MODELING HUMAN PERCEPTION OF PTERYGIUM FIBROVASCULAR REDNESS MEASUREMENT

BY

NORFAZRINA BINTI ABDUL GAFFUR

A thesis submitted in fulfillment of the requirement for the degree of Master of Health Sciences (Optometry)

Kulliyyah of Allied Health Sciences
International Islamic University Malaysia

AUGUST 2017

APPROVAL PAGE

I certify that I have supervised and read this study and that in my opinion, it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation of Master of Health Sciences (Optometry).

.....

Dr. Mohd Zulfaezal Che Azemin
Supervisor

I certify that I have read this study and that in my opinion, it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation of Master of Health Sciences (Optometry).

.....

Dr. Norsham Ahmad
Internal Examiner

.....

Dr. Nashrul Fazli Mohd Nasir
External Examiner

This thesis was submitted to the Department of Optometry and Visual Science and is accepted as a fulfilment of the requirement for the degree of Master of Health Sciences (Optometry).

.....

Dr. Noor Ezailina Badarudin
Head, Department of Optometry and Visual Science

This thesis was submitted to the Kulliyyah of Allied Health Sciences and is accepted as a fulfilment of the requirement for the degree of Master of Health Sciences (Optometry).

.....

Dr. Wan Azdie Mohd Abu Bakar
Dean, Kulliyyah of Allied Health Sciences

ABSTRACT

Pterygium may cause blurring of vision in advanced cases and late treatment may affect the quality of life of a person. The aim of this research is to model a pterygium fibrovascular redness measurement grading scale. The internet enables quick feedback from the experts at the comfort of their home or office. In this study, we demonstrated the use of online form as a tool to get quick feedback from clinicians on clinical grading of pterygium images with various severities. Fifty-one clinicians graded the appearance of thirty images of pterygium fibrovascular redness on a 5-point grading scale with three referent images by an expert. The observers were required to grade each image which was presented in a random order, on a 1 to 3 grading scale. The data collection was analysed by using Statistical Package for the Social Science (SPSS) version 20.0 and Microsoft Excel. The colour space analysis was measured using MATLAB and RAPID MINER Software. The model that we implemented was based on subjective grading by clinicians using descriptive statistics (minimum, 25th percentile, median, 75th percentile, and maximum grade for each of 30 images). The scores were analyzed using quartile analysis and the median was used to construct the benchmark scores for the images. This dataset was tested on assessing human grader and was later trained using artificial neural network to formulate a supervised model using the machine learning algorithm. Intra-class Correlation (ICC) and Bland Altman analyses were performed to assess the performance of human and machine graders. The ICC results for human graders were found to be ranging from 0.57 to 0.89, which indicate poor to excellent agreement with the benchmark scores. The Artificial Neural Network (ANN) exhibits an excellent agreement with an experienced clinician (ICC=0.85), this implies the ANN model was able to mimic the grading of the human expert. This research work has demonstrated the possibility of developing clinical image dataset with its respective grading based on data extracted from an online form. These benchmarked images were shown to be useful in assessing the performance of human and machine learning algorithm. The performance of a newly developed algorithm can also be tested using this dataset in the future.

خلاصة البحث

قد تسبب الظفرة (pterygium) لطخة العين عند ارتفاعها، والتأخر عن علاجها قد يؤثر في جودة حياة صاحبها وطيبها. لذا، كان الهدف من هذه الدراسة هو وضع مقياس لدرجات احمرار الورم الأوعية الدموية. لقد مكّنت الشبكة العنكبوتية للخبراء سرعة الإجابة عن الأسئلة المطروحة إليهم في مساكنهم ومكاتبهم من غير تعب ونصب. ولذا، استخدمت الباحثة في هذه الدراسة استمارة غوغل كآلة للحصول على الإجابة السريعة في المقياس الطبي للظفرة العينية ومراحل خشونتها بالصور من الأطباء. واستجاب ما لا يقلّ عن واحد وخمسين (51) أطباء، ووضعوا لمظاهر الخارجية لاحمرار الورم الأوعية الدموية خمس درجات بجعل ثلاث صور مرجعا في ذلك، ثم طولب المشاهدون بوضع درجة مناسبة من واحد (1) إلى ثلاثة (3) لتلك الصور المرتبة ترتيبا عشوائيا. استخدمت الباحثة لتحليل الاستبانة الإصدار العشرين (20،0) لبرمجة الإحصائي لعلم الاجتماع (SPSS)، وبرنامج مايكروسوفت أيكسيل (Microsoft Excel). واستعملت برمجة ماتلاب (MATLAB) وبرمجة مراقبة السرعان (RAPIDMINER) لتحليل مقياس مساحة اللون. وارتكز المقياس المستعمل على مقاييس الذاتية للأطباء باستعمال الإحصاء الوصفي (الحد الأدنى 25%، والحد الوسطى 75%، والحد الأعلى لكل من ثلاثين صور). واعتمدت على واحد الأرباع (Quartile) في تحليل النتائج، بينما استعملت العدد الأوسط لإنشاء النتائج المرجعية للصور. اختبرت نتائج البيانات بتقدير البشري ثم الشبكة العصبية الصناعية لاستنباط الإشراف المثالي بينهما وخوارزمية الحاسب الآلي. ثم نفذت تحليل الارتباط بين الطبقات (ICC) وتحليلات ألتمان لتقييم التقويم البشري والآلي. ونتيجة (أي سي سي (ICC) تدور بين (0،57) إلى (0،89)، والذي ظهر اتفاقه مع الدرجات المرجعية في الإشارة إلى ضآلة وامتياز. واتفقت الشبكة العصبية الصناعية (ANN) مع رأي الخبيرين من الأطباء في إظهار امتياز (0،85) فحسب. وهذا يعني أن بإمكان قياس الشبكة العصبية الصناعية (ANN) محاكاة تقويم الخبراء. وثبت في آخر الدراسة إمكانية تطوير بيانات الصور الطبية ودرجاتها اعتمادا على البيانات المقتطفة عبر استمارة غوغل. وأظهرت الباحثة هذه الصور المرجعية لاستخدامها في تقييم الإنجاز البشري والآلي. كما يمكن اختبار آلة حلول الحساب المصنوعة جديدا بهذه البيانات التي جمعت مستقبلا.

DECLARATION

I hereby declare that this thesis is the result of my own investigations, except where otherwise stated. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at IIUM or other institutions.

Norfazrina Binti Abdul Gaffur

Signature: ..... Date: .....

INTERNATIONAL ISLAMIC UNIVERSITY MALAYSIA

DECLARATION OF COPYRIGHT AND AFFIRMATION OF FAIR USE OF UNPUBLISHED RESEARCH

MODELING HUMAN PERCEPTION OF PTERYGIUM FIBROVASCULAR REDNESS MEASUREMENT

I declare that the copyright holders of this dissertation are jointly owned by the student and IIUM.

By signing this form, I acknowledged that I have read and understand the IIUM Intellectual Property Right and Commercialization policy.

Affirmed by Norfazrina Binti Abdul Gaffur

....

Signature Date

ACKNOWLEDGEMENTS

In the name of Allah, the Most Gracious and the Most Merciful Alhamdulillah, all praises to Allah for the strengths and blessing in completing this thesis. This thesis would not have been possible without the support of many people. For the accomplishment of this study, I was dependent on the advice, support, and suggestions of my supervisors, friends and family. I owe thanks to many people for their support and consideration, particularly the following:

I render my gratitude, with a deep sense of acknowledgement to my supervisor Dr. Mohd Zulfaezal Che Azemin for the guidance and help during my research work. He did not only supervise my research but also guided me with his valuable suggestions and positive feedback.

I would like to thank my beloved parents, Mr. Abdul Gaffur Bin Allapitchay and Mrs. Faridah Bibi Binti Abu Bakar, my parent-in- law, Mr.Tajudin Sultan and Mrs. Wahida Banun Yusoff and to my brother, sister, grandparents, brother-in- laws and sister-in- laws for their unflagging love and support throughout my education. This research would have been impossible to achieve without their support. Finally, I would like to express my appreciation to my husband, Mr.Putra Tazreenudin Tajudin, for his unconditional love and support, which has given me the confidence to succeed. And not to forget my beloved children Putri Hasya Insyirah, Putra Wazir Ar-Rahman and Putri Husna Marissa.

Lastly, I would like to thank all the helpful and dedicated members of the Department of Optometry and Visual Science, Kulliyyah of Allied Health Science and Department of Ophthalmology Kulliyyah of Medicine for assisting us in making this study possible.

This research is supported by the Ministry of Education Malaysia under Fundamental Research Grant Scheme FRGS14-138-0379.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ANN	Artificial Neural Network
CCLRU	Cornea and Contact Lens Unit
CRT	Cathode Ray Tube
CSO	Construzione Strumenti Oftalmici
HD	High Definition
ICC	Intra-class Correlation
IIUM	International Islamic University Malaysia
IREC	IIUM Research Ethical Committee
LCD	Liquid Crystal Displays
RGB	Red-Green-Blue
ROI	Region of Interest
SLB	Slit Lamp Biomicroscopy
UV	Ultraviolet
MPEG	Motion Picture Experts Group
JPEG	Joint Photographic Experts Group

LIST OF SYMBOLS

™	Trademarked
º	Degree
>	More than
=	Equal to
&	And

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND OF THE STUDY

Pterygium has a worldwide distribution and more common in warm and dry climates especially in countries such as Philippines, Myanmar, South Thailand and Peninsular Malaysia which are originated near the equator belt of the earth and less than 2% in altitudes. Pterygium was more commonly observed in those who worked outside, and it was positively correlated with lower latitudes and high ultraviolet levels (Taylor, 1980). There is another study suggests that pterygium can induce corneal astigmatism. When primary pterygium reaches more than 1.0 mm in size from the limbus, it induces with-the-rule significant astigmatism (> or = 1.0 dioptre) (Avisar, Loya, Yassur, & Weinberger, 2000). One of the causes of the red eye is pinguecula or pterygium. Pterygium is a non-malignant and a slow growing proliferation of wing shaped fibrovascular tissue originating on the conjunctiva and extending onto the cornea. This condition later will disturb the vision (Galor & Jeng, 2008). Symptoms of pterygium include foreign body sensation, persistent redness from smoking and air pollution from vehicles and factories. Besides, other symptoms of pterygium also include inflammation of the eyes, tearing, which can cause bleeding, dry and itchy eyes. In more advanced cases the pterygium can affect vision as it encroaches the cornea with the potential of obscuring the optical centre of the cornea and inducing astigmatism and corneal scarring (Hood, 2009). Moreover, pterygium may cause significant alteration in visual function in some advanced cases. Severe cases of pterygium may cause blurring of vision and would affect the quality of life of a

person. According to (Galor & Jeng, 2008) pterygium can cause eye redness and irritation and if the condition persists it can be surgically removed. However, the pterygium cases are recurrent in several studies. Surgical techniques for pterygium include bare sclera excision, excision with simple conjunctival closure, excision with administration of antimetabolite excision adjuvants such as mitomycin C (MMC), and excision followed by with conjunctival autograft, amniotic membrane transplantation (Mahdy & Bhatia, 2009). The cut and paste technique for pterygium surgery was first reported by Kenyon et al. in 1985 (Huerva, March, Martinez-Alonso, Muniesa, & Sanchez, 2012). Although various studies have compared the safety and recurrence rates of pterygium, there was no such consensus with respect to the question of recurrences and unfortunately, the recurrence rate was not evaluated in many of these studies (Huerva et al., 2012). Some studies however showed lower rates of recurrence when fibrin glue was used in the surgery, while in others, the same rate of recurrence was reported as associated with suturing (Huerva et al., 2012). The previous evidences show the importance of having clinical grading that can better characterise the pterygium before optimal clinical decision can be made to give proper treatment to each case of pterygium.

1.2 STATEMENT OF THE PROBLEM

Red eye is one of the sign of ocular inflammation. Signs and symptoms of red eye include eye discharge, redness, pain, photophobia, itching, and visual changes. The cause of red eye usually can be diagnosed through a detailed patient history taking and comprehensive eye examination. When a patient presents with redness in the eye, the cause needs to be diagnosed quickly. Low redness severity in the eye can be initially

managed by an internist, but higher redness severity may require urgent referral to the ophthalmologist.

The use of numeric scales to grade the severity or advancement of clinical signs is becoming widespread. In clinical practice, there has been a need to grade the magnitude or the severity of the functions and qualities that are assessed in the examination. It is popular to use a discrete step grading scale to categorize the severity of clinical findings. To have a better accuracy and consistency of record purposes, grading scales are very beneficial clinical tool to be used (Allansmith et al., 1977). Previous research emphasized on the clinical grading scales and their influence on the clinician's ability to detect changes (Fieguth & Simpson, 2001). These principles have been applied to grades or measures derived from objective measuring instruments, subjective tests, or techniques in which the clinician makes subjective judgments. A benchmarked image dataset is used to show the severity associated with the images. Computer models can be applied to help to estimate a finer scale and automate the process. Figure 1.1 illustrates the image-based clinical grading process commonly takes place in a routine eye examination.

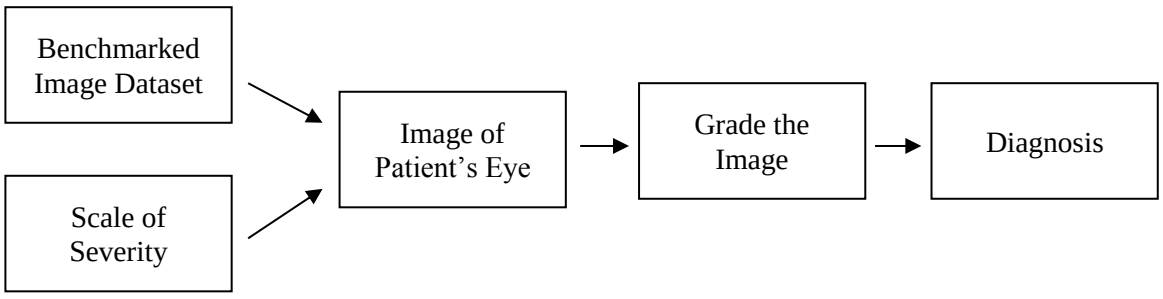

Figure 1.1 Common image-based clinical grading framework

While grading for bulbar conjunctiva redness has been widely formulated, there is lack of research conducted to characterise redness in pterygium tissue.

This study aims to model a grading scale for pterygium fibrovascular redness measurements based on clinicians perception of pterygium patient images. From this scale the clinicians can have better reliability on diagnosing the pterygium cases and need for surgery.

1.3 RESEARCH OBJECTIVES

This study aimed to achieve the following objectives:

i. To obtain subjective grading of pterygium redness from clinicians' perception.
ii. To find the ground truth based on the median value of the grading.
iii. To demonstrate the use the benchmarked pterygium image dataset in assessing the performance of human grader and computer-based model developed using software.

1.4 RESEARCH QUESTIONS

i. What is the median score for each image in the benchmarked dataset?
ii. Is the benchmarked pterygium image dataset useful in assessing the performance of a human grader?
iii. Is the benchmarked pterygium image dataset useful in assessing the performance of a computer model?

1.5 HYPOTHESIS

There is a good agreement between the median score of clinician's grading and the computer model.

1.6 SIGNIFICANCE OF THE STUDY

This study will assist clinicians to better describe the pterygium tissue based on the fibrovascular redness measurement. By characterising the pterygium image, further investigations can be done in clinical research to improve the current decision making process.

1.7 THESIS OVERVIEW

The subsequent chapters of the thesis are organised as follows:

CHAPTER TWO describes the anatomy of the cornea and pterygium tissue component. In addition, it mentions about the previous studies on bulbar redness, pterygium grading scales and colour spaces.

CHAPTER THREE addresses the description of methodology and graphical analysis. Besides, in this chapter, it explains the methodology design including the inclusion criteria, apparatus of the study and data collection process. It also describes the flow of the study and data analysis procedure to obtain the results.

CHAPTER FOUR discussed on the results obtained. The Entropy values, images for multiple colour spaces, the Bland Altman plot and the Intra-class Correlation values for human and the machine graders and the Neural Network model results.

CHAPTER FIVE discussed on the limitation of this study and provided the directions for future work. This chapter also gave the summary of this thesis.

Last but not least, the appendices contained the full details of the online google forms and the reference image (Appendix I), paper and publication (Appendix II) and abstracts that have been submitted for exhibition and conferences (Appendix III).

CHAPTER TWO

LITERATURE REVIEW

2.1 CORNEA AND ITS PROPERTIES

One of the most important element of the ocular refractive system is the cornea. Cornea, as illustrated in Figure 2.1, is a non-vascular and transparent tissue located at the anterior part of the eye.

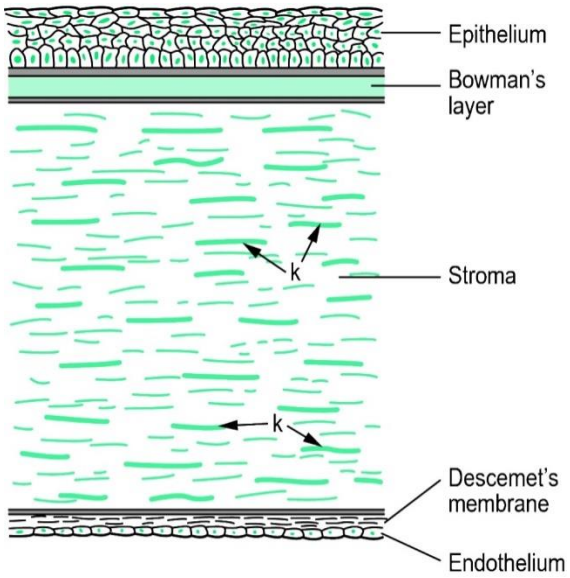

Figure 2.1 The anatomy of the cornea
Source: Millodot (2009)

It is one of the most densely innervated tissues in the body. Human cornea consists of five layers, three cellular layers which are the epithelium, stroma, and endothelium and two interface layers consisting of Bowman's membrane and Descemet's membrane. Corneal stroma composes of cellular (keratocytes) and extracellular components. Cornea also is an immune-privileged tissue due to the

absence of blood and lymphatic vessels. Although normal cornea is an avascular, many conditions can cause neovascularization, scarring, and may lead to corneal blindness (Gandhi & Jain, 2014).

Redness in the eye is related to blood vessel dilation in the conjunctiva and sclera regions. It is another means of assessing severity of the damage in the tissue (Fieguth & Simpson, 2001). This approach is currently underexplored for the assessment of the pterygium tissue. Grading redness is commonly done subjectively by clinicians using a set of reference images as a guide (Galor & Jeng, 2008). While this method is considered repeatable, it must be done by trained graders. Automating this process will result in a highly consistent grading, regardless of the experience of the grader (Hood, 2009).

2.2 PINGUECULA AND PTERYGIUM TISSUE

Pinguecula, as illustrated in Figure 2.2 is a yellowish spot of proliferation on the bulbar conjunctiva in between the junction of the sclera and cornea. It usually occurs on the nasal side. It is likely related to the ultraviolet light exposure and chronic environmental irritation. Pinguecula is frequently seen in elderly people who extensively get exposed to sun exposure (Norn & Franck, 2009).

Figure 2.2 Pinguecula
Source: Pinguecula (2003)

In an electron microscopic study Cameron (1983) concludes that in the cap areas of several pterygia there are presence of active fibroblasts in the natural tissue planes around the Bowman's layer. Thus the hypothesis is that the fibroblasts originate in the limbal connective tissue. The fibroblasts are in the cornea top and bottom of Bowman's membrane, destroying the latter and some of the superficial corneal stroma.

Pterygia is a triangular fold of bulbar conjunctiva in the interpalpebral fissure with its apex advancing progressively towards the cornea usually from the nasal side (Millodot, 2009). A pinguecula often develop due to a degenerative process caused by dryness or irritation from wind and dust or too much exposure to sunlight. It becomes more prevalent with age. Symptoms generally occurs when the pterygium encroaches on the cornea and it may affect the vision. Thus surgical intervention is needed. Some pterygia tend to recur after excision (Millodot, 2009).

Figure 2.3 An advanced case of pterygium
Source : Millodot (2009)

In other words, pterygium is a kind of benign growth that occurs in the eye region where the eyelids is not been obstructed when opened. Blindness can be caused if not been treated for a long period. Pterygium grading is normally developed based on the image characteristics of the fibrovascular tissues.

2.3 PTERYGIUM CLINICAL GRADING SCALE

There are two common clinical grading being used at the moment. One of them is the original work by Tan et al. (1997). The research had proposed a clinical grading, based on its relative translucency of pterygium tissue, with the premise that loss of translucency was related to increased fleshiness or thickness of the fibrovascular component of pterygium (Tan et al., 1997).

i. Grade-I (atrophy) - denoted as pterygium which episcleral vessels underlying the body of pterygium were unobscured and clearly distinguished.
ii. Grade-II (intermediate) - denoted as pterygium which episcleral vessel details were indistinctly seen or partially obscured.
iii. Grade-III (fleshy) - denoted as pterygium which episcleral vessels underlying the body of pterygium were totally obscured.