Machine Learning-Based Quantitative Evaluation of Histological Disease Severity in Ulcerative Colitis

Abstract #1495

Fedaa Najdawi[1], Michael G. Drage[1], Kathleen Sucipto[1], Archit Khosla[1], Christina Jayson[1], Mary Lin[1], Victoria Mountain[1], Stephanie Hennek[1], Ilan Wapinski[1], Richard S. Kinsey[1], Andy Beck[1], & Murray B. Resnick[1]

*[1]PathAI, Boston, USA. *Disclosure: All authors are employees of PathAI and may own company stock.*

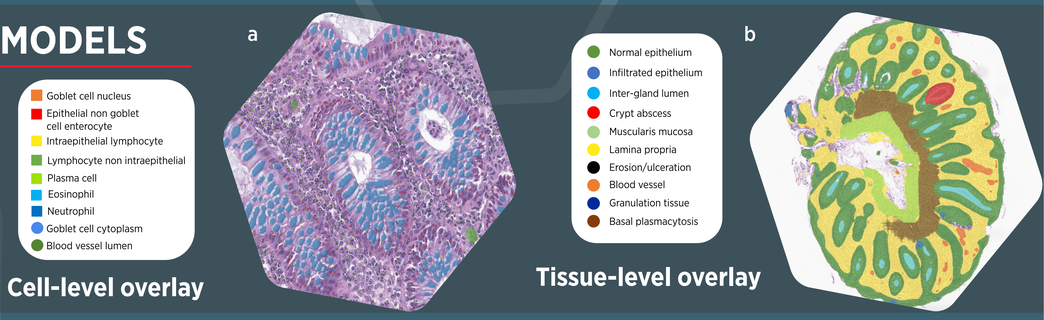
STUDY BACKGROUND

Emerging evidence supports the adoption of histologic improvement as a therapeutic goal and clinical trial endpoint for patients with ulcerative colitis (UC), including reports that show relapse has been associated with residual histologic disease activity in patients who achieved endoscopic endpoints[1-3].

Here we show sensitive and reproducible machine learning (ML)-based pixel-level identification and quantification of histological features of UC, correlation with expert manual pathologist scoring of disease severity, and use of model-derived histological features for prediction of UC disease severity scores.

PATHAI UC MODELS

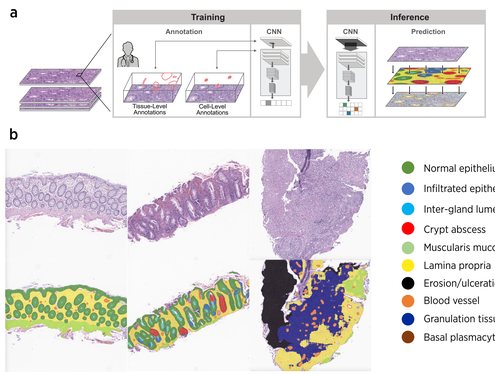
Figure 2. PathAI UC models showing model predictions of relevant histological features. a) Cell-level overlay. b) Tissue-level overlay.



MODEL DEVELOPMENT

- Machine learning models, based on convolutional neural networks, were trained to predict histologic features and generate quantitative, slide-level read-outs using 637 whole-slide images (WSI) of hematoxylin and eosin (H&E) stained biopsies covering the spectrum of disease severity in UC (**Fig. 1a**).
- Models were trained using >130k region- and point-based annotations provided by the PathAI network of board-certified pathologists, indicating relevant tissue (e.g., erosion/ulceration, crypt abscesses, epithelium with neutrophil infiltration, normal epithelium, granulation tissue, basal plasmacytosis) and cell (e.g., neutrophils, plasma cells, lymphocytes, and eosinophils) features (**Figs. 1,2**).

Figure 1. Machine Learning Model Training and Predictions



a) Convolutional neural network (CNN)-based ML models were trained using manual annotations provided by pathologists identifying histological features relevant to UC. Inference of study samples generates tissue- and cell-level predictions. b) Representative fields (4x magnification) from biopsies with corresponding ML overlays: left panel, normal biopsy NHI 0; middle panel, moderate chronic active colitis NHI 3; right panel, severe chronic active colitis NHI 4.

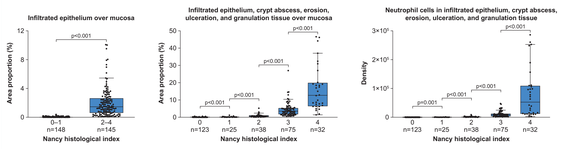
ML MODEL AND PATHOLOGIST CORRELATION

- The models were applied to the validation set of 147 H&E images, and correlation with consensus expert manual pathologist scoring of UC (Nancy Histology Index, NHI) was evaluated. The NHI is a scoring system that measures disease severity in UC with ordinal scores from 0 to 4, where higher scores indicate more severe disease.
- ML-based model predictions were used to generate quantitative "human-interpretable features" (HIFs) measuring tissue area proportions, cell counts, and cell densities.
- ML model-generated HIFs were correlated to manual pathologist NHI scores using Spearman correlation (**Figs. 3,4**). Manual scoring was done by a group of 5 GI-specialized pathologists, and consensus was defined as agreement among 3 out of the 5 pathologists. Slides that did not achieve consensus were excluded (7 slides).

Figure 3. ML-Generated Feature Correlation with Pathologist NHI Scores

FEATURES	CORRELATION	P-VALUE
AREA PROPORTION OF INFILTRATED EPITHELIUM, CRYPT ABSCESS, EROSION OR ULCERATION, AND GRANULATION TISSUE OVER MUCOSA	0.889	<0.001
AREA PROPORTION OF INFILTRATED EPITHELIUM, CRYPT ABSCESS, EROSION OR ULCERATION, GRANULATION TISSUE, AND BASAL PLASMACYTOSIS OVER MUCOSA	0.885	<0.001
AREA PROPORTION OF ALL INFILTRATED EPITHELIUM AND CRYPT ABSCESS OVER ALL EPITHELIUM AND CRYPT ABSCESS	0.883	<0.001
AREA PROPORTION OF ALL INFILTRATED EPITHELIUM OVER ALL EPITHELIUM	0.881	<0.001
AREA PROPORTION OF ALL INFILTRATED EPITHELIUM OVER MUCOSA	0.871	<0.001
AREA PROPORTION OF ALL INFILTRATED EPITHELIUM AND CRYPT ABSCESS OVER MUCOSA	0.871	<0.001
AREA PROPORTION OF CRYPT ABSCESS, EROSION OR ULCERATION, AND GRANULATION TISSUE OVER MUCOSA	0.826	<0.001
AREA PROPORTION OF GRANULATION TISSUE OVER MUCOSA	0.822	<0.001
AREA PROPORTION OF EROSION OR ULCERATION AND GRANULATION TISSUE OVER MUCOSA	0.79	<0.001
AREA PROPORTION OF CRYPT ABSCESS OVER ALL EPITHELIUM AND CRYPT ABSCESS	0.777	<0.001
AREA PROPORTION OF CRYPT ABSCESS OVER MUCOSA	0.766	<0.001
AREA PROPORTION OF EROSION OR ULCERATION OVER MUCOSA	0.743	<0.001
AREA PROPORTION OF BASAL PLASMACYTOSIS OVER MUCOSA	0.721	<0.001
AREA PROPORTION OF GOBLET CELL CYTOPLASM OVER ALL EPITHELIUM	-0.526	<0.001
AREA PROPORTION OF BLOOD VESSEL OVER MUCOSA	0.42	<0.001
COUNT PROPORTION OF NEUTROPHILS OVER ALL CELLS IN ALL EPITHELIUM	0.856	<0.001
COUNT PROPORTION OF NEUTROPHILS OVER ALL CELLS IN MUCOSA	0.734	<0.001
COUNT PROPORTION OF LYMPHOCYTES, PLASMA CELLS, AND EOSINOPHILS OVER ALL CELLS IN MUCOSA	0.692	<0.001
COUNT PROPORTION OF PLASMA CELLS OVER ALL CELLS IN BASAL PLASMACYTOSIS	0.676	<0.001
COUNT PROPORTION OF LYMPHOCYTES AND PLASMA CELLS OVER ALL CELLS IN MUCOSA	0.668	<0.001
COUNT PROPORTION OF PLASMA CELLS OVER ALL CELLS IN MUCOSA	0.555	<0.001
COUNT PROPORTION OF NEUTROPHILS OVER ALL CELLS IN LAMINA PROPRIA	0.513	<0.001
COUNT PROPORTION OF EOSINOPHIL CELLS OVER ALL CELLS IN MUCOSA	0.407	<0.001
COUNT PROPORTION OF INTRAEPITHELIAL LYMPHOCYTES OVER ALL CELLS IN EPITHELIUM	0.325	<0.001
COUNT PROPORTION OF NON-INTRAEPITHELIAL LYMPHOCYTES OVER ALL CELLS IN LAMINA PROPRIA	0.106	0.071
COUNT PROPORTION OF EOSINOPHIL CELLS OVER ALL CELLS IN LAMINA PROPRIA	0.097	0.097
DENSITY OF NEUTROPHILS IN INFILTRATED EPITHELIUM, CRYPT ABSCESS, EROSION OR ULCERATION, AND GRANULATION TISSUE	0.892	<0.001
DENSITY OF NEUTROPHILS IN INFILTRATED EPITHELIUM	0.879	<0.001
DENSITY OF NEUTROPHILS IN LAMINA PROPRIA	0.712	<0.001
DENSITY OF EOSINOPHILS IN MUCOSA	0.549	<0.001

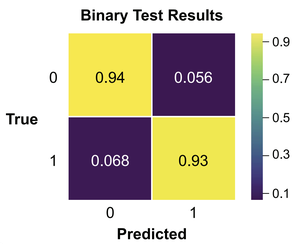
Figure 4. Example ML-Generated Features Showing Correlation with Grouped and Individual NHI Scores



PREDICTION OF UC DISEASE SEVERITY SCORES

- Multivariate analysis was performed to predict the NHI using 16 selected histologic features. The best model, random forest classifier, was selected based on the performance of 5-fold cross validation measure by weighted kappa and yielded a weighted kappa of k=0.93 and Spearman correlation of r=0.93 (p<0.001).
- Multivariate analysis was also performed to predict cases with active disease (binary prediction of chronic active colitis NHI 2-4 vs chronic inactive colitis and normal NHI 0-1). The random forest classifier model yielded an accuracy of 0.94 (weighted kappa k=0.87 and Spearman correlation r=0.87, p<0.001) (**Fig. 5**).

Figure 5. Prediction of UC NHI Scores



Confusion matrix for binarized prediction of chronic active colitis NHI 2-4 vs. chronic inactive colitis and normal NHI 0-1, produced by the random forest classifier trained using 16 model-derived histological features as input.

CONCLUSIONS

- ML model predictions show high correlation with pathologist scoring of UC histological features and assessment of disease severity.
- Model-derived histological features can be used to predict slide-level NHI scores. These quantitative features can potentially be correlated with endoscopic findings, specific treatment response, or patient outcomes.
- This highlights the potential of a robust and reproducible ML-based image analysis for quantitative characterization of UC histology to better guide management decisions.

CONTACT

Fedaa Najdawi
email: fedaa.najdawi@pathai.com

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ACKNOWLEDGMENTS

This poster template was developed by SciStories LLC.
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USCAP 111th Annual Meeting March 19-24, 2022, Los Angeles, CA USA