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A program to analyse optical coherence tomography images of the ciliary muscle

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ABSTRACT

Purpose: To describe and validate bespoke software designed to extract morphometric data from ciliary muscle Visante Anterior Segment Optical Coherence Tomography (AS-OCT) images.
Method: Initially, to ensure the software was capable of appropriately applying tiered refractive index corrections and accurately measuring orthogonal and oblique parameters, 5 sets of custom-made rigid gas-permeable lenses aligned to simulate the sclera and ciliary muscle were imaged by the Visante AS-OCT and were analysed by the software. Human temporal ciliary muscle data from 50 participants extracted via the internal Visante AS-OCT caliper method and the software were compared. The repeatability of the software was also investigated by imaging the temporal ciliary muscle of 10 participants on 2 occasions.
Results: The mean difference between the software and the absolute thickness measurements of the rigid gas-permeable lenses were not statistically significantly different from 0 ($t = -1.458$, $p = 0.151$). Good correspondence was observed between human ciliary muscle measurements obtained by the software and the internal Visante AS-OCT calipers (maximum thickness $t = -0.864$, $p = 0.392$, total length $t = 0.860$, $p = 0.394$). The software extracted highly repeatable ciliary muscle measurements (variability ≤6% of mean value).
Conclusion: The bespoke software is capable of extracting accurate and repeatable ciliary muscle measurements and is suitable for analysing large data sets.

1. Introduction

Despite the involvement of the ciliary muscle in accommodation [1–3], presbyopia [4,5], and possibly myopia development [6–9], there is a relative paucity of *in vivo* ciliary muscle research. Indeed, imaging the ciliary muscle *in vivo* represents a significant challenge due to the obscured position of the ciliary muscle behind the highly pigmented iris.

Traditionally, ultrasound biomicroscopy (UBM) has been utilised to acquire *in vivo* images of the ciliary muscle [7,10–12]. However, sharper image definition obtained with Anterior Segment Optical Coherence Tomography (AS-OCT) permits superior localisation of the scleral spur (a key reference point for ciliary muscle measurements), compared to UBM images [12]. The axial resolution is 8 μm and 25 μm for the Visante AS-OCT (Carl Zeiss Meditec, California, USA) in high resolution corneal mode and the P40 UBM (Paradigm Medical Industries, Utah, USA) at 50 MHz [12], respectively. Additionally, UBM necessitates supine posture, topical anaesthetic, coupling agents and contralateral eye fixation, whereas the Visante AS-OCT permits non-contact ipsilateral imaging of the fixating eye whilst the patient is sitting up-right, which affords enhanced patient comfort and feasibly permits paediatric assessment [2,6]. Therefore, more recent research has progressed to use AS-OCT devices rather than UBM to image the ciliary muscle *in vivo* [1–6,8,9].

Similarly to UBM devices, in-built Visante AS-OCT software allows calipers to be super-imposed onto acquired images to extract measurements. During image analysis, the Visante AS-OCT internal software outlines the boundaries of the ocular media and applies corrective refractive indices (n) to improve measurement accuracy ($n = 1.000$ anterior to the cornea, $n = 1.338$ to the cornea, $n = 1.343$ posterior to the cornea). However, the Visante AS-OCT also fits the same refractive index adjustments to ciliary muscle images, with no option to alter the magnitude of the tiered refractive index corrections. Therefore, previous authors have applied a refractive index of 1.000 to the entire ciliary muscle image [1,4,6]. To provide data more closely associated with physiological *in vivo* ciliary muscle parameters, Sheppard and Davies [1,4] adjusted their ciliary muscle caliper measurements to account for a refractive

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index of 1.382, which is the best estimate of the refractive index of the ciliary muscle based on *in vitro* bovine muscle tissue studies using confocal microscopy [13] and *in vitro* human ventricular muscle studies using OCT [14]. However, the refractive indices of the overlying sclera, as well as the ciliary muscle itself, need to be compensated for to ensure the magnitude of the measured ciliary muscle parameters are as accurate as possible. Furthermore, the ciliary muscle tissue is not accurately represented by the straight lines of the calipers because the scleral and ciliary muscle tissues are curved, to varying degrees in different patients [15]. Therefore, to improve the accuracy of morphological assessment, data have been exported for analysis with external software [15].

Due to the lack of uniformity of the ciliary muscle outline in Visante AS-OCT images, Kao et al. [15] software required manual localisation of the scleral spur before automated image analysis commenced. Once the sclera and ciliary muscle had been outlined, refractive indices of 1.41 and 1.38 were applied across the *y*-axis of the scleral and ciliary muscle image sections, respectively. The software produced vertical thickness measures at 1, 2 and 3 mm behind the scleral spur, maximum thickness and measured the cross-sectional area of the anterior ciliary body. However, the edge detection algorithms appeared to incorporate both the ciliary muscle and the pigmented ciliary epithelium, which may overestimate ciliary muscle measurements. Furthermore, measurements of ciliary muscle length were not obtained.

Despite the Visante AS-OCT's use in previous morphometric studies of the ciliary muscle, the instrument remains susceptible to optical and instrument distortions, and has limited inbuilt capabilities to quantify ciliary muscle parameters. Consequently, to overcome the limitations of previously designed software [15] and to address concerns of the subjectivity of identifying the posterior end point of the ciliary muscle [16], bespoke software was developed. The aim of this study was to describe and validate the bespoke software and to compare data extracted by the software and the internal Visante AS-OCT calipers.

2. Method

The study was approved by the Aston University Research Ethics Committee and was conducted in accordance with the tenets of the Declaration of Helsinki. Informed consent was obtained from all participants after explanation of the nature and possible consequences of the study. One UK registered optometrist (DL) acquired and extracted all the human data.

2.1. Ciliary muscle image acquisition

It is likely that the repeatability of nasal ciliary muscle image analysis is superior to temporal ciliary muscle image analysis because the scleral spur is more easily discernible nasally [17], therefore only temporal ciliary muscle images were analysed in the present study.

Each participant wore an eye patch over their left eye throughout data collection. Participants were asked to place their chin and forehead against the Visante AS-OCT supports and fixate straight-ahead at the centre of the internal star target. The chin rest was adjusted to align the participant's right eye to allow visualisation of the anterior crystalline lens surface, which was guided by the real-time Visante AS-OCT video stream of the external eye. High resolution corneal mode was selected (scanning an area of 10 mm in width and 3 mm in depth) and participants were aligned to ensure the vertical white fixation line was visible through the centre of the image, which indicated the measurement beam was coincident with the optical axis of the eye [18].

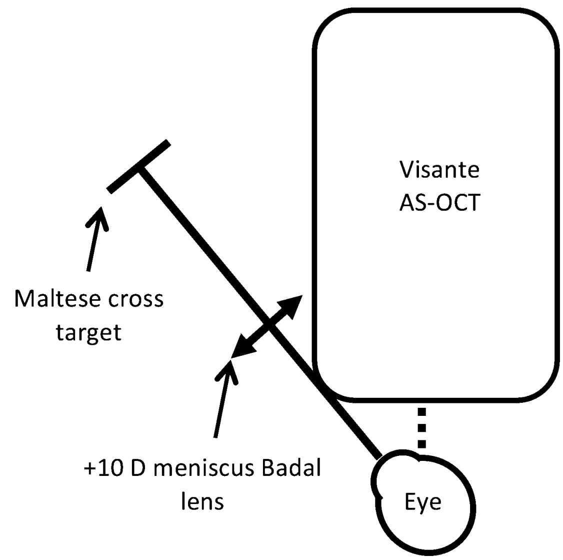

Fig. 1. Schematic diagram of the Visante AS-OCT with bespoke Badal lens system attachment. The dashed line represents the path of the OCT beam through the sclera. The Maltese cross target is positioned 10 cm from the Badal lens in order to stimulate 0.00 D of accommodation in an emmetropic patient.

In order to image the full length of the ciliary muscle using the Visante AS-OCT, patients must avert their gaze to a point external to the central viewing window because the iris blocks visualisation of the ciliary muscle in primary gaze. Fig. 1 illustrates the bespoke Badal lens system with a moveable Maltese cross target, attached to the forehead rest of the Visante AS-OCT to provide a steady peripheral fixation target and to correct for ametropia. The minimum level of horizontal eye movement required to ensure the peripheral target is unobstructed by the instrument casing is 40° from the internal Visante AS-OCT star target. Fixating externally causes the Visante AS-OCT beam to be directed through the sclera, rather than the cornea, reducing optical distortion due to the flatter scleral plane. Since all participants were aligned to the optical axis of the Visante AS-OCT in primary position, only minor vertical alignment adjustments were required once the participant adducted their right eye to view the centre of the external Maltese cross. Horizontal alignment was determined by the real-time Visante AS-OCT video stream of the OCT image, which was adjusted to ensure simultaneous visualisation of the scleral spur and ciliary muscle posterior visible limit, as depicted in Fig. 2.

Once accurately aligned, the Maltese cross target was moved to provide a 0.00 D accommodative stimulus for each participant. Participants were asked to focus on the centre of the Maltese cross

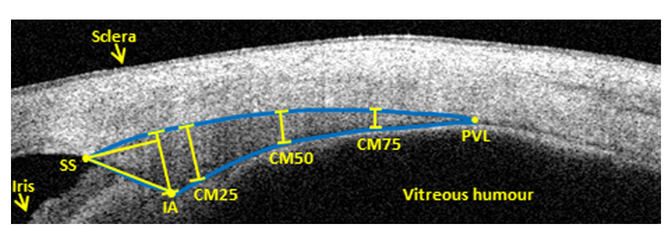

Fig. 2. Visante AS-OCT image of a human ciliary muscle section. The ciliary muscle is outlined in blue with superimposed yellow caliper measurements. PVL = Posterior visible limit; SS = scleral spur; IA = inner apex; CM25, CM50, CM75 = thickness at 25%, 50% and 75% of curved total length (SS to PVL); maximum thickness = perpendicular distance from IA to sclera; anterior length = perpendicular distance from line of maximum thickness to SS. The pigmented epithelium is visible underneath the inner apex and the inferior ciliary muscle border (For interpretation of the colour information in this figure legend, the reader is referred to the web version of the article.).