Trans-scleral Illumination - The Future of Retinal Imaging?

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Abstract. We report how illumination of the retina through the sclera enables the recording of high-contrast reflectance and fluorescence images of the retina, free of the cornea and lens glare and autofluoresence that degrades images recorded using traditional illumination through the pupil.

1 Introduction

High-quality retinal imaging underpins all screening and early detection of retinal disease. The salient objectives are the detection of morphological and structural changes of vascular and neural structure or the chemical abnormalities that may precede them, such as abnormal blood oxygenation or accumulation of chemical waste products. [1–3]. For both reflectance and fluorescence imaging of the retina, both illumination (or excitation) of the retina and imaging of the retina is through the eye pupil. The so-called Gullstrand principle separates the illumination and imaging light paths in the retina to prevent the faint light from the retina from being swamped by the much brighter reflection or fluorescence from the cornea and ocular lens [4]. Typically annular illumination at the pupil is combined with imaging through the centre of the illumination annulus but this is effective only for imaging modest fields of view, and consistent alignment of the annulus with the pupil is difficult to maintain in a handheld device.

Somewhat counter-intuitively the retina may also be efficiently illuminated through the sclera (the white of the eye): in the region of the the pars planar, an annular region a few millimetres outside the iris, a thinning results in light transmission that may be as high as ~ 30% in lightly pigmented eyes, or significantly less for people with high skin pigmentation. It is likely that the impact of the associated stray light at the retina is mitigated by the waveguiding effect of the photoreceptors which tends to limit sensitivity only to light from the centre of the eye pupil.

Here we present retinal imaging systems using trans-scleral illumination for wide-field imaging reflectance and for fluorescence intensity and fluorescence-lifetime imaging.

2 Wide-Field Imaging

An increased field of view of the retina offers the enhanced capabilities for detecting disease but scleral reflections and ocular aberrations increase rapidly with increasing field angle. We have recently reported a proposal to employ multi-camera computational imaging to increase the field of view from a typical 50° to 140° - enabling 80 % of the retina to be imaged [5]. Our multi-camera architecture employs local aberration correction to offer wide-field near-diffraction-limited imaging, but the Gullstrand principle is ineffective for removal of illumination reflections for such wide fields of view. Reflections are however eradicated using trans-scleral illumination and the inherent simplicity also reduces both the optical system complexity and volume. As a step towards realising multi-camera retinal imaging we have demonstrated trans-scleral illumination with a wide-field (80°) single camera, which offers the advantage of a short image acquisition time of < 1 s and of being completely non-contact whilst still being handheld, as shown in Fig. 2 a-c.

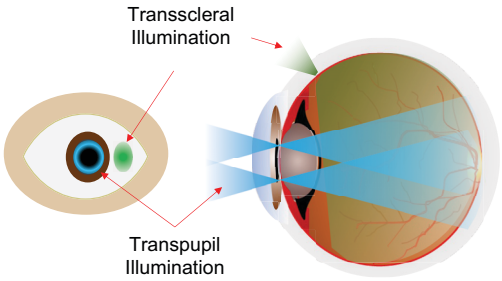

Figure 1: Comparison of annular illumination, where an annulus-shaped field of light is focused onto the cornea and then diverges to both illuminate the retina, and the new technique of trans-scleral illumination where a beam of light is focused onto a spot on the sclera which diffuses and uniformly illuminates the retinal surface.

3 Oximetry

Oximetry of retinal vascular blood exploits oximetric variations in contrast of narrowband spectral images [6, 7].

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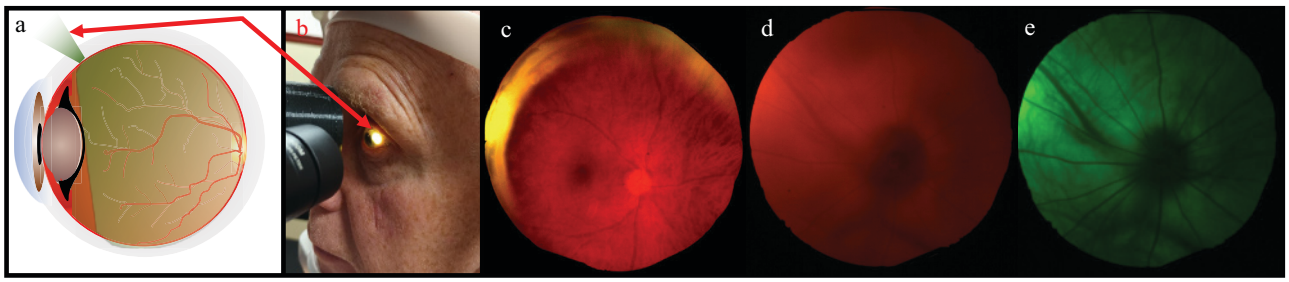

Figure 2: Handheld system utilising trans-slceral illumination. a) Trans-scleral illumination separates illumination and imaging paths b) scleral illumination pattern on a human using a white-light LED c) image human fundus d) red- and green-filtered images of a rat retina for vascular oximetry

Even low-levels of glare from the cornea and lens significantly reduces the contrast, however [8]. We have demonstrated two-wavelength *in vivo* retinal vascular oximetry in rats using scleral illumination, as highlighted in Fig. 2 d-e. This provides promise for anaesthetic-free longitudinal assessment of oximetry in animal models of disease - as well as demonstrating the feasibility of trans-scleral illumination for retinal oximetry in humans

4 Spectral intensity and spectral fluorescence lifetime-imaging

Fluorescence intensity imaging and fluorescence-lifetime imaging (FLIM) of the retina provide additional discrimination for quantification of retinal chemicals associated with metaboloic activity or with residues such as lipofuscin [9]. We record multi-spectral fluorescence images - using a 128 × 192 SPAD array with integrated Time-Correlated Single Photon Counting (TCSPC) module and a co-aligned sCMOS camera (to enable co-registration multiple TCSPC images for enhanced signal-to-noise ratio). We modify the algorithm reported in [10], where phasor analysis and principal component analysis are combined to extract end-member concentrations and lifetimes in photon starved-conditions. However, using trans-pupil illumination, fluorescence images are accompanied by relatively intense lens fluorescence, which degrades accuracy. We have demonstrated the feasibility of trans-scleral fluorescence retinal imaging devoid of contamination by lens fluorescence.

5 Outlook

The transmission of illumination through the sclera, rather than through the pupil, enables almost total eradication of the excitation and reflection of light from the lens and cornea, providing major enhancement of image contrast for quantitative, wide-field reflectance and fluorescence imaging of the retina.

References

[1] D.J. Mordant, I. Al-Abboud, G. Muyo, A. Gorman, A. Sallam, P. Ritchie, A.R. Harvey, A.I. McNaught, Eye **25**, 309 (2011)
[2] C. Dysli, S. Wolf, M.Y. Berezin, L. Sauer, M. Hammer, M.S. Zinkernagel, Progress in retinal and eye research **60**, 120 (2017)
[3] S.N. Patel, A. Shi, T.D. Wibbelsman, M.A. Klufas, Therapeutic advances in ophthalmology **12**, 2515841419899495 (2020)
[4] A.R. Harvey, G. Carles, A. Bradu, A. Podoleanu, in *Computational Retinal Image Analysis* (Elsevier, 2019), pp. 19–57
[5] J. Terry, G. Carles, A.R. Harvey, *Multi-scale Aberration Corrected Imaging of the Retina*, in *Optica Imaging and Applied Optics Congress 2022 (COSI)* (2022), p. ITh5D.2
[6] D.J. Mordant, I. Al-Abboud, G. Muyo, A. Gorman, A. Sallam, P. Rodmell, J. Crowe, S. Morgan, P. Ritchie, A.R. Harvey et al., Investigative Ophthalmology & Visual Science **52**, 2851 (2011)
[7] D.J. Mordant, I. Al-Abboud, G. Muyo, A. Gorman, A.R. Harvey, A.I. McNaught, Eye **28**, 1190 (2014)
[8] G. Carles, M. Preciado, P. Zammit, V. Ochoa-Gutierrez, J. Terry, J.M. Cooper, J. Reboud, A.R. Harvey, *Wide-field, illumination-agile, oximetric retinal imaging with a handheld camera*, in *Computational Optical Sensing and Imaging* (Optical Society of America, 2021), pp. CTh4E–6
[9] D. Geddes, J. Noorbakhsh, , Z. Yang, M. Preciado, M. Normand, K. Smith, , A.R. Harvey, *Quantification of Metabolic Function in the Retina Using Spectral Imaging and Phasor-FLIM*, in *Optica Imaging and Applied Optics Congress 2021 (COSI* (2022), p. JW4C.3
[10] L. Scipioni, A. Rossetta, G. Tedeschi, E. Gratton, Nature Methods **18**, 542 (2021)