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The effect of simulated cataract light scatter on retinal vessel oximetry

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ABSTRACT

To assess the impact of light scatter, similar to that introduced by cataract on retinal vessel blood oxygen saturation measurements using poly-bead solutions of varying concentrations. Eight healthy, young, non-smoking individuals were enrolled for this study. All subjects underwent digital blood pressure measurements, assessment of non-contact intraocular pressure, pupil dilation and retinal vessel oximetry using dual wavelength photography (Oximetry Module, Imedos Systems, Germany). To simulate light scatter, cells comprising a plastic collar and two plano lenses were filled with solutions of differing concentrations (0.001, 0.002 and 0.004%) of polystyrene microspheres (Polysciences Inc., USA). The adopted light scatter model showed an artifactual increase in venous optical density ratio ($p = 0.036$), with the 0.004% condition producing significantly higher venous optical density ratio values when compared to images without a cell in place. Spectrophotometric analysis, and thus retinal vessel oximetry of the retinal vessels, is altered by artificial light scatter.

1. Introduction

In vivo, non-invasive retinal vessel oxygen saturation measurements are relatively novel. Due to the non-invasive nature of this technology and its good reproducibility (Hammer et al., 2008; Lasta et al., 2012), it has attracted interest in the clinical community for the assessment of systemic and ocular disease with a vascular component. Diseases investigated so far include diabetic retinopathy (Hammer et al., 2009; Hardarson and Stefansson, 2012b), glaucoma (Hardarson et al., 2009; Traustason et al., 2009) and retinal vein occlusion (Hardarson and Stefansson, 2010, 2012a). Ease of use and low variability paired with high sensitivity and specificity are essential for any diagnostic technology. Although the eye offers a unique possibility to non-invasively observe the retinal microcirculation, it also requires certain prerequisites in order to obtain good quality images, including clear media (cornea, lens, vitreous and anterior chamber) and an adequate ability to fixate by the individual under observation.

With increasing age and in the presence of systemic or ocular disease, media transmission is invariably altered (Wuerger, 2013; Sakanishi et al., 2012; Artigas et al., 2012; Bron et al., 2000; Polo et al., 1996). This change in ocular media transparency and scattering effect (light diffusion) produced by a cataract can affect both spectral transmission and morphology. By degrading the spatial resolution of the retinal features the detection of the vessel lumen and exterior can thus impact the measurement of optical density of the retinal vessels (Mita et al., 2012). Optical density contributes to the calculation of retinal vessel blood oxygen saturation measurements. Despite this, the impact of lens opacity on the assessment of blood oxygen saturation is unknown. Previous studies from our group have quantified the influence of artificial light scatter on various retinal imaging instruments (Azizi et al., 2007; Burke et al., 2006; Venkataraman et al., 2005). In order to mimic the change in lens morphology, we introduced an additional plano lens, filled with a polybead solution to simulate light scatter.

We hypothesised that light scatter, typical in an ageing lens, could alter retinal vessel oxygen saturation measurements as it might impact upon fundus and vessel reflection which form the basis of the retinal vessel blood oxygen saturation calculation.

2. Materials and methods

The study adhered to the tenets of the Declaration of Helsinki and was approved by the Aston University institutional review

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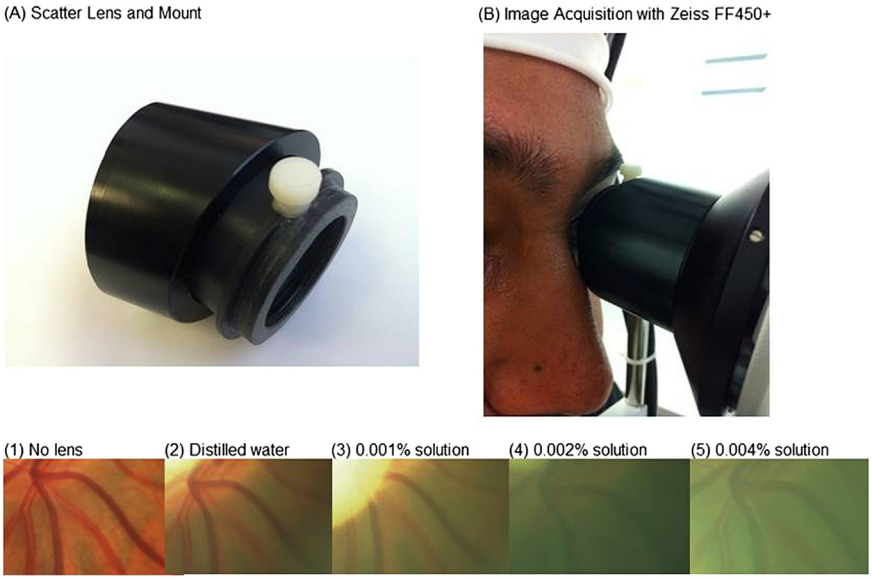

Fig. 1. The lens set up and images taken at each condition for a participant.

board. Written informed consent was provided. We included eight young healthy participants (mean age 32 ± 4 years). All participants were drug free with no systemic disease, no ocular abnormalities, and no history of any ocular surgery. Participants had no lens opacity, exhibited intraocular pressures less than 21 mmHg, a logMAR (logarithm of the minimum angle of resolution) visual acuity of 0.0 or better, and a refractive error ≤±6.00 DS and ≤±2.50 DC.

All measurements were taken in the morning between 9 and 11am with the participants having abstained from caffeinated and carbonated beverages, alcohol, chocolate, red meat, vitamin C or participated in any forms of exercise for a minimum of 4 h. Intraocular pressure was measured using the Keeler IntelliPuff (Keeler Instruments, UK) prior to instillation of one drop of Tropicamide 1% (Minims, Chauvin Pharmaceuticals Ltd, UK) to dilate the pupil. After resting in a sitting position and acclimatizing to a temperature of 22 °C for 15–20 min blood pressure (BP) was measured using a digital BP monitor (UA-779, A7D Instruments, UK) according to best practice guidelines (Williams et al., 2004).

2.1. Artificial light scatter model

The details of the artificial light scatter model have been published elsewhere (Azizi et al., 2007; Burke et al., 2006; Venkataraman et al., 2005). In brief, cells comprising a plastic collar (inner diameter 25 mm) and two 35 mm removable CR39 plano parallel lenses (with a spacing of 4.5 mm between the lenses and a thickness of 2.04 mm each) were filled with solutions of differing concentrations of polystyrene microspheres (Polybead© Polysciences Inc., USA). The total volume of each cell was 2.2 ml. The diameter of the microspheres was chosen to be similar to the mean diameter of aggregated lens proteins (500 nm) that are thought to produce intraocular light scatter in the normal ageing lens. Microsphere concentrations of 0.001%, 0.002%, and 0.004% were made up from a 0.16% stock solution. A cell filled with distilled water only was also used as an additional control. Cells filled with a solution of 0.008% were tested for imaging but proved to produce images which could no longer be analysed.

The cells were re-filled with solution for each subject as the microsphere solution is not constantly homogenous (i.e. the microspheres can deposit and settle with gravity if left over time). Furthermore, cells were checked regularly with a spectrophotometer to ensure consistency of the optical transmission and absorption characteristics throughout the course of the study.

2.2. Image acquisition

The cells were mounted on the objective lens of the Zeiss FF450+ using a custom made adaptor that incorporated a 20° tilt to minimise surface reflections. After full pupil dilation was reached, we obtained a minimum of 5 images per condition (i.e. no lens, distilled water, microsphere polybead concentrations of 0.001%, 0.002% and 0.004%) with the camera angle set at 30° and the optic nerve head centred. A minimum of 5 min resting time between conditions was given (Fig. 1).

Oxygen saturation measurements were performed using the "oxygen tool" (Imedos Systems, Imedos GmbH, Jena, Germany) as described elsewhere (Hammer et al., 2008). In brief, fundus images were taken using a customized dual wavelength filter (transmission bands at 548 and 610 nm; bandwidth 10 nm each). Optical densities of the vessels were measured as the logarithmic ratio of the fundus reflection at the vessel centre and its surrounding. The optical density ratio (ODR) at 610 and 548 nm has been found to be inversely proportional to the vessel haemoglobin oxygen saturation when compensating for the vessel diameter and fundus pigmentation (Hammer et al., 2008).

2.3. Image analysis

For analysis purposes we selected the three best images per condition. Using the Visualis software (Imedos Systems, Jena, Germany), we used a predefined template to measure one retinal arteriole and one retinal venule approximately half a disc diameter (DD) from the ONH and of one DD in length. This distance and length was chosen in order to obtain results which could be used for comparison to earlier publications using the same device. The vessel diameter, optical density ratio, pigmentation (numerical value output from the software) and oxygen saturation were obtained for all three images (per condition) of each participant, using the "multi measurement tool".