Am. A* 24, 1438-1447 (2007).
9. K. Grieve and A. Roorda, "Intrinsic Signals from Human Cone Photoreceptors," *Invest. Ophthalmol. Vis. Sci.* 49 (2) 713-719 (2008).
10. T.Y. Chui, H. Song and S.A. Burns, "Adaptive-optics imaging of human cone photoreceptor distribution," *J. Opt. Soc. Am. A* 25, 3021-3029 (2008).

11. M.K. Yoon, A. Roorda, Y. Zhang, C. Nakanishi, L.C. Wong, Q. Zhang, L. Gillum, A. Green and J.L. Duncan, "Adaptive optics scanning laser ophthalmoscopy images in a family with the mitochondrial DNA T8993C mutation," *Invest. Ophthalmol. Vis. Sci.* 50 (4) 1838-1847 (2009).
12. C. Torti, B. Považay, B. Hofer, A. Unterhuber, J. Carroll, P.K. Ahnelt and W. Drexler, "Adaptive optics optical coherence tomography at 120,000 depth scans/s for non-invasive cellular phenotyping of the living human retina," *Opt. Express* 17, 19382-19400 (2009),
13. R.J. Zawadzki, B. Cense, Y. Zhang, S.S. Choi, D.T. Miller and J.S. Werner, "Ultrahigh-resolution optical coherence tomography with monochromatic and chromatic aberration correction," *Opt. Express* 16, 8126-8143 (2008).
14. O.P. Kocaoglu, S. Lee, R.S. Jonnal, Q. Wang, A.E. Herde, J.C. Derby, W. Gao and D.T. Miller, "Imaging cone photoreceptors in three dimensions and in time using ultrahigh resolution optical coherence tomography with adaptive optics," *Biomed. Opt. Express* 2, 748-763 (2011).
15. J. Carroll, J.T. McAllister, S. Ostler, J. Rha, A.M. Dubis, D.M. Tait and C. G. Summers, "Imaging foveal morphology in ocular albinism using adaptive optics and spectral domain OCT," *J. Vision* 9 (14), article 33 (2009).
16. R.S. Jonnal, J.R. Besecker, J.C. Derby, O.P. Kocaoglu, B. Cense, W. Gao, Q. Wang and D.T. Miller, "Imaging outer segment renewal in living human cone photoreceptors," *Opt. Express* 18, 5257-5270 (2010).
17. A. Dubra, Y. Sulai, and D.R. Williams. "Microscopic in vivo Imaging of Human Inner Retina with a Phase Adaptive Optics Scanning Laser Ophthalmoscope." ARVO Annual Meeting, Fort Lauderdale, Florida, USA (2010).

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