Improved detection of esophageal neoplasia with 3D pathology and deep learning triage

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INTRODUCTION

- **Esophageal adenocarcinoma (EAC):** 5-year survival rate is < 20%
- Patients with precursor (dysplasia) are periodically screened with endoscopic biopsy
- Gold standard: biopsies evaluated with 2D conventional histology which represents < 1% of specimens, leading to sampling errors

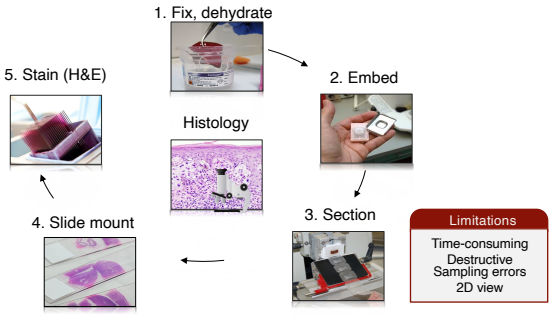


Fig. 1 Conventional histology suffers from sampling limitations due to sparse slide-based representation of clinical specimens

Open-top light-sheet microscopy for 3D pathology

- We have developed **open-top light-sheet (OTLS) microscopy** for comprehensive imaging of clinical specimens in 3D
- Pathologists may evaluate whole biopsies in 3D to make diagnosis

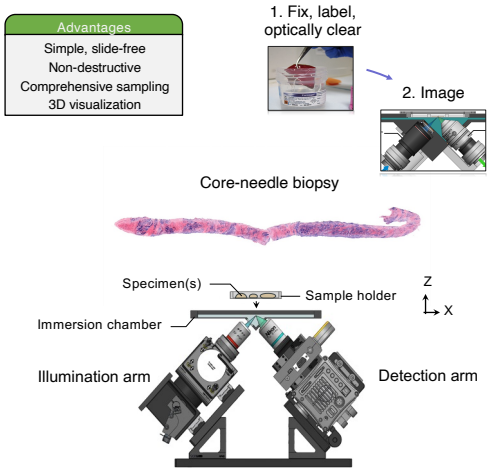


Fig. 2 Tissue processing steps for OTLS imaging (top). CAD diagram of OTLS microscope (bottom).

METHODS

- OTLS microscopy enables detection of EAC and dysplasia
- Esophageal biopsies stained with fluorescent analog of H&E and optically cleared
- Imaged in 3D with OTLS, false-colored to create conventional H&E-like appearance for pathologists

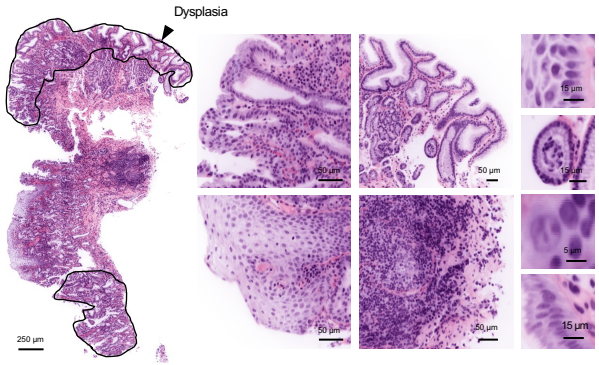


Fig. 3 OTLS microscopy images (en face view) of an esophageal biopsy exhibiting high-grade dysplasia and esophageal adenocarcinoma

Goal: 3D pathology with AI-assisted triage

- Unfortunately, 3D pathology datasets can be very large → manual review is tedious for pathologists
- Goal: streamline 3D pathology evaluation by implementing AI-assisted triage

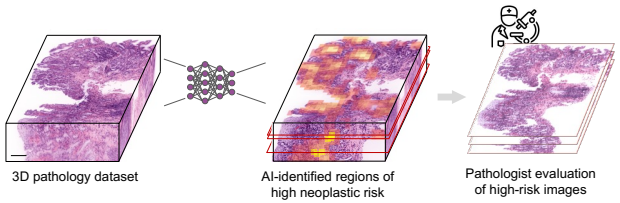
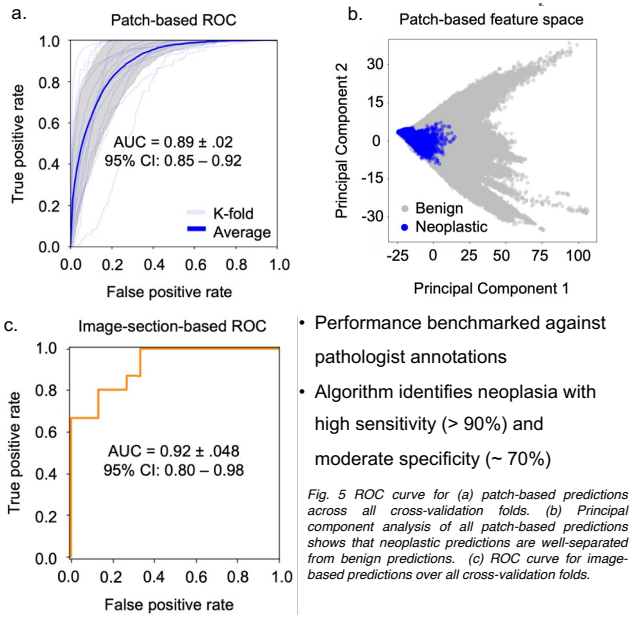


Fig. 4 Diagnostic workflow with 3D pathology and AI-assisted triage.

- We use a deep learning model to identify suspicious regions of interest in 3D OTLS datasets of esophageal biopsies
- A machine classifier evaluates deep learning predictions and identifies the most important 2D images in whole biopsy
- Pathologists are given **top 3** images for diagnosis (reduced workload compared to conventional histology, ~15 images)

RESULTS



- Performance benchmarked against pathologist annotations
- Algorithm identifies neoplasia with high sensitivity (> 90%) and moderate specificity (~ 70%)

Fig. 5 ROC curve for (a) patch-based predictions across all cross-validation folds. (b) Principal component analysis of all patch-based predictions shows that neoplastic predictions are well-separated from benign predictions. (c) ROC curve for image-based predictions over all cross-validation folds.

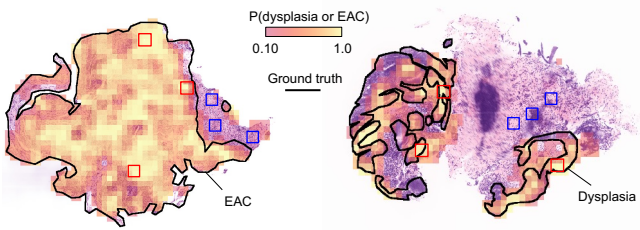


Fig. 6 Example predictions: probability heatmap of predicted suspicious regions (dysplasia or EAC) with ground truth annotations outlined in black for two example cases (top). Examples of correct predictions are shown, i.e. true positives (TP, red) and true negatives (TN, blue).

- We compared our AI-assisted 3D pathology method to conventional histology in an independent clinical validation cohort (n = 20)
- Our method diagnostically upgraded 3 out of 20 cases → improved diagnostic sensitivity in comparison to conventional histology

CONCLUSIONS

- OTLS microscopy + AI-based triage guides pathologist evaluation in 3D pathology datasets
- Our method **improves diagnostic sensitivity** and **reduces pathologist workloads** compared to conventional histology

References: A.K. Glaser *et al.* "Light-sheet microscopy for slide-free non-destructive pathology of large clinical specimens" (2017). L.A. Barner *et al.* "Multi-resolution open-top light-sheet microscopy to enable efficient 3D pathology workflows" (2020). K. He *et al.* "Deep residual learning for image recognition" (2016). I. Tsamardinos et al. "Bootstrapping the out-of-sample predictions for efficient and accurate cross-validation," (2018).