

## MULTIMODAL OPTICAL IMAGING PLATFORM FOR THE EARLY DIAGNOSIS OF ORAL NEOPLASIA

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Early diagnosis is critical to reducing the global burden of oral cancer. In the US, 65% of oral cancer patients are diagnosed after regional metastasis; these patients have a 50% five-year mortality compared to 17% for those with localized disease. A major reason for late diagnosis is that clinicians are unable to accurately distinguish neoplastic lesions, which require treatment, from benign lesions. Furthermore, clinicians are unable to accurately select to biopsy the site with the worst diagnosis within a larger lesion. Many diagnostic adjuncts to address early detection have been explored without strong evidence for clinical benefit. Recently, autofluorescence imaging (AFI) has gained popularity as the basis of the commercially available VELscope device (LED Dental, Inc.). AFI has high sensitivity for neoplasia but suffers from limited specificity, likely due to inflammatory benign lesions. Our group has developed an inexpensive, portable fluorescence microscope coupled to a coherent optical fiber called the high-resolution microendoscope (HRME) that could boost the specificity of AFI by directly imaging nuclei with the topical contrast agent proflavine. We have previously shown that combining automated features calculated from AFI and HRME images improves diagnostic accuracy for neoplasia compared to either modality alone. Here, we introduce a user interface that quickly walks the user through a novel imaging procedure that takes advantage of the strengths of each modality to 1) identify high-risk areas within a single lesion, then 2) predict the diagnosis at the areas and potentially recommend biopsy. First, the user acquires an autofluorescence image of the lesion plus a corresponding reference white-light image and identifies high-risk regions with high sensitivity based on an autofluorescence-based risk heat map overlay. The high-risk regions are then used as a guide to select HRME imaging sites. Finally, the coordinates of the HRME sites on the autofluorescence image are determined, and imaging features from both modalities are combined for a diagnostic prediction. This process is known as multimodal imaging. To address the challenge of correlating specific tissue locations *in vivo* to their locations on the autofluorescence image, a custom image registration algorithm based on mutual information was developed and assessed. The algorithm registers the autofluorescence image with the reference white-light image so that the clinician may interact with the white-light image, which resembles the tissue's appearance to the naked eye. We report initial *in vivo* results of the multimodal imaging system on patients with oral lesions. Future work will focus on assessing the ability of multimodal imaging to guide biopsy location and diagnose tissue sites in a larger group of patients.