Automated Quantitative Assessment of Oral Cavity Dysplasia in Mouse Models of Oral Cavity Squamous Cell Carcinoma

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Background

- **Dysplasia** is an important, yet poorly understood, transition step in the development of oral cavity cancer.
- **Quantitative assessment** of dysplasia is crucial for animal experiments designed to provide biological insights into dysplasia-mediated tumorigenesis.
- However, **assessment of dysplasia remains challenging** due to subjective variability among pathologists.
- For this project, we hypothesize that:
  1. Inter-rater variability of human pathologist labeled dysplasia will be high, *and*
  2. **AI-based image analysis can improve robustness and reproducibility of dysplasia evaluation** in mouse models of oral cancer.

Objectives

The objective of this project is to develop and validate automated, quantitative methods to segment, measure, and grade dysplasia in mouse tongue tissue obtained from animal models of oral cavity squamous cell carcinoma.

Study Design

Mouse models were exposed to a carcinogenic agent to induce oral dysplasia

Mouse Group 1: Exposed to carcinogen (4NQO) first to develop tumors, then treated with tamoxifen (TAM) to knock out the gene

Mouse Group 2: Received TAM first to inactivate the gene before tumor development, followed by 4NQO exposure

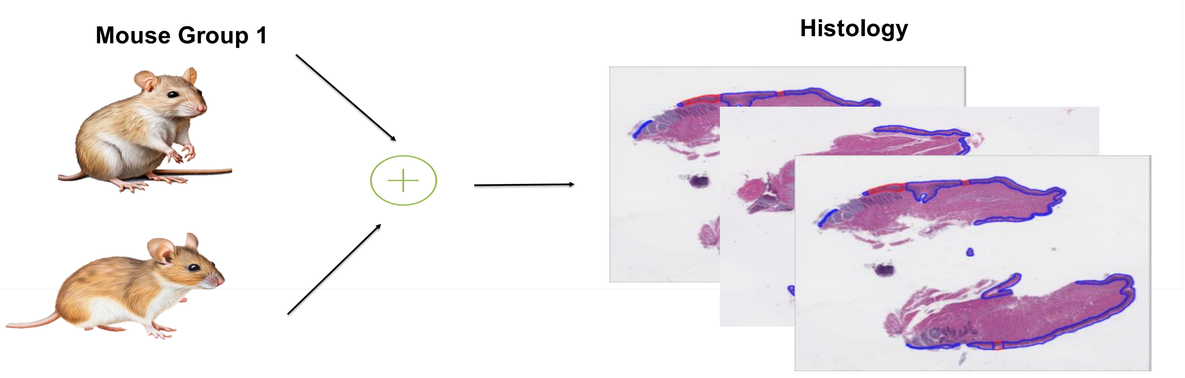
Tissues were labelled by two pathologists

Annotations were compared quantitatively—using metrics such as dysplasia percentage, area, and overlap—to emphasize the inherent subjectivity of current dysplasia assessments

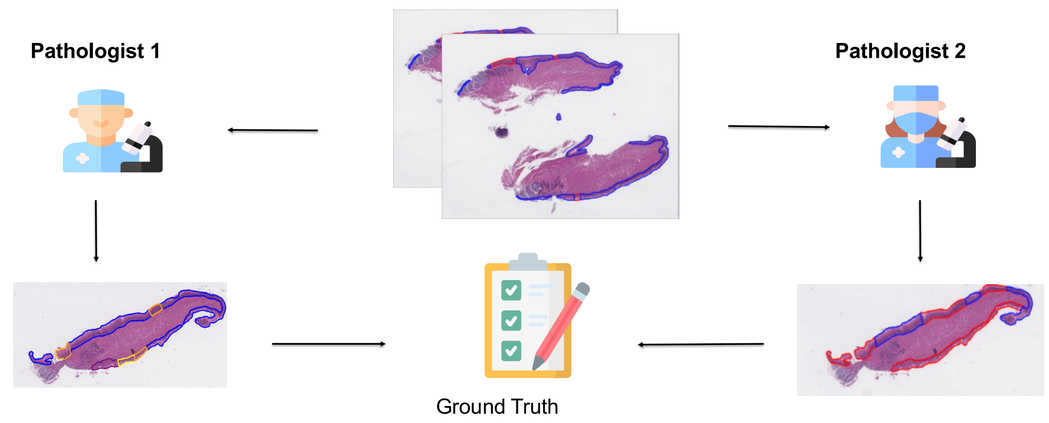
Images will undergo automated feature extraction, followed by unsupervised clustering (e.g., UMAP) to identify distinct dysplasia clusters

Methodology

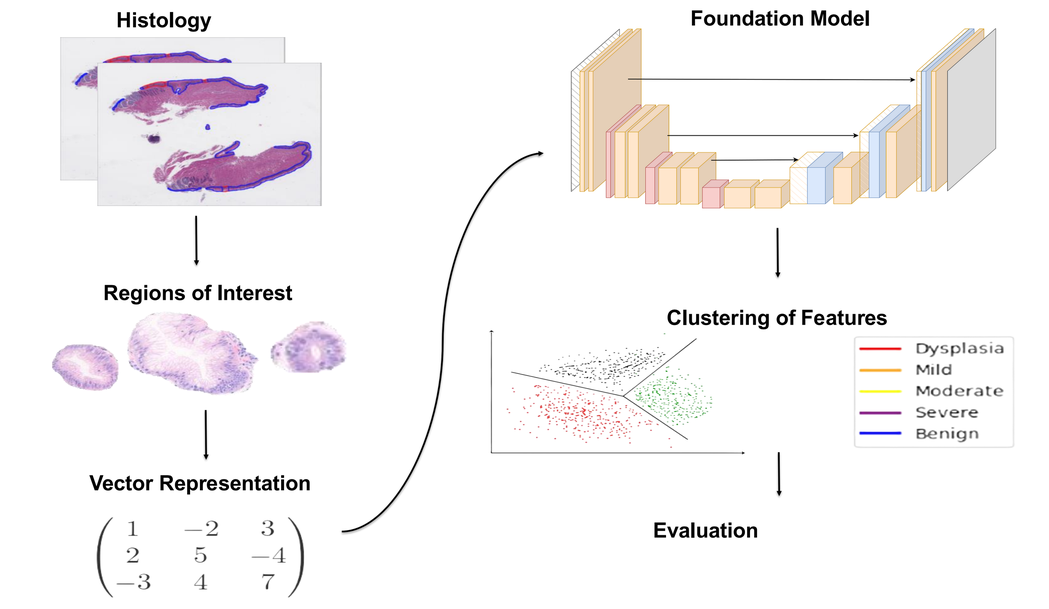
1. Dataset collection



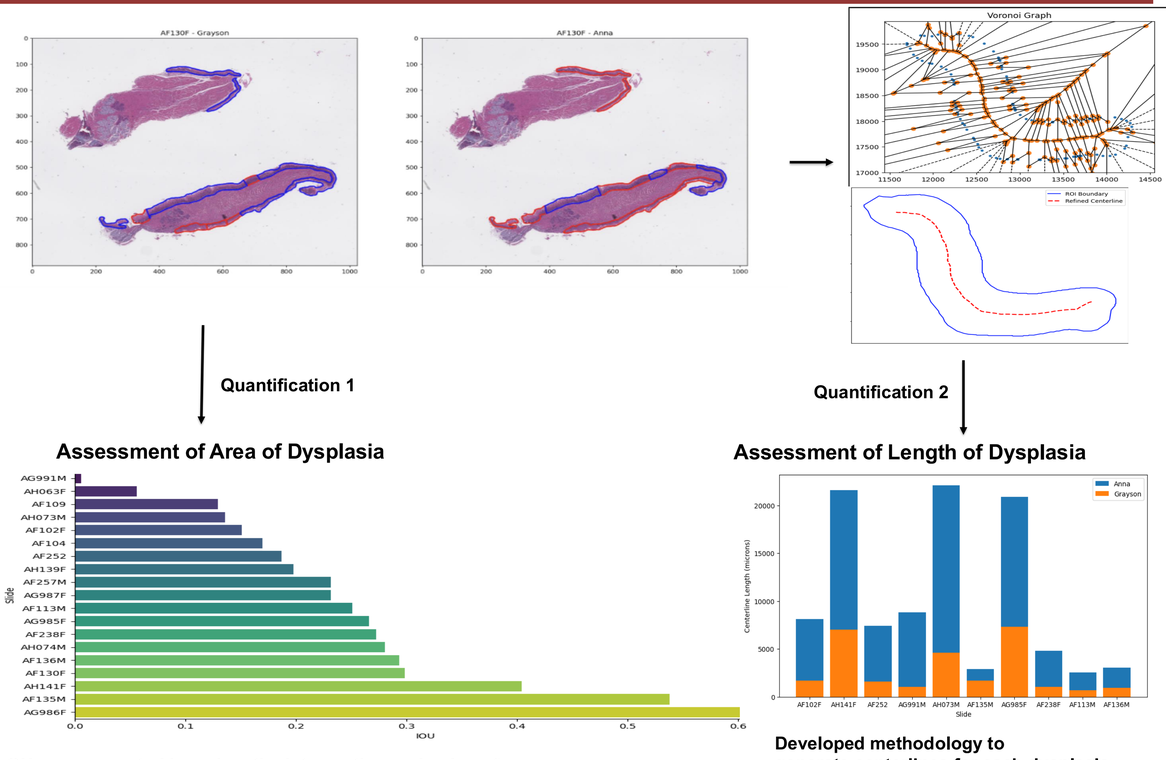
2. Pathologist Annotations



3. Foundation Model



Results



IOU was calculated based on the intersection and union of *area measurements* for dysplasia regions. Median IOU across 19 slides was 0.23

Developed methodology to generate centerlines for each dysplasia region and compute length of dysplastic epithelium. R^2 between pathologists for 10 slides was 0.45.

Conclusion + Future Plans

Our qualitative and quantitative comparisons reveal **significant discrepancies in how pathologists annotate oral epithelial dysplasia**. This variability limits animal model interventions designed to provide biological insights into tumorigenesis when assessment of dysplasia constitutes the primary experimental outcome. Such inconsistencies underscore the urgent need for automated, objective methods to standardize dysplasia evaluation in oral cancer research.

Our next step include clustering analysis of high-dimensional histologic features, as assessed through a pre-trained oral cancer foundation model, to identify *de novo* clusters associated with dysplasia. Image features in this cluster will be assessed as an alternative "ground truth" for dysplasia and compared with human pathologist labels.

References

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2. Ng GTE, Phang SC, Yu KS, Tiwari L, Khurram SA, Sloan P, et al. Understanding interobserver variability of pathologists to improve oral epithelial dysplasia grading. Oral Diseases [Internet]. 2024 Jul 22; Available from: https://doi.org/10.1111/odi.15078