Screening for esophageal dysplasia with nondestructive 3D pathology in conjunction with deep learning triage

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INTRODUCTION

- **Esophageal adenocarcinoma (EAC)** 5-year survival rate < 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

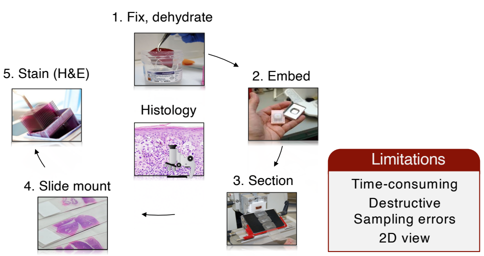


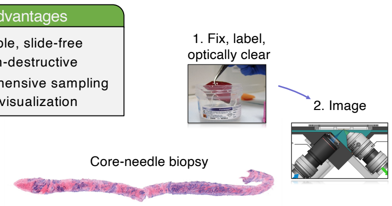
Fig. 1 Conventional histology suffers from sampling limitations due to sparse slide-based representation of clinical specimens

Open-top light-sheet microscopy for 3D pathology

- We have developed multi-resolution open-top light-sheet (OTLS) microscopy for 3D pathology of clinical specimens
- Comprehensive sampling of specimens in 3D
- Non-destructive to tissue
- Multi-resolution imaging enables data- and time-efficient workflows

Advantages

Simple, slide-free
Non-destructive
Comprehensive sampling
3D visualization



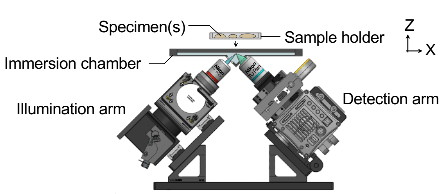


Fig. 2 Tissue processing steps for OTLS imaging (top). CAD diagram of OTLS microscope, side view (bottom).

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

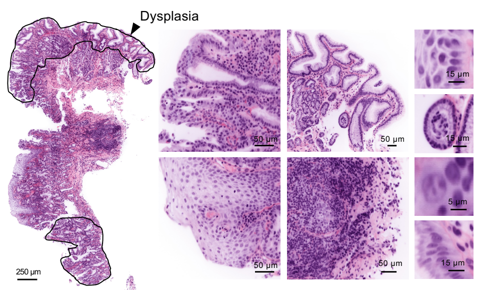


Fig. 3 OTLS microscopy images (en face view) of an esophageal biopsy exhibiting high-grade dysplasia and esophageal adenocarcinoma

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

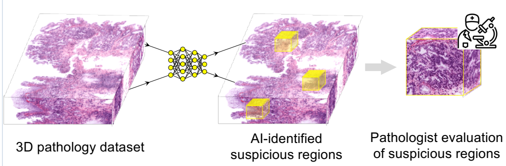
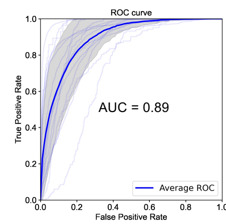


Fig. 4 Diagnostic workflow with 3D pathology and AI-assisted triage.

- We have trained a deep learning model to identify suspicious regions with high sensitivity in OTLS datasets of esophageal biopsies
- Patch-based predictions are aggregated into a heatmap to guide pathologist review

RESULTS



- Performance benchmarked against pathologist annotations
- Area under the curve (AUC-ROC) = 0.89
- High sensitivity (> 90%) and moderate specificity (~ 70%).

Fig. 5 ROC curve for all cross-validation sets (n = 15, light blue). ROC curve averaged over all sets (blue). Standard deviation (gray).

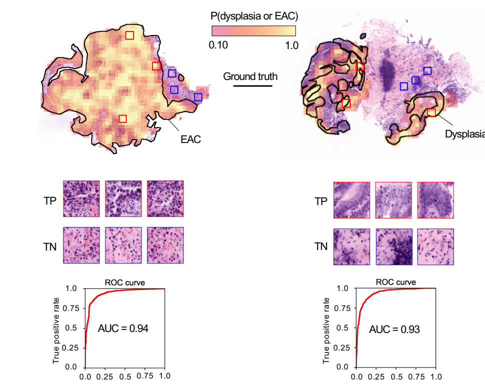


Fig. 6 Probability heatmap of predicted suspicious regions (dysplasia or EAC) with ground truth annotations outlined in black for two example cases (top). Examples of correct predictions are shown, i.e. true positives (TP) and true negatives (TN) (middle). ROC curves for example cases (bottom).

CONCLUSIONS

- 3D pathology may improve diagnostic accuracy in comparison to conventional histology due to comprehensive sampling
- We demonstrate OTLS microscopy combined with an AI-based triage step that identifies dysplasia and EAC with high sensitivity (> 90%) to guide pathologist evaluation

REFERENCES

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