Optics for the Eye

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Master-slave enhanced visible optical coherence tomography imaging of the human eye

Lucy Abbott[1], Gianni Nteroli, Dr Rasmus D. Engelsholm, Dr Patrick B. Montague, Professor Adrian Podoleanu, Dr Adrian Bradu

[1]University of Kent, Canterbury, UK, [2]NKT Photonics , Birkerød, Denmark

Visible-light Optical Coherence Tomography (VIS-OCT) is an emerging imaging modality that provides new capabilities in anatomical and functional imaging of biological tissue. It relies on visible light illumination, whereas most commercial and investigational OCT instruments use near-infrared light. VIS-OCT requires different considerations in engineering design and implementation but brings unique potential benefits to fundamental research and clinical care of several diseases.

Our research is focused on developing a VIS-OCT instrument that can be used to capture in-vivo images of the human retina. To improve image sensitivity, the instrument uses a dual spectrometer detection configuration, known as balanced detection. The complex master-slave (CMS) approach, developed by our research group, is utilised to calibrate the two spectrometers and generate the images. However, as it is difficult to devise identical spectrometers due to various factors such as incorrect alignment of optical components, we have developed a software procedure based on correlating temporal signals collected by the cameras employed, to optimise the benefits of the balanced detection between the two in-house built spectrometers.

A supercontinuum optical source drives our instrument. This source provides sufficient optical power from 450 to 625 nm, resulting in an axial resolution, experimentally measured, of ~1.5μm in tissue. The line cameras used in spectrometers operate at 80 kHz, hence the generation of cross-sectional images at 160 Hz. Two factors affect the sensitivity of these images. Firstly, the intrinsic noise of the supercontinuum lasers and secondly, the low levels of optical power allowed to probe the eye. In the development of the instrument, we have taken into account the safety levels for intra-ocular viewing of a scanned beam and ensured that the maximum permissible optical power for retinal imaging in the visible range is up to only 250μW on the cornea.

If the balance detection scheme is implemented accurately, it can help produce superior OCT images. Currently, the improvement in sensitivity is up to 9 dB, depending on the depth. This improvement allows us to use the instrument to produce enhanced quality images of human tissue showing fine structural information. Once the instrument is fully optimised and equipped with fixation procedures, we are planning to use it for retinal imaging (as a first step of healthy volunteers). More details on the capabilities of our device and its potential future use will be made available during the presentation.

Assessment of Retinal Health using Spectral Fluorescence Lifetime Imaging Ophthalmoscopy

Mr Daniel Geddes[1], Professor Andy Harvey[1]

[1]University Of Glasgow, Glasgow, UK

Motivation

Early diagnosis of eye disease underpins all effective treatment. However, conventional imaging techniques resolve structural changes but only after physical damage to the retina has occurred. Spectral – Fluorescence Lifetime Image Ophthalmoscopy (S-FLIO) is an emergent technique that shows promise for chemical mapping of retinal metabolites and biomarkers such as lipofuscin (A2E), AGE, and FAD – an indicator of local oxygen consumption. This would facilitate the diagnosis of retinal disease at the point of biochemical dysfunction.

The key challenge with this method lies with the feint retinal fluorescence signal is swamped by fluorescent clutter and is degraded by blood resulting in a photon-starved regime wherein images exhibit high noise and require integration times of longer than 90s [1]. The overlapping spectra and fluorescence lifetimes of retinal biomarkers means they cannot be discriminated using spectral imaging or fluorescence lifetime imaging alone.

We demonstrate an imaging device and fluorophore unmixing solution that can robustly discriminate, and quantify, the concentration of retinal fluorophores.

Spectral-Fluorescence Lifetime Ophthalmoscope

We present a modified off-the-shelf ophthalmoscope (Topcon TRC 50D) fitted with a new generation 128 X 192 pixel SPAD array with 47ps time bins (Horiba FLIMera) [3] to record fluorescence lifetime images of the retina, over a 15° Field-of-View (FOV), in series of snapshots using 6 spectral filters optimised for detecting retinal biomarkers as well as a 4096 x 2160 pixel science camera to compensate for saccade movements in the eye. Fluorescence is excited in the retina between 460-467nm using a picosecond pulsed supercontinuum white light source (NKT SuperK EX12W) filtered by an Acousto-Optic Tuneable Filter (AOTF) allowing for agile targeting of specific fluorophores.

Tensor-Based Spectral-FLIM Unmixing

We have developed a bespoke tensor-based unmixing solution, based on the solving of multilinear systems of equations [4]. Our fit free technique utilises the recorded emission spectra in tandem with the entire fluorescence decay profile – avoiding the common comprise of simplified lifetime models due to limited photon counts. From the results of simulations our solution shows promise in quantifying retinal FAD using photon fluxes where previously only a single lifetime could be resolved [1].

Conclusion

We have constructed an S-FLIO device which coupled with our new fluorophore unmixing technique shows promise in quantitatively assessing retinal health. Our device utilises new generation SPAD arrays to record S-FLIM images in a series of snapshots. Using our new unmixing algorithm we can recover the concentration of retinal metabolites and biomarkers from SFLIM images despite the low photon fluxes typical to fluorescence imaging in the retina.

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High diffusion efficiency holographic diffusers for managing diplopia.

Matthew Hellis[1,2], Suzanne Martin[1,2], Matthew Sheehan[1,3], Kevin Murphy[1,2]

[1]Centre for Industrial and Engineering Optics, TU Dublin, Dublin, Ireland, [2]FOCAS Research Institute, TU Dublin, Dublin, Ireland, [3]School of Physics, Clinical and Optometric Sciences, TU Dublin, Dublin, Ireland

In a retrospective secondary care study, binocular diplopia, which is a distressing condition with numerous potential causes, was observed in 88.5% (146 individuals) of diplopia cases, indicating a prevalence of binocular over monocular diplopia [1]. If the magnitude of binocular deviation exceeds what can be corrected practically via relieving prisms, it is typical that monocular occlusion be considered to remove the visual confusion, which can be debilitating. Indeed, the visual system will often achieve the same ends via suppression if sufficient adaption time is allowed.

It is proposed that holographic diffusers offer a new potential treatment modality, adding to various established methods such as patch occlusion and spectacle lens frosting or taping. Holographic diffusers have been produced via a single-beam recording method and have demonstrated consistent and replicable fabrication [2]. The structure of the diffuser is developed by optically patterning the internal structure of the photopolymer layer on a micro-scale [2]. Initially introduced for amblyopia treatment [3], this study explores their potential application in treating diplopia.

Previous work characterising Holographic diffusers shows that elements exhibiting high diffusion efficiency can effectively suppress all spatial frequencies, behaving similarly to an occluder in terms of visual disruption [3], but with arguably improved cosmesis and only minor reduction in irradiance. Their advantage in terms of aesthetics, compared to conceptually similar treatments such as Bangerter foils, lies in the holographic diffusers' angular dependence, which results in a notably clearer optical element (affixed to the individual's spectacles) from the perspective of an observing bystander.

It is expected that high diffusion efficiency (a metric that indicates how much light is removed from the optical axis) will be a beneficial property in treating diplopia. While a range of holographic diffusers have been developed in both acrylamide (AA) and diacetone acrylamide (DA) [3], this study will focus on the development of 99% diffusion efficiency holographic diffusers and their characteristics which may be beneficial as a treatment modality. Using a beam intensity of 1.0 mW/cm² and recording durations between 50 and 70 seconds, holographic diffusers with 99% diffusion efficiency have been successfully produced in DA-based photopolymer. These elements display diffusion envelopes extending up to 30^0, with a maximum 10% reduction in efficiency and the ability to reduce visual acuity by >1.0 logMAR.

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Subclinical changes detected in diabetes mellitus using high resolution retinal imaging and colour vision assessment

Dr Emily J. Patterson[1,2,3], Megan Vaughan[2,3,4], Nicole Tay[2], Dr Angelos Kalitzeos[2,3], Thomas Kane[2,3], Navjit Singh[2,3], Adrian Zheng[2,3], Mira Dixit[2,3], Bishwanath Pal[3], Ranjan Rajendram[2,3], Konstantinos Balaskas[3], M. Pilar Martin Gutierrez[3], Jose Carlo Artiaga[3], Georgios Koutsocheras[3], Hanan Nussinovitch[3], Khadra Adan[3], Marisa Rodriguez-Carmona[5], John L. Barbur[5], Michel Michaelides[2,3]

[1]Occuity, Reading, UK, [2]UCL Institute of Ophthalmology, University College London, London, UK, [3]Moorfields Eye Hospital NHS Foundation Trust, London, UK, [4]Anglia Ruskin University, Cambridge, UK, [5]City, University of London, London, UK

Purpose: Diabetic retinopathy (DR) is the leading cause of vision loss in working-age adults in the developed world. Although it is known that photoreceptor damage and colour vision loss occur in patients with diabetes mellitus (DM), the relationship between these structural and functional changes remains unclear. By using highly sensitive measures of photoreceptor structure and function, we aim to determine whether early loss of colour sensitivity in DM is also accompanied by decreased cone density.

Methods: Monocular data from 25 patients with DM and varying severity of DR, along with 25 normally-sighted controls without DM, were examined to assess the integrity of their cone photoreceptors and their red/green (RG) and yellow/blue (YB) colour vision. The retina was imaged using a custom-built adaptive optics scanning light ophthalmoscopy (AOSLO) system. Cone density was assessed, when possible, using confocal images from 0.5 and 1 degree eccentricity along the temporal meridian (0.5T, 1T) using 55 x 55 μm regions of interest. Colour vision was assessed using the Colour Assessment and Diagnosis (CAD) test, which yields both RG and YB color detection thresholds.

Results: Both RG and YB thresholds were significantly greater in patients with DM than in controls (RG: $p<0.001$; YB: $p<0.001$), and there were statistically significant differences in confocal cone density between the two groups at 1T ($p=0.016$), but not at 0.5T ($p=0.094$). In patients with DM, cone density at 1T was inversely correlated with RG and YB chromatic discrimination thresholds (RG: $p=0.014$; YB: $p=0.007$), whereas for 0.5T only YB was correlated with cone density ($p=0.009$), and not RG ($p=0.152$). No relationship between RG and YB chromatic discrimination thresholds and cone density was evident in the control group for 0.5T (RG: $p=0.808$; YB: $p=0.693$) nor 1T (RG: $p=0.874$; YB: $p=0.166$).

Conclusion: Although the CAD test and AOSLO are currently being used as outcome measures in clinical trials for gene therapy, they have not been validated against each other. This is the first study to investigate the relationship between cone density and colour detection in patients with DM. The significant inverse relationship observed between cone density and CAD thresholds could have important implications for understanding retinal structure-function relationships (oculomics) in DM, potentially providing a valuable screening tool for early detection of DR.

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