

Oral Cancer Detection: Prospective comparison of clinical, visual, cyto- and histo-pathological tests

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Oral cancer stage at the diagnosis remains the best predictor of survival, yet the majority of oral cancers are discovered at later stages. Clinical examination (CE) remains the principal method for detection of oral mucosal lesions. A variety of techniques have emerged to assess the malignant potential of oral lesions with inconclusive results due to methodological limitations. This study prospectively examined the performance of current techniques for detecting oral premalignant / malignant lesions (OPML) compared to "gold standard" histopathology. This study was approved by institutional review boards.

Methods. Subjects with potentially OPML were enrolled, demographics and risk factor histories collected, and calibrated examiners assigned a risk classification of low or high to every lesion. An additional group of subjects with histopathologically confirmed oral cancer were also enrolled. Every lesion in every subject underwent: chemiluminescent visualization using Vizilite® (VL), toluidine blue staining using T-Blue® (TB), cytopathological assessment using the OralCDx brush test® (BB), and except for the known oral cancers group, every lesion underwent biopsy for histopathology (HP). The outcome of each technique (positive vs negative) was compared to the histopathology (dysplastic/cancer vs benign).

Results. 269 subjects (67% male) with 376 oral lesions were enrolled across low (132, 49%), high (97, 36%) and known cancer (40, 15%) risk classification groups. Mean age at enrollment was 53.7±13.2 years. Individual technique performance (sensitivity (CI)/specificity (CI)) for detecting OPML was: **CE**: 87 (0.78, 0.93) / 71 (0.65, 0.77); **VL**: 58 (0.47, 0.68) / 40 (0.33, 0.46); **TB**: 80 (0.75, 0.85) / 53 (0.47, 0.59); and **BB**: 80 (0.75, 0.85) / 81 (0.76, 0.86). Examination of test combinations using logistic regression models and score statistic revealed significantly improved detection with the combination of CE+BB, modest improvement with CE+TB, and no improvement with CE+VL.

Conclusion: CE alone results in a significant number of false negatives for OPML. CE performance is significantly improved with the addition of BB and somewhat improved with the addition of TB. However, the indications for BB and TB use, based upon clinical risk assessment, must be considered before test selection. Finally, CE, BB, and TB all require visual identification of the lesion which compromises the opportunity for earliest detection of OPML. Techniques to detect at-risk patients or identify lesions not visible during standard clinical examination could further improve early OPML detection.

Supported by NIDCR/NIH: U54 DE14257 and NYUCI CCSG NIH/CI: P30 CA16087