A Novel Multi-Parameter Point-of-Care Tear Film Test for Diagnosis of Dry Eye Syndrome, Severe Meibomian Gland Dysfunction, and Responsiveness to Therapy

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INTRODUCTION

- Dry Eye Syndrome (DES) is a common disorder in which there is a decline in tear production or tear quality is impaired.
- Moderate and severe DES may cause pain and discomfort and impair vision quality.
- Accurate diagnosis of DES is complex and requires a battery of tests to assess signs and symptoms which lack consistency and often do not associate with each other.
- Most DES cases have an evaporative component originating from Meibomian Gland Dysfunction (MGD), which when severe, often requires broader treatment options.
- Cyclosporine A (CysA), a proven immunomodulatory therapy for DES, requires long treatment periods to exhibit effectiveness, often elicits local pain, and thus, most of the patients are reported to discontinue therapy within the first 3 months.

OBJECTIVES

Assessing the capability of **TeaRx™** a novel, point-of-care, multi-parametric technology to:

- Distinguish between DES patients and healthy controls and between severe and non-severe cases of DES
- Identify Severe MGD cases within DES patients, and
- Predict objective responsiveness to CysA therapy at baseline.

EXPERIMENTAL SETUP

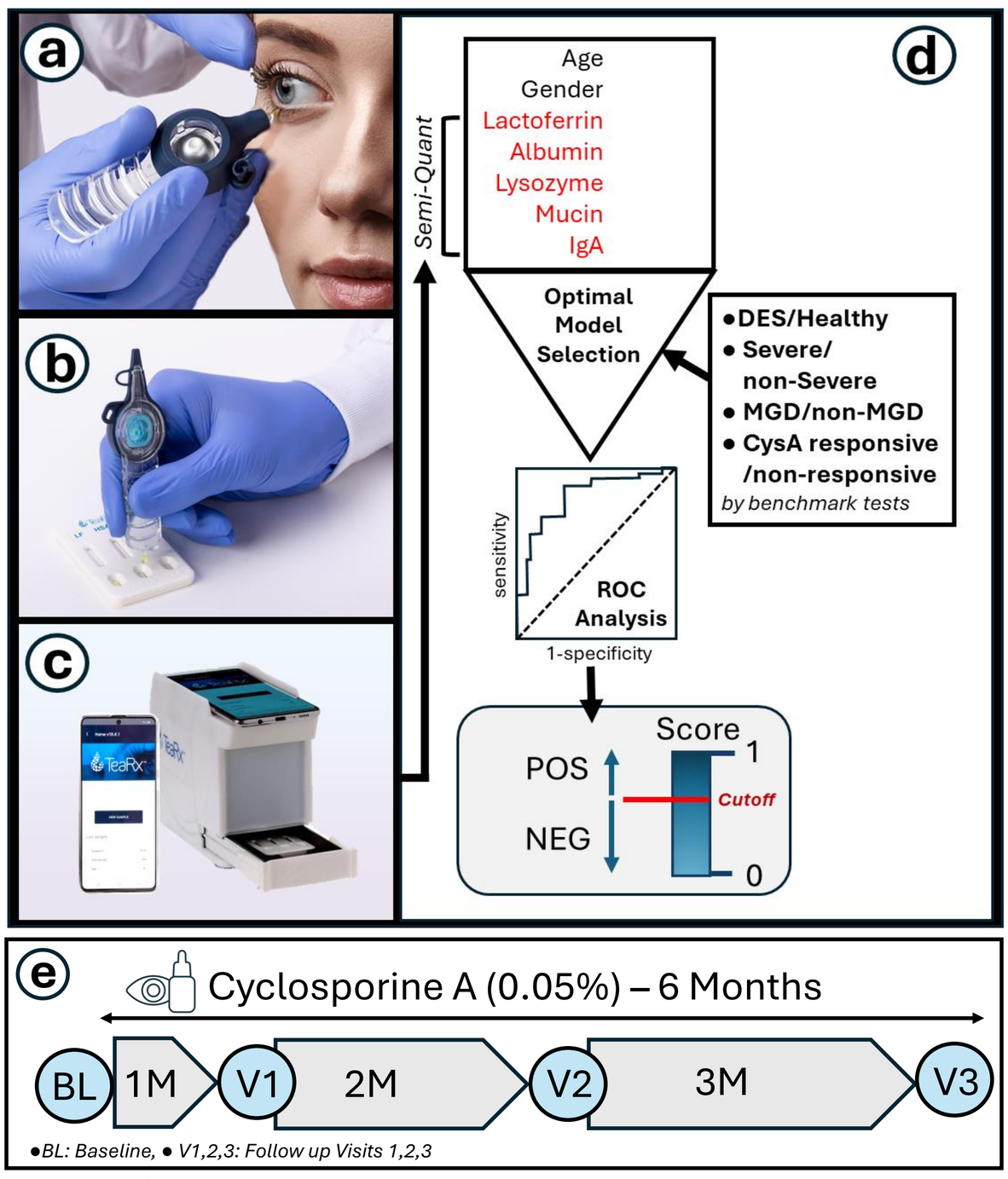

Figure 1: *Experimental Setup*

METHODS

The TeaRx™ technology is based on minimally invasive collection of tear fluid using a novel microfluidic device and semi-quantitative assessment of 5 tear proteins (Lactoferrin, Albumin, Lysozyme, Mucin and IgA) by immunochromatography (Fig 1 a-c).

In this study 593 participants were graded by the TFOS-DEWS II criteria: 495 DES – of which 83 severe MGD (Meibograde 3-4), 29 no-MGD controls (Meibograde 0), and 98 healthy controls . In addition, 35 eligible DES patients were analyzed by TeaRx™ at baseline before topical CysA 0.05% (Cyclomune®, Sun Pharma) therapy was initiated. A positive response was defined as a non-relapsing decrease in DES grade at 3 and/or 6 months (Fig 1e). 16/19 patients were defined as responders/non-responders, respectively. Optimal logistic regression models were selected for associating the semi-quantitative readouts of the 5 proteins, ages and genders of the subjects to the DES and MGD status/severeness, and responsiveness to CysA therapy (all assessed independently). The performance of the selected models was evaluated using ROC analysis. Youden's Index was used to find the optimal combination of sensitivities and specificities (Fig 1d).

RESULTS

- TeaRx™ differentiated between **DES subjects at all severity levels vs. healthy controls** at sensitivity, specificity, and accuracy levels of 72%, 63% and 70.1%, respectively (Fig. 2a), and between severe DES (Grades 3-4) vs. non-severe and healthy (Grades 0-2) at sensitivity, specificity, and accuracy levels of 80.6%, 66.7% and 68%, respectively (Fig. 2b).
- In addition, TeaRx™ identified the presence of **severe MGD vs. non-MGD**, within the tested cohort of eligible DES patients, at sensitivity, specificity, and accuracy levels of 80.6%, 61.3% and 76%, respectively (Fig. 2c).
- Finally, TeaRx™ was capable of **predicting CysA responsiveness** at baseline at sensitivity, specificity, and accuracy levels of 94%, 63% and 77%, respectively (Fig. 2d). Notably, NPV was 92.3%, indicating the promising potential of TeaRx™ to identify non-responders before therapy initiation.

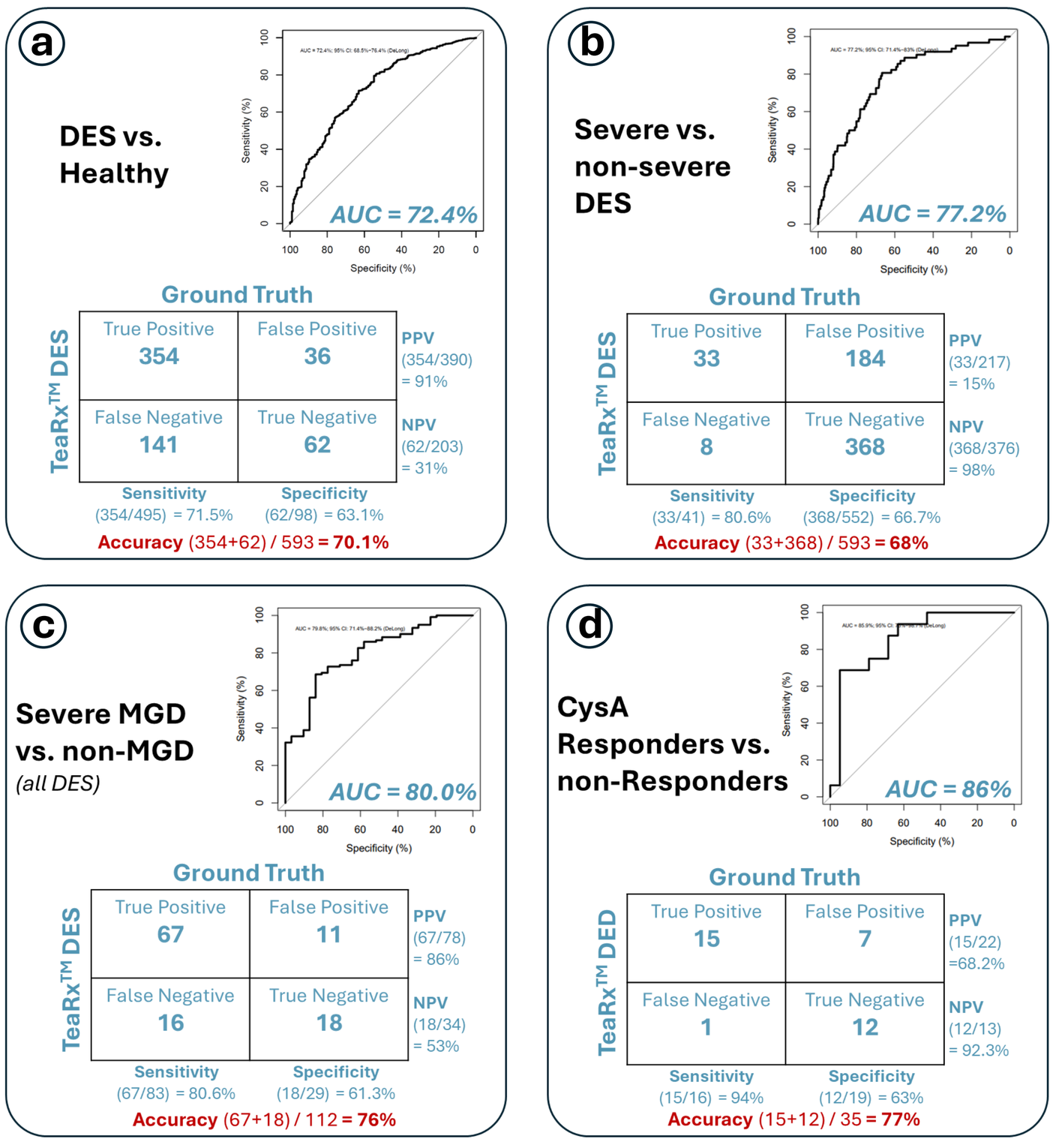

Figure 2: *Diagnostic performance of the various models*

CONCLUSIONS

Based on the results of this explorative study, and pending future validation on a separate cohort of subjects, we conclude that the TeaRx™ technology may be used:

- As a single point-of-care diagnostics for assessment of DES
- For differentiating severe and non-severe DES cases,
- For predicting cases of severe MGD in DES pre-diagnosed patients
- For effective selection of patients for CysA therapy
- For proper selection of DES therapeutic alternatives based on the underlying etiology and the severeness of the disease.

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TeaRx™