Furthermore, in keratinized tissue we observed that normal-appearing sites in healthy volunteers typically had moderate to low fluorescence intensity, while histologically normal sites in patients tended to have substantially higher fluorescence intensity (Fig. 5b). This makes classification of keratinized sites in a mixed population of patients and healthy volunteers more challenging. One contributing factor to this difference between healthy volunteers and patients may have been that gingival sites in healthy volunteers were typically located adjacent to teeth, while teeth were often missing at the corresponding sites in patients. The difference was much less evident in nonkeratinized tissue (Fig. 5a). Despite these issues, the diagnostic algorithm proved to be sufficiently robust for use with both nonkeratinized and keratinized tissue.

It is believed that the presence of inflammation can be a potential source of false positive results for diagnostic methods based on tissue autofluorescence [35]. The design of the depth-sensitive probe is intended to minimize this effect by interrogating the epithelium and minimizing the signal from the stroma. In this study three of the six false positive non-neoplastic sites (50%) were found to have inflammation present. This percentage was higher than the fraction of all non-neoplastic sites which had inflammation present (28%). Based on this very small sample of sites, inflammation may have been a contributing factor but not the dominant factor in the false positive results obtained in this study.

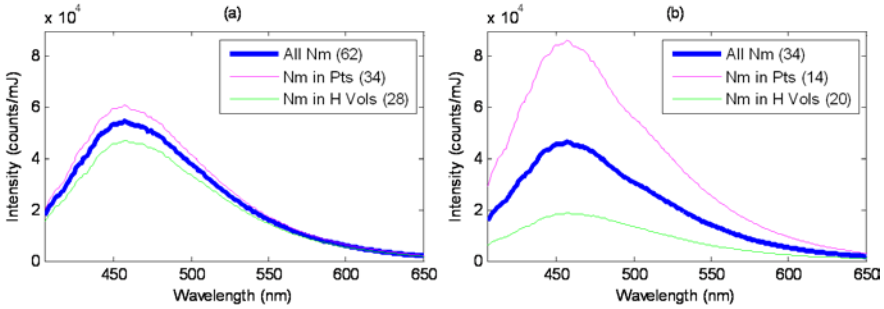

Fig. 5. Average fluorescence spectra of normal oral sites, measured using the medium depth channel, in (a) nonkeratinized tissue and (b) keratinized tissue. All Nm: All normal sites. Nm in Pts: Normal sites in patients only. Nm in H Vols: Normal sites in healthy volunteers only. Number in parentheses indicates number of spectra represented in the average.

The portable spectroscopy device has proven to be well suited for clinical use due to its compact size and its rapid measurement capability. The device is rugged and can be easily transported between clinical sites without the need for optical realignment. Measurements are performed in a darkened room; however, the system performs well even in the presence of a low level of ambient light, which is useful in many clinical situations. We typically perform two successive 5-second measurements at each site; by verifying that the two sets of spectra are consistent, the operator can ensure that no patient movement or probe slippage occurred during the measurement.

In summary, the diagnostic performance of a portable depth-sensitive spectroscopy device was evaluated in a clinical study involving 33 subjects. A previously developed classification algorithm was implemented to classify measured sites. Sensitivity and specificity were 84% and 91%, respectively, for nonkeratinized sites using a preestablished threshold. Sensitivity and specificity were 86% and 83%, respectively, for keratinized sites using a retrospectively established threshold. The development of portable clinical instrumentation and the implementation of algorithms for real-time diagnostic prediction should facilitate the translation of optical spectroscopy to community and low-resource settings where it can be used to aid in early diagnosis of oral cancer.

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