

## Reliability of Pterygium Redness Grading Software (PRGS) in Describing Different Types of Primary Pterygia Based on Appearance

(Kebolehpercayaan Perisian Penggredan Kemerahan Pterigium (PRGS) dalam Mengelaskan Pelbagai Jenis Pterigium Berdasarkan Perawakan)

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### ABSTRACT

*The aim of this study was to evaluate the reliability of Pterygium Redness Grading Software (PRGS) in describing different types of primary pterygia. Ninety-three participants with primary pterygia who visited an ophthalmology clinic were recruited in this study. PRGS is a semi-automated computer program used to measure fibrovascular pterygium redness by analysing digital images of the pterygium and grading it on a continuous scale of 1 (minimum redness) to 3 (maximum redness). An ocular surface expert graded all 93 images in random order. The reliability of PRGS was determined by comparing pterygium redness measured using the software and by the expert. The mean and standard deviation of redness of the pterygium fibrovascular images measured using PRGS and by the expert were  $1.81 \pm 0.58$  and  $1.73 \pm 0.61$ , respectively ( $P = 0.396$ ). A comparative analysis based on pterygium type showed an increase in redness according to pterygium type (Type I:  $1.43 \pm 0.32$ ; Type II:  $1.67 \pm 0.55$ ; and Type III:  $2.31 \pm 0.46$ ), without significant differences compared to redness measured by the expert (Type I:  $1.38 \pm 0.34$ ; Type II:  $1.78 \pm 0.62$ ; and Type III:  $2.02 \pm 0.66$ ) (all  $P > 0.05$ ). PRGS could describe and classify pterygia according to their redness, and PRGS-based classification was in agreement with the established classification of pterygia. Therefore, PRGS can be used in addition to the existing pterygium grading system.*

*Keywords: Automate; morphology; pterygium; redness; translucence*

### ABSTRAK

*Matlamat kajian ini adalah untuk menilai kebolehpercayaan Perisian Penggredan Kemerahan Pterigium (PRGS) dalam mengelaskan jenis-jenis pterigium primer. Kajian ini berjaya merekrut 93 pesakit daripada klinik oftalmologi yang menghidap pterigium primer. PRGS merupakan program komputer semi-automatik yang berfungsi untuk mengukur darjah kemerahan pterigium fibrovaskular yang diperolehi daripada imej digital pterigium, dalam bentuk pengredan berterusan (1 untuk kemerahan minimum dan 3 untuk kemerahan maksimum). Kesemua 93 imej pterigium telah digredkan secara rambang oleh pakar permukaan okul. Kebolehpercayaan PRGS telahpun ditentukan dengan membandingkannya dengan kemerahan yang dicerap oleh pakar. Nilai min dan sisihan piawai untuk kemerahan pterigium fibrovaskular adalah  $1.81 \pm 0.58$  (PRGS) dan  $1.73 \pm 0.61$  (pakar), ( $P = 0.396$ ). Analisis berasaskan jenis pterigium menunjukkan terdapat peningkatan kemerahan pterigium fibrovaskular apabila diukur menggunakan PRGS (Jenis I:  $1.43 \pm 0.32$ ; Jenis II:  $1.67 \pm 0.55$ ; Jenis III:  $2.31 \pm 0.46$ ) berbanding pakar (Jenis I:  $1.38 \pm 0.34$ ; Jenis II:  $1.78 \pm 0.62$ ; Jenis III:  $2.02 \pm 0.66$ ), tetapi perbezaan ini tidak signifikan untuk semua jenis pterigium ( $P > 0.05$ ). Skala pengredan PRGS dapat mengelaskan pterigium berdasarkan kemerahan dan ia selaras dengan pengelasan pterigium sedia ada. Skala kemerahan ini boleh digunakan sebagai tambahan kepada pengredan pterigium yang sedia ada.*

*Kata kunci: Automatik; kemerahan; morfologi; pterigium; translusen*

### INTRODUCTION

Pesticides Pterygium is an abnormal fibrovascular growth which originates from the conjunctiva and encroaches the central cornea (Manzar & Mahar 2013; Mohd Radzi et al. 2017), and it is caused by chronic exposure to ultraviolet rays (Bradley et al. 2010; Chui et al. 2011; Hilmi et al. 2018; Modenese & Gobba 2017; Oellers et al. 2013). The severity of pterygium has been

clinically described on the basis of its length (extension) (Gumus et al. 2011; Kheirkhah et al. 2012a; Kheirkhah et al. 2012b; Mohammad-Salih & Sharif 2008) and size (Altan-Yaycioglu et al. 2013; Farhood & Kareem 2012; Vives et al. 2013). However, studies on the morphological features of pterygium, such as redness, which could also act as an indicator of disease severity are lacking. Pterygium Redness Grading Software (PRGS) was

developed to address this issue by introducing redness as an indicator to determine the effects of different types of pterygia on corneal curvature (Azemin et al. 2014; Che Azemin et al. 2015, 2014; Mohd Radzi et al. 2017).

Preliminary studies (Azemin et al. 2014; Che Azemin et al. 2015, 2014) attempted to quantify and describe pterygium redness using extensive image analysis combining colour-space conversion, colour layers, textural descriptors, and feature selection technique. The introduction of the semi-automated PRGS has allowed the grading of pterygium redness on a continuous scale of 1 (minimum redness) to 3 (maximum redness) (Mohd Radzi et al. 2017). Recent histological evidence (Altan-Yaycioglu et al. 2013; Park et al. 2015) suggests that pterygium is composed of fibrovascular tissue; hence, redness is an important element in describing pterygium. Redness indirectly signifies tissue growth, whereby more redness reflects more aggressive pterygium growth and faster progression. Thus, with the development of PRGS, this clinically important pterygium morphology can be clinically applied for evaluating and managing patients with pterygium. To the best of our knowledge, no previous study has described pterygium redness.

In 1997, Tan et al. proposed a clinical grading based on pterygium translucency which corresponds to an increase in the fleshiness of the fibrovascular components of pterygium. This clinical grading is based on the morphological appearance of pterygium. Other authors had proposed different subjectively measured clinical grading systems based on the extent of pterygium progression from the limbus to the central cornea via slit-lamp biomicroscopy examination (Farhood & Kareem 2012; Manzar & Mahar 2013; Mohammad-Salih & Sharif 2008). Although both these grading systems have clinical applicability, the inter-grader variability is high, especially in the latter approach. Hence, the current study aimed to determine the repeatability and reliability of the semi-automated PRGS in describing different types of pterygia based on pterygium redness.

#### MATERIALS AND METHODS

This study recruited 93 eyes of 93 participants with primary pterygia who visited an ophthalmology clinic. We

used digitised pterygium images and other data obtained during the baseline visit. Image acquisition, analyses, and clinical grading were performed as previously described (Che Azemin et al. 2015, 2014; Hilmi et al. 2019; Mohd Radzi et al. 2017). All participants were selected on the basis of the following specific criteria: participants with an established diagnosis of primary pterygium; participants of both sexes with ages ranging from 20 to 70 years; and those without any history of ocular trauma, ocular surgery, contact lens wear, and any ocular anterior segment disease other than pterygium which may affect vision (Che Azemin et al. 2015, 2014; Hilmi et al. 2019; Mohd Radzi et al. 2017). Assessment of primary pterygium and its classification were carried out by a consultant ophthalmologist (KMK). The study was conducted according to the recommendation of the tenets of the Declaration of Helsinki and was approved by the International Islamic University Malaysia (IIUM) ethical research committee (IIUM/310/G13/4/4-125). Written informed consent was obtained from all participants before they underwent any procedures.

For reliability testing, the consultant ophthalmologist (KMK) graded each of the 93 images on the basis of Tan's classification (Tan et al. 1997) into Type I (atrophic), Type II (intermediate), and Type III (fleshy), and subjectively graded pterygium redness on the basis of previous scales (Mohd Radzi et al. 2017) by using PRGS. The set of images was randomised using Research Randomizer software (Urbanik & Plous 2013). Thereafter, PRGS was employed, and the amount of redness was recorded for each image. Comparative analyses were conducted by evaluating the association between the redness measured using PRGS and each type of pterygium, as graded by the consultant ophthalmologist.

Statistical analyses were carried out using IBM SPSS Statistics for Windows/Macintosh, Version 24.0 (IBM Corp., Armonk, NY, USA). The reliability of PRGS was assessed using intraclass correlation coefficients (ICCs). The alpha significance level was set at  $P < 0.05$ . The difference between PRGS and expert grading was compared using a paired t-test for each pterygium group. All data were described according to pterygium types (Type I: atrophy; Type II: intermediate; and Type III: fleshy) as shown in Figure 1.

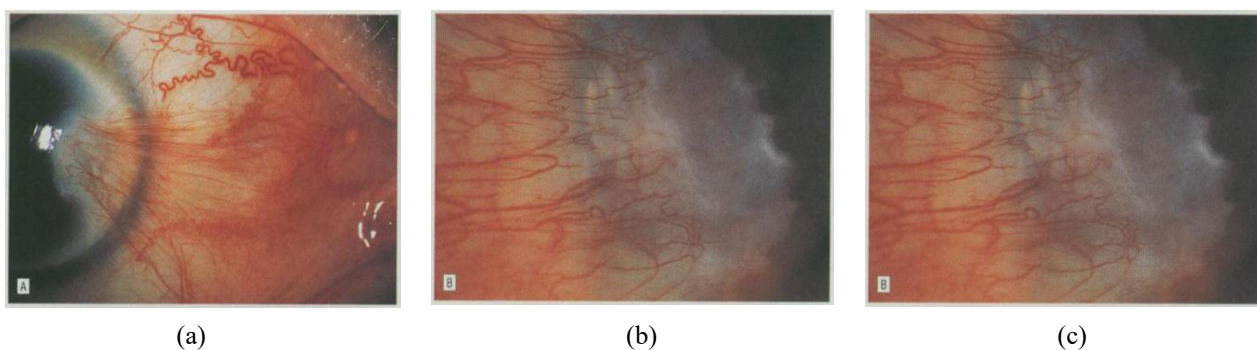


FIGURE 1. Tan's Classification of Pterygia (a) Type 1, (b) Type 2, (c) Type 3

## RESULTS AND DISCUSSION

This study recruited 93 participants, and 50.5% ( $n = 47$ ) were men. The mean ( $\pm$  standard deviation) age and computed redness (PRGS) were  $57.42 \pm 11.55$  years and  $1.81 \pm 0.58$ , respectively. Descriptive analysis ( $n = 93$ ) showed that redness measured using PRGS was comparable to expert grading, with values of  $1.81 \pm 0.58$  and  $1.73 \pm 0.61$ , respectively ( $P = 0.396$ ).

In all 93 cases, primary pterygia were further classified into three groups based on pterygium types, and comparative analysis using a paired t-test was performed to evaluate the difference in redness measured using PRGS and expert grading in each pterygium group. The results of the paired t-test showed no significant difference in pterygium redness measured using PRGS and expert grading in all pterygium groups (all  $P > 0.05$ ; Table 1). ICC analysis was employed to evaluate and compare the reliability of redness measured using PRGS to that of expert grading in each pterygium group. The analysis showed robust associations between redness measured using both approaches in all pterygium groups ( $r > 0.9$ ).

Table 2 describes the reliability estimates based on PRGS and expert grading in all pterygium groups. The ICC findings showed that PRGS could distinguish pterygium types based on their redness appearance (ICC, all  $r > 0.90$ ).

This study aimed to verify the validity and reproducibility of PRGS in describing pterygia based on redness. PRGS was developed to address an essential issue regarding the lack of standardisation in assessing pterygia. Currently, several methods are available for describing pterygia, including methods based on pterygium size, length, and morphology. However, these methods are based on subjective grading. Hence, individual variations could lead to a bias.

PRGS aimed to standardise the assessment of pterygia based on redness which was objectively measured. The study results showed that redness measured using PRGS was comparable to expert grading ( $n = 93$ ,  $P > 0.05$ ). When primary pterygia were categorized into different groups, PRGS could cluster all primary pterygia ( $n = 93$ ) into three groups based on redness which was graded on a continuous scale of 0–0.99 (minimum redness), 1.00–1.99 (moderate redness), and 2.00–3.00 (maximum redness), and these findings were in agreement with those of a previous study (Mohd Radzi et al. 2017). The current study highlights that pterygium redness measured using PRGS was in agreement with the pterygium types shown in Table 2. This indirectly showed that PRGS can be used to differentiate pterygium types. Thus, by adopting Tan's classification of pterygia, the combination of a translucent appearance of pterygium and its redness could indicate a higher probability of pterygium progression.

Redness has been used as a clinical predictor in automated assessments of anterior eye structures, such as the bulbar conjunctiva, eyelid, and cornea (Downie et al. 2016; Efron 1998; Fieguth & Simpson 2002). PRGS adopts a similar concept of integrating redness into the assessments of anterior eye structures; however, PRGS was developed specifically for evaluating pterygia and for clinically predicting the changes in oculo-visual function (Mohd Radzi et al. 2020). PRGS was developed (Mohd Radzi et al. 2017) using a combination of selective hybrid features, including entropy, vesselness, texture analysis, and average pixel values on images using specific colour spaces. This is important as the pterygium surface on the conjunctival area is not smooth, and is in fact quite rough. Thus, if a measurement was made considering that the pterygium surface is smooth, it would yield inaccurate findings.

Previously, many methods have been used to provide an objective grading, including edge detection (Amparo et al. 2017; Chun et al. 2014; Peterson & Wolffsohn 2009; Sánchez Brea et al. 2016), colour extraction (Chun et al. 2014; Efron 1998; Papas 2000; Sumi et al. 2013), smoothing (Peterson & Wolffsohn 2009; Schulze et al. 2008, 2007; Zhao et al. 2014), thresholding (Amparo et al. 2017; Fieguth & Simpson 2002; Jiang et al. 2014; Papas 2000; Schulze et al. 2009; Wolffsohn & Purslow 2003), densitometry (Chun et al. 2014), and morphometry (Romano et al. 2017), with the aim to mimic normal human colour perception. An objective assessment of pterygia may improve the reliability and consistency of measurements (Fieguth & Simpson 2002; Papas 2000; Peterson & Wolffsohn 2009; Schulze et al. 2009, 2007; Wolffsohn 2004), thereby indirectly reducing subjective bias and individual variability (Peterson & Wolffsohn 2009; Schulze et al. 2011; Zhao et al. 2014).

In this study, PRGS could detect a significant difference in pterygium types relative to their translucency. The study results also showed an increased amount of redness with a higher grade of pterygium ( $P < 0.05$ ). Pterygium redness might signify an active lesion which could grow into a larger or thicker pterygium lesion. Previous studies reported that mast cell degranulation was twice as high in pterygium tissue than in normal tissue (Džunic et al. 2010; Qin et al. 2016; Ribatti et al. 2009, 2007; Sha et al. 2014; Touhami et al. 2005), thereby indicating that chronic inflammation is a possible cause of pterygium. Hence, this study demonstrates that PRGS could be used to further classify pterygium groups according to their redness measurements. PRGS can be further utilised and refined to meet its purpose which is to predict the effect of pterygium morphology on the changes in anterior corneal curvature.

TABLE 1. Comparison of redness measurements between PRGS and expert grading based on different types of pterygia

Variable	Pterygium type			P-value*
	Type I <sup>a</sup> (n = 30)	Type II <sup>b</sup> (n = 32)	Type III <sup>c</sup> (n = 31)	
PRGS	1.43 ± 0.32	1.67 ± 0.55	2.31 ± 0.46	0.594 <sup>a</sup>
Expert	1.38 ± 0.34	1.78 ± 0.62	2.02 ± 0.66	0.446 <sup>b</sup> 0.185 <sup>c</sup>

PRGS: Pterygium Redness Grading Software

\*: Based on the independent t-test, with significance level set at 0.05 (two-tailed)

<sup>a</sup>: P-value between PRGS and Expert for Type I

<sup>b</sup>: P-value between PRGS and Expert for Type II

<sup>c</sup>: P-value between PRGS and Expert for Type III

TABLE 2. Reliability estimates for redness measurements in different types of pterygia based on PRGS and expert grading

Inter-grader (PRGS and Expert)	ICC*	95% CI <sup>#</sup>
Type I (n = 30)	0.910	0.86, 0.93
Type II (n = 32)	0.922	0.90, 0.94
Type III (n = 31)	0.954	0.92, 0.96

PRGS: Pterygium Redness Grading Software

\*: Based on the intraclass correlation coefficient (ICC)

<sup>#</sup>: Confidence interval

## CONCLUSION

This study describes the use of PRGS in describing pterygium redness in different pterygium groups. A better understanding of pterygium morphology is important in predicting pterygium progression and in clinical decision-making.

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