

## REVIEW

**Dissertation title:** Infrared Imaging of the Meibomin Gland Structure

**Author:** Laura Rico del Viejo, MSc

**Supervised by:** Prof. Robert Iskander, PhD, DSc  
Prof. David Madrid Costa, PhD  
Prof. José Manuel Benítez del Castillo, PhD

Review of the dissertation by Laura Rico del Viejo, MSc was commissioned by Dean of the Faculty of Fundamental Problems in Technology, Wrocław University of Science and Technology, Prof. Arkadiusz Wójs, PhD, DSc on 16.04.2019.

### 1. Importance, originality and scope

Dry eye disease, being a disorder of the tear film due to tear deficiency or excessive tear evaporation, is considered as a significant impact on the quality of life. Moreover, eye care practitioners consider it as one of the most frequently encountered ocular morbidities. Since the prevalence of the dry eye disease increases linearly with age and the global population of the elderly is expected to double by 2050, the disease becomes a growing public health concern.

Due to the latest techniques for the ocular surface assessment, the meibography has become a widely employed tool for researchers and clinicians employed in the area of the assessment of the Meibomian Gland (MG) under various illumination techniques. It provides diagnostic morphology information including meibomian gland loss, dropout, shortening, dilation, distortion, etc. Recently, the introduction of the non-contact infrared meibography, has improved the quality of the acquired images.

Thus, the Ph.D. study under consideration, related to the assessment of changes in the meibomian gland structure is fully justified and compatible with current research studies and clinical demands.

The work contains 201 pages divided into 6 chapters, preceded by an index, abstracts written in English, Spanish, and Polish, lists of abbreviations, figures and tables, and followed by references of 339 positions, Epilogue, that contains authors scientific dissemination and research activities. Annex includes the approval from the Ethics Committee, Participant information sheet and informed consent, Clinical sheet, DED questionnaires, The ocular surface, Disease index (OSDI), Symptom assessment in dry eye (SANDE), Standard patient evaluation of eye dryness (SPEED), Dry eye questionnaire (DEQ-5; short version), Personal images permissions, Description of the methodology to obtain the MG morphology parameters by an automatic algorithm.

The first chapter provides a wide background about the several aspects of the ocular surface. Chapter 2 summarizes the justification, hypothesis and objectives stated in the dissertation. Chapter 3 describes the clinical protocol, methodology, material and the statistical analysis applied in each of four studies performed within the PhD thesis. Chapter 4 presents results of all four studies in figures and tables. Chapter 5 discusses the results of these studies separately. Chapter 6 summarizes the conclusions and gives some remarks about future studies.

In the dissertation two hypotheses have been stated and proven by the author: (1) Information revealed by NIM (Non-contrast Infrared Meibography) can be used for assessing changes in the morphology of the meibomian gland (such as loss of glandular tissue, shortening and distortion of the glands) related to the Dry Eye Disease (DED). (2) Changes in MG structure can affect the ocular surface integrity.

The main objective, established by the author was to study the relationship between the Meibomian Gland Loss (MGL) revealed by NIM and the ocular surface parameters. The secondary objectives include (1) the study of the relationship between the MGL revealed by NIM and the ocular surface parameters, (2) the assessment of the effect of ageing on the ocular surface parameters and to study its role on the DED diagnosis, (3) study of the relationship between new objective MG morphology parameters and the ocular surface parameters, and (4) study and comparison of the thermal characteristics of Dry Eye Disease and healthy subjects using non-contrast IR thermography.

In order to prove the hypotheses and accomplish the objectives, a carefully selected and approved by the Ethics Committee of San Carlos University Hospital in

Madrid clinical protocol has been designed. Then, measures are presented and statistical methods employed for their analysis are described. Finally, the results are discussed.

The clinical protocol includes invasive and non-invasive clinical tests performed in an order from the least invasive to the most invasive once. The clinical examination starts with the patient interview, followed by the tear film osmolarity and an automated measure with Keratograph 5M. Then, a thermal registration of the ocular surface is followed by a biomicroscopic general assessment that observes the ocular surface staining and the tear break-up time. Next, the fluorescein dye is applied in order to evaluate the tear film stability and the corneal staining. The conjunctival integrity and the eyelid margin are assessed by applying lissamine green strips. A meibography image of each eyelid has been obtained by using the Keratograph 5M. Finally, the Schirmer test has been performed with measuring the length of wetting.

Based on the parameters, extracted during the clinical procedures, experimental studies have been performed. They are organized into four independent parts. The goal of each study is related to the objectives summarized above.

The first study refers to an analysis of the ageing influence on the ocular surface parameters. This study gives an input to the knowledge of the effect of ocular surface ageing to the dry eye diagnosis. It confirms a decline in the tear film with ageing.

The second study evaluates the relationship between the meibomian gland loss and the ocular surface parameters and symptomatology. The meibomian gland loss has been extracted from the infrared images acquired by the camera integrated with the Keratograph 5M. Its value higher than 50% is accompanied by signs of increased osmolarity, redness and staining of the ocular surface. Due to the mean age of participants, this study could not ascertain where the abnormal signs were related to the meibomian gland loss or the age.

The third study finds the relation between objective meibomian gland parameters and the ocular surface parameters. It is an attempt to objectively report the irregularity of the meibomian gland. The author rightly notices the influence provided by the age.

In the fourth study a trial of employing IR thermography to distinguish dry eye disease for a healthy eye has been performed. The camera has measured the ocular surface temperature. In this study a control group has been used.

## **2. Substantive assessment of the dissertation**

The PhD Student has correctly assessed the problem and applied the appropriate tools of modern meibomian gland structure assessment methods. The most important achievements of PhD student in my opinion include:

1. extended and comprehensive state-of-the-art study on dry eye disease as a multifactorial problem of the ocular surface
2. verification of the research hypothesis by designing the study protocol
3. statistical data analysis that indicates the following results:
  - a. effect of ageing on the ocular surface parameters
  - b. relationship between Meibomian Gland Loss assessed by Non-contrast Infrared Meibography and the ocular surface parameters and symptomatology
  - c. relationship between objective Meibomian Gland morphological parameters and the ocular surface parameters
  - d. evaluation of the thermal changes of the ocular surface in patients with dry eye disease and healthy eyes.

## **3. Comments and remarks**

The reading of the dissertation also raises some remarks of a discussion or polemic nature.

1. The parameter evaluation is mentioned once in the entire dissertation mentioned (Sec. 3.1.11.1). No information are given about the methodology employed at this stage, no results are shown. This part of the study is essential to assess the reliability of the final results.
2. In Sec. 4.3.1. an “automated algorithm that processes successfully meibography images” is mentioned. I can only guess that it refers to the poster presented at page 201. The evaluation of data subjected to the analysis within the evaluated dissertation would be valuable?

## **4. Summary**

The doctoral dissertation presented for review contains a correctly formulated and solved research problem and constitutes a valuable contribution to the fields of optometry and medical data statistical analysis. The original research included in the

dissertation contains the development and verification of a clinical protocol yielding interesting results related to the support the dry eye disease assessment.

In summary, in my opinion Laura Rico del Viejo, MSc demonstrates the knowledge and skills required to obtain a PhD in technical sciences in the discipline of Biomedical Engineering. The dissertation meets the requirements of the doctoral dissertations and in reference to the Act of 14 March 2003 on academic degrees and the academic title and on the degrees and title in the field of art, I am asking for its acceptance and admission of the author to doctoral finals.

G. Rico