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Title: The effects of ocular magnification on Spectralis spectral domain optical coherence tomography scan length

Irene Ctori (1), Stephen Gruppetta (1) and Byki Huntjens (1*),

1. Applied Vision Research Centre, The Henry Wellcome Laboratories for Vision Sciences, City University London, Northampton Square, London, EC1V 0HB, UK

E-Mail:

Irene.Ctori.2@city.ac.uk

Steve.Gruppetta.1@city.ac.uk

Byki.Huntjens.1@city.ac.uk;

* Corresponding author:

Byki.Huntjens.1@city.ac.uk

Tel.: +44-20-7040-0145

Fax: +44-20-7040-8355 (not private)

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Abstract (180 words)

Purpose: To assess the effects of incorporating individual ocular biometry measures of corneal curvature, refractive error and axial length on scan length obtained using Spectralis spectral domain optical coherence tomography (SD-OCT).

Methods: Two SD-OCT scans were acquired for 50 eyes of 50 healthy participants, first using the Spectralis default keratometry (K) setting, then incorporating individual mean-K values. Resulting scan lengths were compared to predicted scan lengths produced by image simulation software based on individual ocular biometry measures including axial length.

Results: Axial length varied from 21.41 to 29.04mm. Spectralis SD-OCT scan lengths obtained with default-K ranged from 5.7 to 7.3mm and with mean-K 5.6 to 7.6mm. We report a stronger correlation of simulated scan lengths incorporating the subject's mean-K value ($\rho = 0.926$, $P < 0.0005$) compared to Spectralis default settings ($\rho = 0.663$, $P < 0.0005$).

Conclusions: Ocular magnification appears to be better accounted for when individual mean-K values are incorporated into Spectralis SD-OCT scan acquisition compared to using the device's default-K setting. This must be considered when taking area measurements and lateral measurements parallel to the retinal surface.

Key Words: Optical Coherence Tomography; axial length; scan length; Spectralis; keratometry.

Introduction

Optical Coherence Tomography (OCT) allows a direct cross-sectional view of the human retina [1] correlating well with retinal histology [2]. SD-OCT provides increased acquisition speed and higher image resolution compared to older time-domain OCT techniques [3,4]. OCT technology is increasingly employed in the clinical diagnosis of ocular pathology such as age-related macular degeneration [5], macular holes [6], vitreo-macular traction [7], and glaucoma [8]. Quantitative evaluation of retinal thickness using both automatic and manual measuring techniques is used to aid clinical diagnosis and design treatment protocols [9-11]. It is known that segmentation algorithms employed by individual OCT instruments result in variability in retinal thickness measurement complicating comparison across different platforms [12,13]. In addition, ocular magnification of retinal images is affected by refractive error, corneal curvature, refractive index, axial length and anterior chamber depth [14,15]. The distance of the eye to the measuring device can also influence the magnification effect [16]. In the case of OCT scan images, ocular magnification may affect lateral measurements i.e. those made parallel to the retinal plane [17]. The optical set-up of the OCT instrument as well as the software program for calculating image size will govern image size calculation in computerized fundus imaging [18]. If lateral measurements such as drusen diameter, geographical atrophy area in dry age-related macular degeneration or foveal width measurements for example are to be used for establishing diagnosis and treatment protocols, the potential impact of ocular magnification on lateral measurements must be considered.

An inverse correlation between retinal nerve fibre layer thickness, optic nerve head parameters and axial length has been reported [19-22]. However, these correlations became negligible when corrections accounting for axial length were applied to the measured values [19,22,23]. This suggests that axial length should be taken into account when assessing the reliability of OCT data [24]. However, not all OCT platforms account for axial length induced ocular magnification, and various attempts have been made to correct for the magnification of an individual nominal scan length produced by the OCT instrument [22]. In a study by Wagner-Schuman et al., a ratio of the individual's axial length to that assumed by the instrument was applied to lateral measurements [25]. Others have addressed the issue of lateral scaling by applying a correction based on the SD-OCT instrument manufacturer's formula using modified Littman's method [14], which incorporates individual refractive error, corneal radius and axial length [22,26]. An alternative approach used in studies of retinal morphology has been to exclude subjects with refractive error greater than ±5.00 or ±6.00DS to minimize potential errors [27,28]. In contrast to these other SD-OCT platforms, the Spectralis (Heidelberg Engineering, Heidelberg, Germany) applies an automatic modification process to cancel out the effect of ocular magnification, generating individual scan lengths based on three parameters. It assumes a non-modifiable pre-set axial length of 24.385mm based on the Gullstrand schematic eye [29] (personal communication with Heidelberg Engineering, Germany; July 2013). Secondly, by allowing the operator to focus the retinal image, the subject's refractive error is taken into account. Thirdly, a default corneal curvature i.e. keratometry (K) setting of 7.70mm equal to the K-value of Gullstrand's model eye [29] is assumed by the device, as described in its technical specifications. Alternatively, an option to use the subject's actual mean-K is provided. The present study was carried out to investigate the effect of individual mean spherical error (MSE), mean-K and axial length on B-scan length obtained using the Spectralis SD-OCT.

Methods

Study protocol

The study was conducted from October to December 2013 at the Division of Optometry and Visual Science, City University London. A total of 50 volunteers took part; all presented Log MAR visual acuity better than 0.3 log units in the eye being tested. Exclusion criteria were: ocular pathology, medication that may affect retinal function and previous laser eye surgery. By default, measurements were taken for the right eye unless it did not meet the inclusion criteria, in which case the left eye was used. Each participant had measures of MSE (based on an average of five autorefractor readings) and mean-K (average of three horizontal and vertical K readings) taken with the Auto Kerato-Refracto-Tonometer TRK-1P instrument (Topcon, Tokyo, Japan).

The Spectralis SD-OCT was used to scan the undilated test eye of each participant in a dark room [30,31]. Two high resolution 20° x 10° volume scans (97 B-scans 30 microns apart, ART 16 frames including 1024 A scans) were acquired for each participant. The first scan was obtained using the default corneal curvature setting of 7.70mm; while the second had the subject's mean-K entered into the software prior to scan acquisition. The participant was instructed to look at the central fixation target while the infrared fundus image was focused with a dial corresponding to their MSE. During scan acquisition, the investigator independently monitored the participant's fixation via the live fundus image. All scans had a minimum quality level of 25 decibels, as recommended by the manufacturer guidelines. The resulting "*default-K*" and "*mean-K*" scan length was recorded from the Spectralis mapping software, Heidelberg Eye Explorer (Version 1.7.0.0 © 2011). Axial length was measured using the IOLMaster (Carl Zeiss Meditec, Dublin, CA, USA). This is a well-known non-contact device based on partial coherence interferometry shown to have good axial length measurement repeatability [32,33]. Zemax optical design software (Zemax, LLC, Redmond, WA, USA) was used for simulation of an image from a 20° SD-OCT incorporating individual subject's MSE, mean-K and axial length data. The Gullstrand's exact model eye [29] was applied to the simulation since Spectralis software image size calculations are based on this model. Within the Zemax model, mean-K values and axial length were modified for each subject by changing the radius of curvature of the anterior corneal surface and the axial distance between posterior lens surface and retinal plane respectively. MSE was modelled as a paraxial lens immediately before the model eye. An object with a field of 10º (with respect to the optical axis, resulting in 20º overall field) was set and the size of the image at the retinal plane calculated by the software was used to represent the simulated scan length. This was compared to the default-K and mean-K scan lengths.

Ethical approval and consent

The study was approved by Optometry Research & Ethics Committee City University London. Written informed consent was obtained from all subjects conforming to the tenets of the Declaration of Helsinki.

Statistical analysis

All statistical analyses were performed using SPSS version 21.0 for Windows (SPSS Inc., Chicago, USA). Values in the text and tables are presented as the mean ± standard deviation (SD). Preliminary analyses were performed to ensure no violation of the assumptions of normality, linearity and homoscedasticity. Since Kolmogorov-Smirnov test revealed a significant deviation from a normal distribution for scan length and MSE, Spearman's Rank Correlation Coefficient ρ was calculated to explore the correlation between default-K and mean-K with simulated scan lengths. Statistical significance was accepted at $P < 0.05$.

Results

A total of 22 males and 28 females were included in the study. The mean age was 21 ± 2.9 years. Mean, minimum and maximum values of mean-K, MSE, axial length, and scan lengths are summarised in Table 1.

[insert Table 1 approximately here]

A Wilcoxon Signed Rank Test revealed a statistically significant difference in scan lengths obtained using default-K, mean-K and from simulations (Figure 1). There was a significant correlation between mean-K ($\rho = 0.926$, $P < 0.0005$) and default-K scan length with the simulated scan length ($\rho = 0.663$, $P < 0.0005$), shown in Figure 2. We explored the effect of axial length and

MSE on these relationships and found that the correlation between mean-K and simulated scan length remained strong and significant when controlling for axial length (ρ = 0.822, P < 0.0005) and for MSE (ρ = 0.875, P < 0.0005). The correlation was weakened for default-K measurements when controlling for axial length (ρ = 0.473, P < 0.001) and became non-significant when controlling for MSE (ρ = 0.221, P = 0.128).

[insert Figure 1 and Figure 2 approximately here]

Discussion

The Spectralis SD-OCT generates individual scan lengths based on refractive error, corneal curvature and a non-modifiable pre-set axial length of 24.385mm according to the Gullstrand schematic eye. We explored the correlation of Spectralis SD-OCT scan length acquired using the instrument's default-K setting of 7.70mm versus using the subject's mean-K, when compared to Zemax software simulated scan length. The aim was to ascertain whether the effect of ocular magnification on SD-OCT scan length was represented more accurately using an individual's mean-K value as opposed to the Spectralis default-K setting in comparison to simulated output based on Gullstrand exact eye model [20]. We included individuals with axial length of 21.41mm to 29.04mm resulting in mean-K scan lengths ranging from 5.6 to 7.7mm (Figure 1). Whilst direct comparisons cannot be drawn from other studies with different subject demographics, individual scan lengths ranging from 5.3 to 7.0mm have been reported whereby the nominal 6mm scan was corrected using each subject's axial length (varying from 21.56 to 28.36mm) based on the Cirrus eye model [20]. Of note, the most accurate model eye to calculate ocular magnification has yet to be determined [18], although differences between modified Littman's technique [14] and the Gullstrand eye model are less than 2% for axial lengths from 22 to 26.5mm [34].

While there was significant correlation of mean-K ($\rho = 0.926$, $P < 0.0005$) and default-K scan length with the simulated scan length ($\rho = 0.663$, $P < 0.0005$), the correlation was much stronger for mean-K scan length. The within-subject SD of K measurements have been shown to range from 0.05mm to 0.18mm depending on the instrument used [35]. According to the Spectralis technical guidelines, a 0.1mm error in K will result in an error in lateral measurement of 0.8%. This translates to a 0.1mm change in scan length for every 0.2mm deviation from the individual's mean-K. The TRK-1P gives repeated measurements within ±0.12DS on test eyes (personal communication with Topcon; June 2014) that may explain the lack of perfect agreement between the mean-K and simulated scan lengths in the current study. Another consideration is that subjective refraction was not carried out to estimate MSE. However, it has been shown that using an autorefractor is an accepted method to approximate refractive error [36]. Nonetheless, accuracy of ocular biometry measurements is potentially a limitation of the study. We incorporated individual's mean-K and MSE values into Spectralis scan acquisition as well as the Zemax simulation. Any error in these values would therefore have the same effect on both occasions. We postulate that the discrepancy from perfect correlation is more likely to be caused by some other assumption built into the OCT software. Furthermore, Tan et al. explored the effect of different lens powers and varying eye-scanner distance on image magnification while maintaining a constant axial length [37]. This was repeated keeping a constant lens power while varying eye-scanner and axial length. The results showed that even with accurate axial length measurement, in eyes not complying with standard assumptions (for example cataract) or in eyes that over-accommodate during imaging, the magnification is still not sufficiently corrected. In addition, there was no option to include separate horizontal and vertical K values in the Spectralis software. The mean-K value underestimates or overestimates the horizontal K value depending on whether the individual has with- or against-the-rule astigmatism. The latter may explain the lack of perfect agreement between the mean-K and simulated scan lengths in the current study. However, as the mean-K value has to be inserted prior to scan acquisition and cannot be changed retrospectively, using mean-K allows subsequent analyses of vertical frames or measurements of area.

There was a strong and significant correlation between scans taken with mean-K and the simulated scan length when controlling for the effect of MSE ($\rho = 0.875$, $P < 0.0005$) and axial length ($\rho = 0.822$, $P < 0.0005$). This was not the case for scans taken using the default setting of K = 7.70mm. A recent study aimed to address the issue of the influence of axial length on OCT data acquired from Spectralis SD-OCT scans [38]. The study involved a novel method of measuring the known distance of a sub-retinal visual implant *in vivo*. The results confirmed the accuracy of lateral measurements taken from Spectralis SD-OCT measurements of emmetropic medium (22.51 to 25.5mm) length eyes. The authors did recommend that caution should be exercised when comparing measurements obtained from very short (<

22.5mm) or very long (> 25.51mm) eyes. Contrary to this, when the data was examined in the current study, the largest deviation of either mean- or default-K scan length from the simulated scan length did not belong to those with the higher MSE or those with axial length that deviated most from the Gullstrand exact eye model value of 24.385mm (Figure 2). Moreover, optic nerve head area measurement from Spectralis SD-OCT scans has been found to be independent of axial length when transverse scaling is applied using measures of ocular biometry including K and axial length [39]. It therefore does not seem to be necessary to measure axial length to minimise potential lateral measurement errors resulting from not correcting for ocular magnification [20].

The simulated scan length consistently overestimated the mean-K and default-K scan length output. Nonetheless, we observed a stronger correlation between scan length obtained with mean-K compared to default-K. Scan lengths above 5.9mm produced by the default-K setting were increasingly under-estimated compared to those obtained with mean-K (Figure 2). This implies that lateral measurements of drusen size and foveal width for example are likely to be underestimated if SD-OCT scans larger than 5.9mm are obtained with the default-K setting. We recommend incorporating the individual's mean-K and MSE during lateral retinal measurements when using the Spectralis SD-OCT. In addition, it is important to consistently use the individual's mean-K value for subsequent scans of the same patient for long-term monitoring in a clinical setting, for example measuring progression of non-exudative pigment epithelial atrophy.

CONCLUSION

This study provides useful information on the effect of ocular biometry measures on Spectralis SD-OCT scan length. The effect of ocular magnification on scan length appears to be better accounted for when an individual's mean corneal curvature value is incorporated into Spectralis SD-OCT scan acquisition as opposed to using the device's default setting. We recommend performing scan acquisition incorporating a measured mean keratometry value, with the fundus image focussed according to the individual's refractive error. This should be considered when taking area measurements and lateral measurements parallel to the retinal surface. These results may be of interest for clinical trials using SD-OCT for area or lateral measurements.

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Conflict of Interest Statement

All authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Legends

Table 1 Summary of variations in mean keratometry, axial length and mean spherical error within the study sample

Figure 1 Box and whisker plot to show scan lengths obtained from SD-OCT scans obtained with default-K settings; mean-K values; and from software simulations incorporating axial length values. The length of each box is the interquartile range and the band inside the box represents the median. The whiskers show the smallest and largest values, with outliers indicated by the circles and extreme outliers by the asterisks. The mean and median scan length for scans using the default-K was 6.04 ± 0.28mm, Md = 5.95mm; for the mean-K group 6.10 ± 0.33mm, Md = 6.00; and for the simulated-K group was 6.23 ± 0.38mm, Md = 6.21mm

Figure 2 Scatterplot of mean-K (black squares) and default-K (grey triangles) scan lengths against Zemax simulated scan length (x-axis). There is a statistically significant correlation of mean-K (ρ = 0.926, $P < 0.0005$) and default-K (ρ = 0.663, $P < 0.0005$) with the simulated scan length. Dashed grey line represents perfect agreement, $r = 1.00$

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