Harnessing AI to infer novel spatial biomarkers for the diagnostics of immune inflammatory conditions in EoE

Ariel Larey¹,², Eliel Aknin²,³, Nati Daniel², Garrett A. Osswald⁴, Julie M. Caldwell⁴, Keren Yizhak¹,⁵, Margaret H. Collins⁶, Marc E. Rothenberg⁴, Yonatan Savir²

¹ Dept. of Computer Science, Technion
² Dept. of Physiology, Biophysics & System Biology, Rappaport Faculty of Medicine, Technion
³ Dept. of Industrial Engineering, Technion
⁴ Division of Allergy and Immunology, Cincinnati Children’s Hospital Medical Center, University of Cincinnati College of Medicine, OH, USA.
⁵ Department of Cell Biology and Cancer Science, Rappaport Faculty of Medicine, Technion
⁶ Division of Pathology, Cincinnati Children’s Hospital Medical Center, University of Cincinnati College of Medicine, OH, USA.

Abstract

Histology is critical for the diagnosis of various immune inflammation conditions. In particular in EoE (Eosinophilic esophagitis) disease, the dependency on histology is crucial. This task is very laborious, expensive, time-consuming and requires trained pathologists. In this work we harness Artificial Intelligence (AI) to infer non-trivial novel spatial biomarkers for diagnostics of immune inflammatory conditions. We developed a platform that is able to identify EoE features rapidly and accurately. The implementation included a segmentation phase that achieved mean IOU of 84%, and eventually the process yields a classification accuracy of 86.7%.

Background

Clinical Introduction

- EoE (Eosinophilic esophagitis) disease is a chronic allergic inflammatory condition of the esophagus
- EoE’s main symptoms are nausea, vomiting, food impaction, pain and malnutrition
- EoE is characterized by eosinophils infiltrate in the esophagitis
- Peak Eosinophil Count (PEC) from the biopsy is crucial for biological diagnostic. A common EoE active/not-active PEC threshold in the High-Power-Field (HPF) resolution is 15
- Remission condition diagnostic method uses also a scoring system of 8 features (EoEHSS), including, eosinophilic inflammation (Ei), and basal zone hyperplasia (BZH)
- EoE’s main treatments are: Dietary management, Steroids, PPI therapy and Endoscopic dilatation

Goals

- Segmenting significant EoE features: Eos intact and Basal Zones (BZ)
- Utilize the segmentation for remission diagnostic
- Improve EoE’s medical diagnosis process using AI

Challenges

- Dimensionality obstacle: biopsy slides size are ~ 100,000² pixels resolution while known deep learning models require much smaller images
- Lack of labeled data: data should be labeled and annotated by experts pathologists
- EoE is not a common disease, and its literature sources are limited

Local Segmentation

- The segmentation model was based on UNNet++ and included several updates.
- The model was trained over annotated local patches and was tested over a different test set. Validation achieved 84% mean IOU score

Novel Global Scores

- Our model, scans the biopsy slide with a HPF size kernel, segments both features and calculates their local score per HPF: Eos-Intact count and Basal Zone (BZ) area rate
- This process’s output is a score map for each feature. The system extracts from each map the peak and spatial scores, yielding four novel scores: Peak Eosinophil count (PEC), Spatial Eosinophil count (SEC), Peak Basal Zone (PBZ) and Spatial Basal Zone (SBZ).
- They showed significant correlations to the pathologists’ corresponding EoEHSS scores

Remission Classification

- The 4 scores were concatenated to a vector and were applied to an MLP classifier to predict remission status
- An improved model selects a classifier based on the PEC score in the first step

Achievements

- Developing a model that is able to segment EoE local features with SOTA mIOU results of 84%
- Leveraging the segmentation model into a platform that allows us to construct four novel biomarkers and prove that they are clinically significant
- This platform achieved SOTA results of 86.7% accuracy in classifying the remission condition of EoE patients
- Our platform is currently in the process of adaptation for real-world application in Cincinnati Children’s Hospital Medical Center (CCHMC)