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## RESEARCH ARTICLE

# Utilization of Anterior Segment Optical Coherence Tomography Enhanced High Resolution Corneal In Measuring Pterygium Thickness

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***ABSTRACT***

***Introduction:*** *A significant degree of corneal astigmatism can be induced by the encroachment of a pterygium onto a cornea. As various pterygium morphologies have been advocated as contributing factor on corneal astigmatism, little support in the literature available in establishing techniques in measuring pterygium thickness as clinical indicator.* ***Objective:*** *The aim of this study was to describe a quantitative method in determining pterygium thickness using anterior segment optical coherence tomography (AS-OCT).*

***Methods:*** *Anterior segment imaging was performed using enhanced high resolution cornea (EHRC) of Visante™ AS-OCT in 120 primary pterygium eyes. Prior to imaging, corneal topography assessment was performed on each pterygium eye in order to identify its topographic location. Based on topography mapping, three meridians (in degrees) were selected as close as possible to the pterygium border, which signify the demarcation of pterygium from the cornea. Reliability testing between intra and inter-observer of AS-OCT imaging modality was examined using intraclass correlation and scatter plot.*

***Results:*** *The overall (n = 120) mean and standard deviation of pterygium thickness EHRC of AS-OCT modality were 0.48 ± 0.10 mm (confidence interval: 0.45 – 0.50). EHRC of AS-OCT also showed excellent intra and intergrader reliability in measuring pterygium thickness with intraclass correlation of 0.997 (confidence interval: 0.994 – 0.998).*

***Conclusions:*** *EHRC of AS-OCT imaging modality is a better choice in assessing pterygium compared to traditional slit-lamp biomicroscopy. This tool is applicable for future work related to better understanding on the role thickness in pterygium morphology, its progression and prediction of induced corneal astigmatism and visual impairment due to pterygium.*

***Keywords:*** *pterygium; anterior segment OCT; AS-OCT; morphology; thickness; reliability*

## INTRODUCTION

Previous studies had shown that AS-OCT is useful in making accurate measurement of anterior segment structures. These studies generally focused on the dimension of the anterior segment such as depth and width of anterior chamber angle (Nakakura et al, 2012; Bueno-Gimeno et al, 2013), corneal thickness (Kheirkhah et al, 2011; Kheirkhah et al, 2012), refractive surgery (Doors et al, 2010), evaluation of various lesions of anterior segment (Buchwald et al, 2003; Bianciotto et al, 2011; Soliman and Mohamed, 2012; Rojas et al, 2012).

Pterygium thickness is considered as a new parameter of pterygium and to the best of literature search, information available which addresses this issue is still scarce. Hence with introduction of AS-OCT, this suggests that measurements of pterygium thickness are now permitted as high quality cross-sectional images are now can be easily obtained via AS-OCT. There are two (2) modes Visante™ OCT: the standard and high resolution imaging. The standard resolution imaging provides broader view of the anterior segment with a 16 mm width and 6 mm depth image by performing 256 scans in 0.125 seconds. This enables a full overview of anterior segment structures such as cornea, iris and both angles. In contrast, high resolution imaging (High Res Mode) provides a more detailed image of with dimension of 10 mm width with 3 mm depth by performing 512 scans in 0.25 seconds (Ashrafzadeh and Steinert, 2009). Hence, the high resolution mode is more appropriate for imaging of anterior segment structures in need of detailed evaluation. In this study, High Res Mode was employed with aimed to determine an accurate dimension of pterygium.

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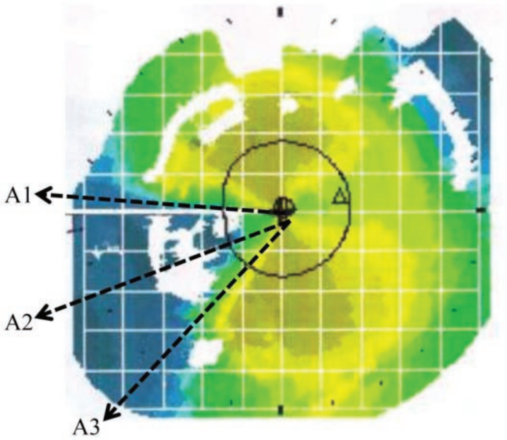



**Figure 1. Illustration on reference meridians based on the topographic map**

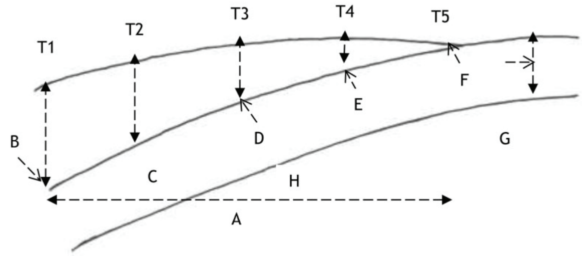
Tan et al, (1997) had postulated that pterygium fleshiness may provide some information on pterygium thickness as they suggest that increase of fleshiness could signify thickness of pterygium. Recently, Welch et al, (2011) had demonstrated the usage of AS-OCT in measuring the length of pterygium, and based on their results thickness of pterygium was clearly seen and could be measured. However, no study has been conducted to quantify pterygium thickness solely. Moreover, reliability testing of this instrument in measuring pterygium thickness are not yet been explored. This aim of the paper is to explore the usage of AS-OCT and its reliabilities in measuring pterygium thickness.

## METHODS

120 eyes from 120 primary pterygium patients were enrolled. This study adhered to the tenets of the declaration of Helsinki and was approved by the Institutional Research Ethics Board (IIUM/310/G13/4/4-125).Consent form was given to all participants. Inclusion criteria were selected as described by previous study (Oh and Wee, 2010) and patients with significant ocular surface diseases were excluded. Measurement of pterygium thickness comprised of two stages; corneal topography and AS-OCT assessments.

### Corneal Topography Assessments

Zeiss Atlas 995™ corneal topography (Carl Zeiss Meditec Inc, Dublin, USA) was employed as the baseline data in order to determine the specific location of pterygium. All data were processed via its built-in software (MasterVue™ software, version A12.2). Previous study had demonstrated the usage of




A. Total length of pterygium
B. Limbus (border of bulbar conjunctiva and cornea), Thickness (Point 1, T1)
C. Midpoint between limbus and midpoint of total length of pterygium, Thickness (Point 2,T2)
D. Midpoint of total length of pterygium, Thickness (Point 3,T3)
E. Midpoint between apex and midpoint of total length of pterygium, Thickness (Point 4,T4)
F. Apex of pterygium, Thickness (Point 5, T5)
G. Cornea
H. Pterygium

$$\text{Thickness of each meridian} = \frac{(T1 + T2 + T3 + T4 + T5)}{5}$$

$$\text{Total average thickness of pterygium} = \frac{(M1+M2+M3)}{3}$$

**Figure 2. Schematic diagram of calculation formula for pterygium thickness based on cross-sectional view of pterygium.**

corneal topography in determining the exact location of pterygium (Maheshwari, 2007). Location of pterygium can be identified as local corneal flattening (indentation) from the corneal mapping which was marked in the display in different colour (Figure 1). Only high quality images from corneal topography assessments which fulfil the criteria as previously described (Gumus et al, 2011) were included this study. It is important to obtain high quality corneal mapping images as it would later used to determine the exact location of pterygium according to its meridian. By having good topographic mapping, it is now permissible to pinpoint three (3) different meridians to act as reference meridians in determining the average thickness of pterygium via AS-OCT.

Hence, the other two (2) meridians serve as the upper and lower border of pterygium. Border of pterygium was defined as approximation of 5° from the furthest meridian observed on topographic mapping based on local indentation (blue colour) which taken as the location of pterygium (Maheshwari, 2007) (Figure 1). The reason why between 0 - 4 ° of meridian was not taken into consideration was due to the margin of pterygium are sometimes vague and topographic mapping might misinterpret it due to small changes on corneal curvature. These meridians act as the angles for AS-OCT to scan in determining the horizontal length and average thickness of pterygium.

A1, A2 and A3: Border of pterygium based on pterygium location taken as reference meridians

## AS-OCT Assessments

Based on the output from topographic mapping, a total of three meridians were taken from each pterygium image. Two meridians as close as possible to the pterygium border were measured, which indicates the furthest part of reference meridian for pterygium thickness measurement (A1 and A3). Horizontal meridian (A2) were chosen and measured from apex to limbus of pterygium as previously described (Welch et al, 2011). Each meridian angle was manually configured in AS-OCT and scanned using enhanced high resolution corneal (EHRC), OCT imaging modality of Zeiss Visante™ OCT (Zeiss Meditec Inc, Dublin, USA).

Previous studies had suggested that pterygium surface is not uniform (Soliman and Mohamed, 2012; Kieval et al, 2012). Therefore, it is suggested that multiple points are needed to signify the average thickness of pterygium. Thickness of pterygium was defined as the average thickness of pterygium from base to apex for all three (3) meridians. In order to obtain the approximate thickness, total horizontal length of pterygium obtained from OCT imaging was divided into five (5) points. The thickness of pterygium for each meridian was calculated by summed up the total five (5) different thicknesses points and then divided by five (5) points. And to obtain the average thickness of pterygium tissue, it is suggested that the thickness in all three (3) meridians were totalled and divided by three (3), as three meridians were measured for each pterygium eyes. The schematic diagram of calculation formula for pterygium thickness based on cross-sectional view of pterygium is shown in Figure 2.

## Reliability Testing of Pterygium Thickness Measurement

Reliability testing of pterygium thickness using OCT imaging tools of EHRC modality was performed. For OCT imaging, measurements were based on its hyper-reflective (red colour), which allows to differentiate between pterygium from other structures via colour coding (Buchwald et al, 2003; Soliman and Mohamed, 2012; Nanji et al, 2015) by two (2) independent observers. For intergrader, each grader measured all 120 pterygium images in single session. For intragrader reliability testing, all 120 pterygium images were measured by a single grader twice with different sequence at least one (1) month apart. On each session and sequence, all images were randomized using randomization software (Research Randomizer, Version 4.0, downloaded from www.randomizer.org).

Normality of data was tested using ratio of kurtosis and skewness of ± 2.50 (George and Mallery, 2010). Intra and intergrader reliability were assessed using intraclass correlation coefficients (ICC) and scatter plot. The alpha significance level was set at $P < 0.05$. All statistical analyses were performed using IBM SPSS (Predictive analytics software) (version 12, SPSS Inc., Chicago, IL, USA).

## RESULTS

Analysis included data from 120 primary pterygium eyes. The mean of age for the study group was 57.42 ± 11.55 years (Confidence interval (CI): 55.04 – 59.80). The overall (n = 120) mean and SD of pterygium thickness via OCT modality were 0.48 ± 0.10 mm (CI: 0.45 – 0.50). In terms of reliability testing, the intra-grader agreement in measurement of pterygium thickness between initial and the grading 1 month apart later was 0.997 (95% CI, 0.994 – 0.998; $P < 0.001$). Inter-grader agreement was 0.955 (95% CI, 0.924 – 0.973; $P < 0.001$). Table 1 shows that intra and inter-grader reliability estimates based on objective measurement in the subsample were excellent, with ICC of 0.955 to 0.997. In Figure 3 and 4, Scatter plot shows excellent intra and inter-observer agreement of pterygium thickness measurement respectively.

**Table 1. Reliability of Measurement of Pterygium Thickness (n = 120) Based on OCT Imaging Modality**

| Variables | Rater | ICC |
|---|---|---|
| Intragrader | Grader 1 | 0.997 |
| | Grader 1 (1 month apart) | |
| Intergrader | Grader 1 vs Grader 2 | 0.955 |

## DISCUSSION

Pterygium thickness is considered as a new parameter of pterygium and to the best of literature search, information available which addresses this issue is still minimal. Tan et al., (1997) had postulated that pterygium fleshiness may provide some information on pterygium thickness as they suggest that increase of fleshiness could signify thickness of pterygium. Though, no study has been conducted to quantify pterygium thickness solely.

Recent study (Sarac, Demirel and Oltulu, 2014) demonstrated a method in quantifying pterygium

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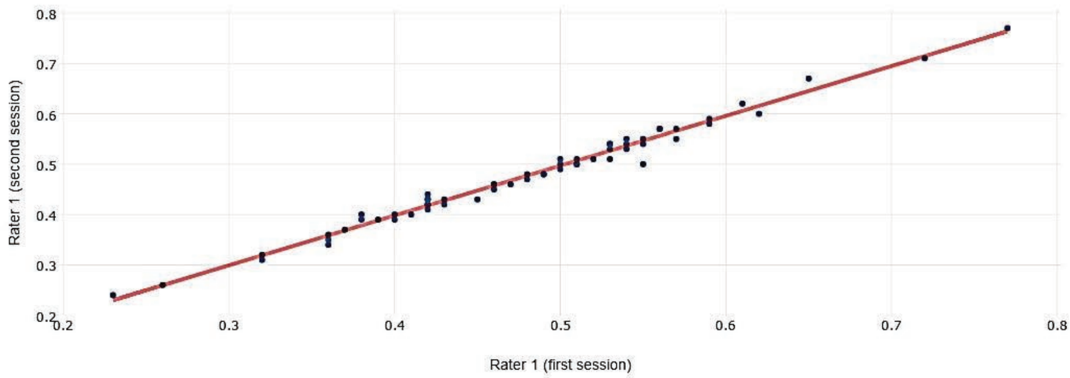


**Figure 3.** **Scatter plot of intra-observer agreement in measuring pterygium thickness based on OCT imaging modality. ICC was 0.997 (95% CI, 0.994 – 0.998).**

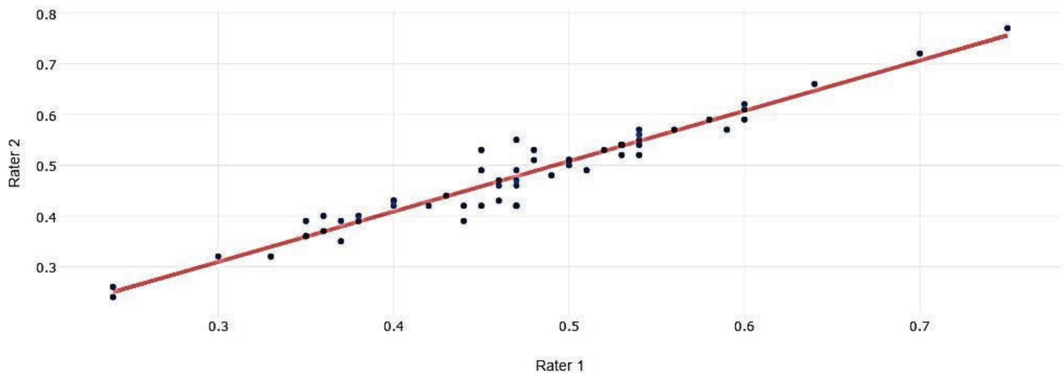


**Figure 4.** **Scatter plot of inter-observer agreement in measuring pterygium thickness based on OCT imaging modality. ICC was 0.955 (95% CI, 0.924 – 0.973).**

thickness by comparing the thickness of combination of cornea and pterygium between pre and post-surgical excision in conjunction with Bevacizumab. The authors measured pterygium thickness manually at any point of the corneal thickness map via mouse click. This process were performed in the same horizontal and vertical coordinate in each pterygium patient, and the difference in thickness between pre and post-surgical excision were taken as reduction in pterygium thickness due to Bevacizumab treatment. However, this method (Sarac, Demirel and Oltulu, 2014) could be improved further. For example, this substraction method might not indicate the true pterygium thickness as the corneal tissue may be thicker than the previous measurement due to direct hydration effect from tear film.

Hence with introduction of AS-OCT, the measurements of pterygium thickness are now permitted as high quality cross-sectional images are now can be easily obtained via AS-OCT. Recently, previous work (Welch et al, 2011) had demonstrated the usage of AS-OCT in measuring the length of pterygium, and based on their results thickness of pterygium was clearly seen and could can be measured. Unfortunately, the author did not address the issue, yet they only literally describe pterygium thickness based on the AS-OCT cross-sectional images. Moreover, reliability testing of this instrument in measuring pterygium thickness are not yet been explored. Hence, this study aims to investigate pterygium thickness and its effects of induced astigmatism based on types of pterygium using previous study (Welch et al, 2011) as the basis for future research.

This present study had demonstrated a new method as described in this study which proposed a method to quantify pterygium thickness using OCT imaging tool of EHRC modality of AS-OCT. The benefits employing this method was the ability of EHRC which can decode the ocular anterior segment structures based on its reflectivity, which allows pterygium to be differentiated easily from other structures via colour coding (Buchwald et al, 2003; Soliman and Mohamed, 2012; Nanji et al, 2015). These authors (Buchwald et al, 2003; Soliman and Mohamed, 2012; Nanji et al, 2015) reported that pterygium appeared as a hyper-reflective (red colour) lesion in the printable output. Likewise, this present study also found similar findings, which support the claim. For this study, OCT imaging tool of EHRC was employed in measuring pterygium thickness based on its hyper-reflective appearance.

Reflectivity of OCT is related to the intensity of the light which backscattered from a specific tissue. In case of hypo-reflective images, it could due to cystoid spaces or fluid as they are serous in nature (Keane et al, 2012). However, hyper-reflective could signify several factors such as high concentration of fibrous component such as fibrin (Keane et al, 2008) and aggregation of inflammatory reactions (Liakopoulos et al, 2008; Keane et al, 2012; Koo, Shin and Lim, 2014). Hence, a postulation can be made that cross-sectional image of hyper-reflective appearance of pterygium from its cross-sectional image could represents the actual thickness of pterygium as pterygium in nature comprises of fibroblasts, inflammatory cells and connective tissues (Dzunic et al, 2010; Soliman and Mohamed, 2012; Altan-Yaycioglu et al, 2013; Liu et al, 2013; Park, Kim and Lee, 2015).

This study found that OCT imaging also showed excellent reliability in measuring pterygium thickness with ICC of 0.997 (intragrader) and 0.955 (intergrader). Reasons for the good outcomes could be due to three factors. Firstly, inclusion of adequate points of measurements would give rise to an appropriate estimation of the average pterygium thickness. This present study suggested and measured pterygium average thickness at three (3) different meridians; which is appropriate with present methodology and study timeline. However, it is suggested that more meridians could be better in describing the uneven surface of pterygium (Rojas et al, 2012). This is important as this method currently measure the average thickness of pterygium. Improvement can be made with more meridians and more points of measurement.

Secondly, the utilisation of OCT imaging that employed colour codes in distinguishing between pterygium and cornea. Hence, by taking colour as separation factor, it is easier to measure pterygium thickness. Thirdly, based on the present study sample size and power of study, it is proved that pterygium thickness, as measured via OCT imaging of EHRC using AS-OCT were reliable in measuring this parameter. EHRC modality also was found better in terms of image quality compared to conventional AS-OCT modality as it provides enhanced view with less graininess, higher contrast and density within the image (Ashrafzadeh and Steinert, 2009). This study postulate that apart from pterygium length (Kampitak, 2003; Mohammad-Salih and Sharif, 2008; Öner et al, 2016) and total area (Gumus et al, 2011; Altan-Yaycioglu et al, 2013; Vives et al, 2013; Öner et al, 2016), pterygium thickness also could play a role as possible factors, which caused changes on cornea curvature. Therefore, there is a need to investigate further on how this factor contributes to these changes.

## CONCLUSION

Based on this current work, it is suggested that OCT imaging of EHRC using AS-OCT can provide better measurement of pterygium thickness rather than solely relying on the standard SLB. To the best of the author's knowledge, this is the first report that describes an objective method in measuring pterygium thickness. In conclusion, this present study demonstrated an objective method using EHRC of AS-OCT could provide a reliable measurement of pterygium thickness.

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## CONFLICT OF INTEREST

The authors report no conflicts of interest

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