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Diagnosis of response and non-response to dry eye treatment using infrared thermography images

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HIGHLIGHTS

- Responders and non-responders of dry eye (DE) treatment are classified using infrared (IR) images.
- DE treatments hot towel, EyeGiene®, and Blephasteam® are performed twice daily and Lipiflow® for 12 min.
- IR images are taken at week 0 (baseline), weeks 4 and 12 after treatment.
- Various entropy and energy features are extracted from the IR images.
- Features coupled with K nearest neighbour classifier yielded an average accuracy of more than 99%.

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ABSTRACT

The dry eye treatment outcome depends on the assessment of clinical relevance of the treatment effect. The potential approach to assess the clinical relevance of the treatment is to identify the symptoms responders and non-responders to the given treatments using the responder analysis. In our work, we have performed the responder analysis to assess the clinical relevance effect of the dry eye treatments namely, hot towel, EyeGiene®, and Blephasteam® twice daily and 12 min session of Lipiflow®. Thermography is performed at week 0 (baseline), at weeks 4 and 12 after treatment. The clinical parameters such as, change in the clinical irritations scores, tear break up time (TBUT), corneal staining and Schirmer's symptoms tests values are used to obtain the responders and non-responders groups. We have obtained the infrared thermography images of dry eye symptoms responders and non-responders to the three types of warming treatments. The energy, kurtosis, skewness, mean, standard deviation, and various entropies namely Shannon, Renyi and Kapoor are extracted from responders and non-responders thermograms. The extracted features are ranked based on *t*-values. These ranked features are fed to the various classifiers to get the highest performance using minimum features. We have used decision tree (DT), K nearest neighbour (KNN), Naves Bayesian (NB) and support vector machine (SVM) to classify the features into responder and non-responder classes. We have obtained an average accuracy of 99.88%, sensitivity of 99.7% and specificity of 100% using KNN classifier using ten-fold cross validation.

1. Introduction

Dry eye (DE), one of the most common problems encountered by ophthalmologists, is a challenge to diagnose and to treat due to its multiple causes. One of the main causes of DE is meibomian gland dysfunction (MGD), also termed as posterior blepharitis and is chronic abnormality of the meibomian glands (MG) in the eyelids [37]. It is estimated that MGD affects 46.2–69.3% Asians and 3.5–19.9% Caucasians [51,52]. MGD is characterised by the alterations in the glandular secretions due to terminal duct obstruction. These alterations in glandular secretion results in the eye discomfort [50], irritation, the ocular surface inflammation, tear film instability [37], rapid tear evaporation and finally the DE [16]. The

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standard procedures and tests are conducted based on the symptoms exhibited to diagnose MGD and DE. The irritation, tear break up time (TBUT), Schirmer's test, corneal staining symptoms tests are used to diagnose MGD and to decide on further treatments plan. One of the non-invasive diagnostic tests used is infrared thermography (IR) [39] for the diagnosis of MGD and DE. In 1960s IR thermography is discovered as a body imaging modality for medical sciences [49]. The thermography images taken with IR cameras provide information about physical abnormalities such as, cancer, infection, eye disease. In terms of medical applications, the usefulness of this IR thermography diagnostic method can be expressed in terms of the ability to deliver a correct diagnosis. The IR thermography in the application of eye measures temperature changes in the vascular tissues [22]. These temperature changes can be linked to DE. Thus this technique is beginning to play an important role in the field of ophthalmology [22] for the study of tear film and its deficiencies in the diagnosis of DE [47,25,23,56,24]. The OST, which is affected by tear film stability [21] are studied by researchers using IR thermography [1,22,23,25].

The standard MGD treatment methods are manual warm compresses [16], commercialised compressive devices [38,35,33,36], self-administered lid massage [7,27]. The main objective of these treatment methods is to relieve meibomian gland obstruction thus prevent it from causing further complications. These conventional and commercial eyelid-warming treatments have showed to improve patient's symptoms [38,32,17,30,18,59,33,13], tear film stability [38,32,17,30,18,59,33,41], slow down tear evaporation [17,41], and reduce ocular surface damage [33,42]. Benefits or results always go hand in hand with few limitations or compromises. The warm compresses and self-administered lid massage are normally inefficient, and can be very painful for the patient [3]. And also the warm compress method can be both time-consuming and labor intensive [15,4], which can be avoided by using the commercialised compressive devices. So far no method has reported any optimal warm compress method regime to reduce significantly the blockage of the upper and lower eyelids of the meibomian gland [31]. The studies on compressive devices result in measurable improvements in lipid layer thickness [38,27], meibomian gland expressibility [17,36,27], and DE symptoms.

Various eyelid-warming devices that are convenient to use and safe in heat delivery have been developed recently [32,30,43]. Three examples are EyeGiene® (Eyedetec Medical, Inc., Danville, California, USA), Blephasteam® (LaboratoriesThea, France) and LipiFlow (TearScience, Morriville, NC). EyeGiene® is a convenient and portable system with an eye mask and sachets containing heat-generating chemicals. It applies warmness to eyelids for a duration of 10 min during rest or travelling. Blephasteam® is an eyelid warming device consisting of pair of goggles which delivers a latent moist heat therapy to the eyelids in standardised conditions. This system provides a heat therapy to melt meibomian secretions by unblocking the glands with a real efficacy in only 10 min.

The conventional types of eyelid heating devices are known to apply heat to the eyelid outer surface only even though they are claimed to be effective in melting the eyelid block. Therefore before reaching the meibomian glands, the applied heat must diffuse through the surface of the eyelid skin, muscle, and the insulating tarsal plate. The thick anterior lid vascular supply poses a further thermal challenge to the conventional compressive devices as it transfers away a major amount of the delivered heat from the ocular surface [8,20]. An innovative LipiFlow® system developed addresses the shortcomings of current therapeutic methods to alleviate obstruction of MGs and to safely deliver therapeutic levels of heat and pressure [30]. The LipiFlow® system applies the heat to the upper and lower eyelids directly above the MGs and at the same time exerting graded pulsatile pressure to the eyelid outer surfaces [26,14,34]. The LipiFlow® system showed significant effectiveness and safety in the treatment of MGD and DE symptoms.

The short and long-term effectiveness of these eye-lid warming devices are lacking in evidence. The combined use of EyeGiene® (controlled heat to the eyelid margin) and eyelid massage treatment show efficacy in reducing symptoms in MGD. Combined use affect the MGs by increasing the tear film lipid concentration and improved tear film stability [18]. Though Blephasteam® warming device is considered as a promising alternative to conventional method, no short-term effects are observed to this treatment [44].

The outcome of efficiency of the treatments is determined by the number of symptoms responders and non-responders, though the complete recovery from the treatments is very difficult task. Successful outcomes or long-term efficacy of the conventional devices treatments are not well known/studied. Therefore in our work, we are analysing the clinical significance of treatment effect using responder analysis [55]. In this analysis study, we are developing a system which will automatically identify and classify the IR thermography images into symptoms responders and non-responders to the compressive treatments namely, Towel, EyeGiene®, Blephasteam® and LipiFlow®. Initially, the irritation, TBUT, corneal staining and Schirmer's symptoms tests are used to identify the responders and non-responders to the four types of treatments. The images of the two classes are further studied and analysed to develop classification system which will automatically classify the images into responders and non-responders classes using image processing techniques.

The proposed system block diagram is shown in Fig. 1. In this study, the outcome of the treatments (warm towel, EyeGiene®, Blephasteam® and LipiFlow®) or symptoms responders and non-responders to the treatments (warm towel, EyeGiene®, Blephasteam® and LipiFlow®) groups are identified using the irritation, TBUT, corneal staining and Schiermer's symptoms tests. The IR thermography images of symptoms responders and non-responders to the treatments are subjected to pre-processing to select the region of eye. From the pre-processed images, we have extracted salient features (Energy, mean, standard deviation, kurtosis, skewness and entropies). These features are ranked using t-test based on their p-values. The ranked features are fed to classifiers (DT, KNN, NBC and SVM) one by one to obtain the highest classification performance using minimum number of features. The flow of the paper is as follows. Section 2 discusses about the data acquired, image processing, feature extraction, feature ranking, and different classifiers. Results are of the proposed method are tabulated in Section 3 and discussed in Section 4. Finally the paper is concluded in Section 5.

2. Materials and methods used

2.1. Data acquisition

The required IR thermal image sequences of the DE/MGD patients who have responded and not responded to the given treatments were collected using VarioTHERM head II device from Singapore eye research institute (SERI), Singapore. The study had parallel treatment groups using the eyelid-warming devices, EyeGiene® and Blephasteam®, LipiFlow® and warm towel compression in MGD participants. We have taken the recordings between 10 AM and 4 PM, with room temperature and humidity controlled at around 20–23 °C and 60–68% respectively. Each thermal sequence lasted 20s long, and in each second 25 images were recorded. The size of each thermal image is 442 × 299 pixels, stored in JPEG format. A total of 81 subjects (40 subjects those who have responded and 41 those who have not-responded were included in this study. Fig. 2 shows the typical image of non-responder and responder to the DE