

Appendix 3.2

Report of Publishing Journal Papers

Name: (Presenter)	Laily Azyan Ramlan												
Affiliation:	Universiti Kebangsaan Malaysia												
Project Title:	Integrated Decision Support System for Non-Communicable Ocular Diseases using Machine Intelligence												
Journal Name: (Website if any)	MDPI Diagnostic website: https://www.mdpi.com/journal/diagnostics												
Title of Research Paper:	Non-Invasive Dry Eye Disease Detection using Infrared Thermography Images: A Proof-of-Concept Study												
Name of all Co-authors (if any)	Wan Mimi Diyana Wan Zaki, Marizuana Mat Daud and Haliza Abdul Mutalib												
Reviewers' Questions and Comments: <u>Round 1 Revision</u> Reviewer 1: This manuscript discusses a non-invasive screening tool for the detection of Dry Eye Disease by integrating infrared thermography with deep learning and machine learning algorithms. Below are my comments and recommendations: In general: - The manuscript does not provide a sufficient number of references to adequately support its claims. - Please, ensure that the following criterion is met in all tables: Rounding the mean: Identify the position of the first significant digit of the standard deviation, and round the mean to the same decimal place. Examples: <table> <tr> <td>Age</td> <td>31.30</td> <td>±</td> <td>17.60</td> <td>25.60±</td> <td>10.60</td> </tr> <tr> <td>NC</td> <td>0.60 ±0.20</td> <td></td> <td>0.50 ±0.20</td> <td></td> <td></td> </tr> </table> - Lines 54-56: When the authors state, "Multiple clinical studies have highlighted the significant role of inflammation in the ocular surface, meibomian glands, lacrimal glands, autoimmune diseases, and systemic conditions, as well as age-related dysfunction, in the pathogenesis of DED." they must include bibliographical references to support these statements. - Lines 89 and 90: Please remove the space in the ratio values 1:12729 and 1:10000. - Line 89: Reference [15] appears to be incomplete. - Lines 145-146: Please indicate the standard formula to calculate the Ocular Surface Disease Index		Age	31.30	±	17.60	25.60±	10.60	NC	0.60 ±0.20		0.50 ±0.20		
Age	31.30	±	17.60	25.60±	10.60								
NC	0.60 ±0.20		0.50 ±0.20										

(OSDI)

- Table 1: Could the authors clarify the meaning of the abbreviations NK, PK, and TK?
- Figure 3a, 3b, and 3c: All images are of poor quality and should be replaced. Figure 3b: the curve labels are missing.
- Lines 284-286: When the authors state, "Overall, the study demonstrated that DITI-derived features, when integrated with appropriate ML algorithms, offer a promising pathway for non-invasive, automated screening of DED with high accuracy and meaningful clinical applicability" Please move this sentence to the Conclusion Section for better placement.
- Lines 304-305: When the authors state, "which aligns with established epidemiological patterns linking higher DED prevalence to females" a reference should be inserted here.
- Table 2: According to the authors, OSDI exceeding 13 was interpreted as suggestive of DED. The table shows that the mean OSDI value for the normal group is 15.90 ± 8.48 . What is the explanation for this relatively high value?
- Line 431: When the authors state "... are illustrated in Figure 7," maybe they mean "Figure 5."
- Table 6: The meaning of the abbreviations Acc, Sen, Spe, and Err must be included in the table title.
- Lines 572-575: the comment "Accordingly, individuals with severe DED, as well as those with recent ocular surgery, medications affecting tear film stability, pregnancy, or breastfeeding, were excluded from initial model training to maintain generalizability for standard screening applications" has already been mentioned in the section (2.1. Study Design and Data Acquisition). Please remove it.

Reviewer 2:

Thank you for the opportunity to review your manuscript. The concept explored is of potential interest, but several key methodological and interpretive issues limit the strength of the current submission. The following points outline areas that would need to be addressed in a substantially revised or newly designed study.

- 1- The study is not framed appropriately. Given the limited sample size, lack of external validation, and absence of a controlled diagnostic comparison, the work would be more appropriately presented as an early-stage proof-of-concept rather than as a clinically applicable method.
- 2- A recognized diagnostic gold standard is not established. TBUT and OSDI are used to label the data and to assess model performance, which introduces circularity. Diagnostic accuracy should be evaluated against an independent, clinically accepted reference.
- 3- While TBUT and OSDI are measured, they are not analyzed as separate diagnostic tools. There is no comparative evaluation of how the proposed method performs relative to existing diagnostics, which limits the ability to assess its added value or practical utility.
- 4- The conclusions overstate the evidence provided. Claims regarding diagnostic potential and accuracy go beyond what is justified by the current data and design. These should be clearly tempered or omitted.

5- The dataset is small and limited in scope, with no power calculation or confidence interval reporting. The exclusion of severe DED cases also narrows the applicability of the findings and supports an exploratory classification rather than a diagnostic one.

6- The analysis appears to treat both eyes from the same subject as independent data points, without addressing intra-subject correlation. This can compromise the statistical validity of the results and should be corrected in any future study.

7- To move forward, the authors should either substantially rewrite the manuscript as a proof-of-concept study using appropriately cautious language, or repeat the work with a larger sample size and a properly controlled design that includes a defined diagnostic gold standard and comparative evaluation of multiple diagnostic methods applied to the same subjects.

Reviewer 3:

Thank you for giving me the opportunity to review your manuscript entitled “*Non-Invasive Dry Eye Disease Detection using Infrared Thermography Images.*” I very much enjoyed reading your manuscript.

Summary:

This study presents a novel approach to screening Dry Eye Disease (DED) by integrating smartphone-based infrared thermography (IRT) with machine learning (ML) classifiers. By analyzing ocular surface temperature (OST) cooling rates across three corneal regions, the study demonstrates a significant correlation between thermal patterns and clinical indicators like Tear Film Break-Up Time (TBUT) and Ocular Surface Disease Index (OSDI). Among the tested models, the k-Nearest Neighbours (k-NN) classifier with Euclidean distance achieved the highest accuracy (91.89%), while Quadratic Support Vector Machine (SVM) also showed strong performance. The manuscript effectively addresses the need for accessible, non-invasive, and portable DED screening tools, particularly in resource-limited settings. Your study provides valuable evidence supporting IRT’s feasibility for early DED detection and offers a solid foundation for future advancements in automated ocular diagnostics.

Comments:

1) Theory Contribution

- You may explicitly state how this method differs from or improves upon similar IRT-ML approaches for DED (e.g., higher accuracy, better cost-efficiency, ease of use) and discuss how this platform could influence clinical practice or telemedicine applications.

2) Methods

- You may Clarify the inclusion/exclusion criteria for patient selection and whether controls were age- and gender-matched.
- You may mention adherence to the Declaration of Helsinki or equivalent ethical guidelines.

3) Figures

- Figure 3: You may user higher-resolution figures

- All figures: You may make legends to be more descriptive.

4) Tables

- All Tables: You define all abbreviations in table footnotes for clarity.
- Table1: You may add rows for each NK, PK and TK, and instead of mentioning them in each in each column and you may name the figures row as DITI image or similar relevant term. The first row may be time.
- Table 2: You may ensure tables follow consistent formatting (e.g., decimal). You may rewrite change $<.001$ to <0.001
- Table 5: You may ensure tables follow consistent formatting (e.g., decimal). You may rewrite change $<.001$ to <0.001 . You may use the same font size.

Round 2 Revision

Reviewer 1:

The authors have adequately addressed the reviewer's comments thoroughly and satisfactorily. I have just one comment:

Table 1 title: Contrary to the authors' claim of a 5-second capture duration, Table 1 includes DITI images acquired over only 4 seconds, as the image corresponding to the 5-second was excluded. Please correct the title accordingly

Reviewer 2:

As I suggested before In my previous review I think the whole article should be rewritten as a proof of concept article with a toned down conclusion considering its limitations and resubmitted. The authors have agreed with most of my primary critique but have failed to adequately change the structure of the article to a proof of concept case series article.

Editor's Decision:

Accept in current form

Comments:

Manuscript improved with revisions

Contribution to the project:

This study introduces a proof-of-concept for a non-invasive, cost-effective, and portable screening method for Dry Eye Disease (DED) by integrating infrared thermography (IRT) with machine learning (ML) techniques.



ICT Virtual Organization of ASEAN Institutes and NICT (ASEAN IVO)

Leveraging smartphone-based thermal imaging and AI-driven feature extraction, the approach enables early, efficient, and scalable detection of DED, particularly in regions with limited access to specialized care. The work contributes to the ASEAN IVO project's goal of developing integrated AI-based systems for ocular disease detection and is currently progressing within the machine intelligence and cloud-based development phase.

[Required Documents]

- A) Presentation Materials (PDF file)
- B) Journal Cover Page and Contents Page of PDF file

Reporter: Laily Azyan Ramlan