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EDITORIAL

Imaging the visual system: from the eye to the brain

Imaging technologies have revolutionized the study of human anatomy and physiology. Nowhere is this more evident than in the vision sciences, where imaging has provided unprecedented insights into the structure and function of the entire visual pathway *in vivo*. Ocular and retinal imaging techniques such as optical coherence tomography (OCT)[1,2] have become established clinical tools, providing highly detailed images of ocular structures that are now used routinely to support the diagnosis and management of ocular disease. The expanding scope of measurements possible with ocular imaging technology is resulting in even more accurate diagnostic and prognostic clinical instruments and progressing our understanding of the eye's structural and functional properties.[3]

On the other hand, brain imaging technologies such as functional magnetic resonance imaging[4,5] and diffusion tensor tractography[6] are not yet widely utilized in the clinical management of visual disorders. This is likely to change. There is increasing evidence that the impact of ocular disease on visual function cannot be fully understood without considering associated changes in the structure and function of the brain.[7] Furthermore, attempts to restore vision using electrical prosthetics[8–10] or regenerative medicine[11] require an understanding of the entire visual pathway in patients with vision loss. For example, any neurodegenerative effects of long-term visual cortex deafferentation will limit the extent to which vision can be recovered when retinal input to the brain is restored. Therefore future advances in the field of vision restoration are likely to rely critically on information from a combination of both eye and brain imaging techniques.

This feature issue had two main goals. The first was to identify new imaging technologies and recent progress in established imaging methodologies that can be applied to the visual system. The second was to highlight advances in our understanding of the visual system and visual disorders that have been achieved through the use of imaging techniques. These broad goals allowed us to assemble a collection of papers that span the entire visual system from the cornea to the extrastriate visual cortex.

The feature issue begins with two invited reviews that together provide comprehensive overviews of both retinal and brain imaging. The first review, by Jessica Morgan, describes recent developments in retinal imaging resulting from the use of novel OCT techniques, adaptive optics and their combination.[3] These techniques allow for detailed, cellular level imaging of retinal layers and vasculature, visualization of the photoreceptor mosaic (both cones and rods) and even perimetry at the level of individual photoreceptors. Morgan also describes the exciting possibility of high-resolution functional imaging of the retina.[3] These cutting edge technological advances in retinal imaging have direct implications for the early detection of retinal dysfunction and improved assessment of treatment outcomes.

The second review, by Brown *et al.*[7], deals with the application of structural, functional and spectroscopic magnetic resonance imaging (MRI) techniques to the study of vision disorders. The visual system is particularly amenable to functional MRI (fMRI) because it is relatively straightforward to present participants with well-controlled stimuli for psychophysics within the scanner environment. In fact, the very first human functional magnetic resonance imaging (fMRI) studies involved measurements of visual cortex activation.[4,5,12] It is perhaps not surprising then, that fMRI has been used extensively to study the functional organization of the human visual system. Precisely organized retinotopic maps have been visualized within the primary and extrastriate visual cortex[13–16] as well as in thalamic areas such as the pulvinar.[17] Recent advances in retinotopic mapping techniques have even allowed for the estimation of average receptive field size within specific regions of the visual cortex.[18] In more general terms, structural and functional MRI has advanced our understanding of visual pathway disease mechanisms and the extent to which the brain can reorganize in response to impaired visual input.

Brown *et al.*[7] provide an introduction to structural and functional brain imaging techniques as well as a technique called magnetic resonance spectroscopy that enables the measurement of metabolite concentration in targeted brain areas. They then describe studies that have used these techniques to unveil the cortical and subcortical effects of anophthalmia, macular degeneration, retinitis pigmentosa, glaucoma, albinism and amblyopia in humans.[7] It is clear from this review that the impact of ocular disease and dysfunction does not end at the eye.

Both review papers highlight the remarkably rapid technical advances that imaging technologies have undergone, and the substantial contributions that imaging has made to vision science. It is also evident from both reviews that significant breakthroughs in the clinical application of imaging technologies are imminent. This theme is reflected in the original research papers included in the feature issue.

The first two papers relate to anterior eye-imaging technologies. Iskander *et al.*[19] report on the Eye Surface Profiler: a device that utilizes fourier transform profilometry to measure the topography of the anterior eye in high resolution, extending across cornea, limbus and sclera. The possibility of accurately mapping the topography of the limbus and sclera provides exciting new opportunities to further our understanding of the anterior eye's topography, which in turn has the potential to impact upon contact lens fitting and design.

In order to properly interpret the exceptionally precise anterior eye measurements that can be achieved with contemporary OCT techniques, it is essential to understand the normal physiological factors that influence anterior eye structure. Read *et al.* highlight this issue by showing that scleral and conjunctival thicknesses vary significantly throughout the 24 h sleep/wake cycle.[20] This result demonstrates the ability of high resolution imaging to reveal new physiological changes, and underscores the importance of considering normal variations in ocular tissues when interpreting anterior eye measurements.

Moving from the anterior eye to the retina, Chui *et al.*[21] report the use of adaptive optics scanning light ophthalmoscopy (AOSLO) to document the remodelling of the retinal microvasculature in a patient with diabetic retinopathy. The longitudinal changes in microvasculature that can be detected using this technique are striking and demonstrate the potential of AOSLO to track disease processes and quantify treatment outcomes.

The next two papers highlight the utility of imaging technologies for the detection of ocular disease. Ly *et al.*[22] review the use of infrared reflectance imaging to detect age related macular degeneration (AMD) and to differentiate between different phenotypes of the disease. The authors also provide case images to guide clinicians in the use of infrared reflectance imaging for the diagnosis of AMD. Pang and Franz demonstrate that the Heidelberg Retinal Tomograph (HRT) has higher sensitivity and specificity for detecting congenital optic nerve hypoplasia than the standard measurement of disc-to-macula/disc diameter ratio.[23] An optimal HRT disc area cut-off value for distinguishing between optic nerve hypoplasia and a healthy optic nerve head is also provided.

The final set of three papers deal with the use of MRI techniques to assess the impact of visual disorders on the brain. Two of these papers use functional MRI to address a fundamental question in visual neuroscience: does the human visual system have sufficient plasticity to "remap" in response to disease or injury? Fracasso *et al.*[24] investigate the structure of retinotopic maps in a patient with congenital hemihydranencephaly, a disorder that causes the complete absence of one hemisphere due to abnormal prenatal cortical development. The absence of one hemisphere represents an extreme challenge to the visual system because the entire cortical representation of one visual hemifield is absent. However, visual field testing revealed that the patient's vision extended into the left visual field despite the absence of a right cerebral hemisphere. Subsequent high-field fMRI measurements showed that the remaining right hemisphere contained population receptive fields that encoded both the left and right hemifields.[24] This is a dramatic demonstration of extensive visual cortex plasticity occurring in response to a prenatal developmental abnormality.

In contrast to Fracasso *et al.*'s finding, Haak *et al.*[25] report an absence of cortical reorganization following visual system damage. The key difference is that while Fracasso *et al.*'s patient had an abnormal visual pathway from birth,[24] the patients studied by Haak *et al.*[25] lost vision later in life due to juvenile macular degeneration. Despite extended periods of vision loss, these patients exhibited normal patterns of functional connectivity between the primary and extrastriate visual cortex indicating a lack of cortical reorganization. This is perhaps good news, since this result suggests that the neural systems required to process information from retinal implant technologies remain intact despite having been deprived of visual input for extended periods of time.

In the final paper of this feature issue, Boucard *et al.*[26] explore the impact of normal-pressure tension glaucoma on subcortical white matter microstructure using diffusion tensor imaging. Glaucoma is of particular interest from a brain imaging perspective because the neurodegenerative effects of the disease extend beyond the retinal ganglion cells to the lateral geniculate nucleus and cortex.[27,28] Boucard *et al.*[26] report evidence of white matter abnormalities in the optic radiations, forceps major (a large fibre bundle that connects the two occipital lobes) and the corpus callosum (the primary white matter connection between the two hemispheres). These white matter changes may reflect neurodegeneration. Therefore, the presence of white matter changes in structures that are remote from the retinal ganglion cells, such the corpus callosum, raises the intriguing possibility that glaucoma may involve brain-specific neurodegeneration.

As a whole, the papers that make up this feature issue highlight how rapid technological advances have provided us with the ability to image all aspects of the visual system with unprecedented resolution. The expanding capabilities and scope of imaging technologies and continued multidisciplinary approach to imaging the eye and brain promises to further broaden our knowledge of the entire visual system: from the anterior eye, to the retina and the cerebral cortex. We envision that the developments in imaging on the horizon have the potential to further transform clinical practice and patient management and enable continued research breakthroughs and discoveries.

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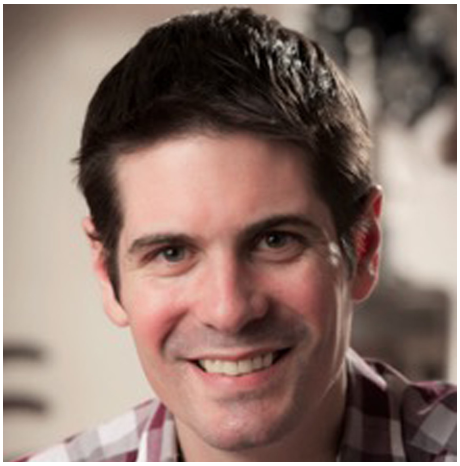
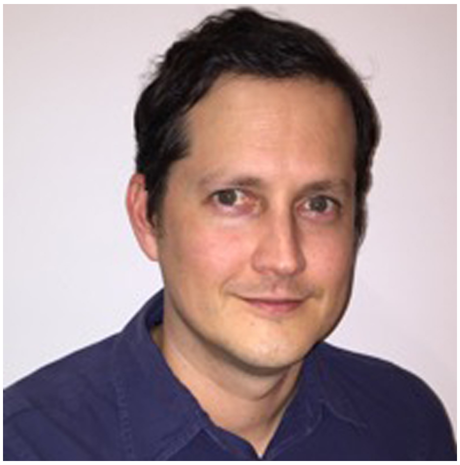
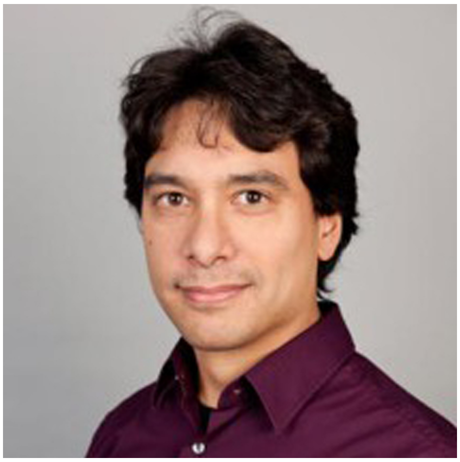


Benjamin Thompson. Ben holds a BSc and DPhil in experimental psychology from the University of Sussex, UK and completed postdoctoral training in the Department of Psychology, UCLA, USA and the Department of Ophthalmology, McGill University, Canada. He joined the faculty of the University of Auckland, New Zealand in 2008, where he retains a research position. In 2014 Ben moved to the University of Waterloo, Canada as an Associate Professor. Ben is a member of the *Ophthalmic & Physiological Optics* editorial board, an academic editor for *PLOS One* and a guest editor for *Vision Research*. His research involves the use of psychophysics, non-invasive brain stimulation and magnetic resonance imaging to investigate development and plasticity of the human visual system.



Scott A. Read. Scott is an Associate Professor and Director of Research in the School of Optometry and Vision Science at the Queensland University of Technology, Brisbane, Australia. Since the award of his PhD in 2006, for work examining the normal corneal topography and astigmatism in the population, Scott has been involved in a wide scope of research activities. A feature of Scott's work has been his use of optical imaging techniques to broaden our understanding of human myopia, and in particular the role of the choroid. Dr Read recently received the "*ZEISS Young Investigator Award in Myopia Research*" for his distinguished contributions to the myopia research field, which also involved the presentation of the keynote "Josh Wallman Memorial Lecture" at the 2015 International Myopia Conference. He has also been an Associate Editor and Editorial Board Member of *Clinical and Experimental Optometry* and acts as a Topical Associate Editor for *Optometry and Vision Science*.



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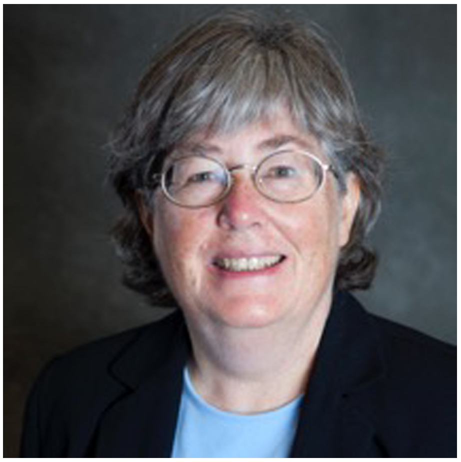

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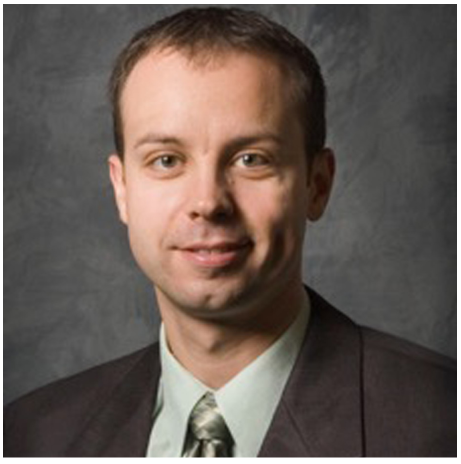

Jason Porter. Jason earned his BS, MS and PhD degrees in Optics from the University of Rochester's Institute of Optics, USA. As a graduate student and postdoc with David Williams, he worked in the areas of ocular aberration measurement, customized correction and high-resolution retinal imaging of photoreceptors and ganglion cells using adaptive optics (AO). Jason is now an Associate Professor in Vision Science and Biomedical Engineering at the University of Houston's College of Optometry. His laboratory investigates mechanisms responsible for the development and progression of optic nerve head and retinal-related diseases (e.g., glaucoma, inherited retinal degenerations) using advanced imaging techniques, including AO. Jason was lead editor for the book entitled, "*Adaptive Optics for Vision Science*" a collaborative work that describes the principles and practices of AO in vision science. He is an Editorial Board Member for *Ophthalmic & Physiological Optics* and a writer and panel member for the Optical Society's (OSA's) Spotlight on Optics series.

Austin Roorda. Austin received his PhD in Vision Science & Physics from the University of Waterloo, Canada in 1996. For over 15 years, Dr. Roorda has been pioneering applications of adaptive optics, including mapping of the trichromatic cone mosaic while a postdoc at the University of Rochester, designing and building the first adaptive optics scanning laser ophthalmoscope at the University of Houston, tracking and targeting light delivery to individual cones in the human eye at UC Berkeley, and being part of the first team to use AO imaging to monitor efficacy of a treatment to slow retinal degeneration. Since January 2005, he's been at the UC Berkeley School of Optometry where he is the current chair of the Vision Science Graduate Program. He is a Fellow of the *Optical Society of America* and of the *Association for Research in Vision and Ophthalmology* and is a recipient of the Glenn A. Fry award, the highest research honor from the *American Academy of Optometry*.