Sensitivity of direct tissue fluorescence visualization in screening for oral premalignant lesions in general practice

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Various specialty clinics and research centers have conducted studies of direct tissue fluorescence visualization as a screening technique for oral premalignant lesions and early oral squamous cell carcinoma (OSCC). The effectiveness of the VELscope in a private practice setting is unknown. This pilot study is the first report to assess the VELscope system as a screening adjunct among lower-risk populations seen by a primary care clinician in a general practice setting. This study involved a retrospective comparison of two oral cancer screening examination protocols conducted on a presumably low-risk patient population seen in a private general dentistry practice. For one year, all patients age 12 or older received oral examinations, according to a standard oral cancer screening protocol. The following year, the same population was examined according to the same protocol with the addition of direct tissue fluorescence visualization using the VELscope.

Screening with incandescent light examination yielded a prevalence of mucosal abnormalities of 0.83%, none of which were premalignant. Screening with incandescent light examination combined with direct tissue fluorescence visualization yielded a 1.3% prevalence of mucosal abnormalities; based on surgical biopsy and histopathologic examination, 83% of these were potentially premalignant epithelial dysplasia.

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Approximately 34,000 people in the U.S. are diagnosed annually with oral squamous cell carcinoma (OSCC) occurring in the oral cavity proper and oropharynx, contributing to more than 8,000 deaths each year.[1] Oral cancer is one of the most curable forms of cancer, provided it is diagnosed early. With appropriate early intervention, success rates are greater than 90%, as determined by five-year survival rates. Early detection of premalignant oral mucosal abnormalities and SCC is desirable because early diagnosis and appropriate treatment reduces patient morbidity and improves survival.[2]

The clinical signs of premalignant lesions and early OSCC are varied and may be misdiagnosed as other conditions, including mucosal inflammation, hyperkeratosis, or traumatic ulceration, all of which are benign. OSCC generally is not symptomatic in its early stages. A wide range of normal benign abnormalities—such as morsicatio buccarum (cheek biting), melanotic macules, amalgam tattoos, leukoedema, and so forth—may be confused as disease processes.

For many years, dentists screening for oral cancer have been limited to using incandescent light illumination to visually inspect the oral cavity and manual palpation. Recently introduced adjunctive screening technologies may allow clinicians to detect early epithelial dysplasia and OSCC.[3] However, one cannot substitute any adjunctive screening device into the examination process as a replacement for the ability to recognize basic oral pathological findings and normal variations in the appearance of oral tissues. One sophisticated but easy to use screening modality is the VELscope (LED Dental, White Rock, British Columbia, Canada; 888.541.4614), a non-invasive, direct tissue fluorescence (narrow band) visualization technology. This device emits a particular wavelength and intensity of light that illuminates the oral mucosa and excited natural fluorophores in the tissue. The tissues emit fluorescence that is visualized through a filter by a human observer.[4]

Incorporating new screening technologies into private practice may be challenging. As new technologies are developed, general practitioners must decide whether to implement such adjunctive screening measures, basing their decisions on the current literature.[5,6] This retrospective pilot study compared the efficacy of adding direct tissue fluorescence visualization to a standard oral cancer screening protocol performed in a private general dentistry practice.

Materials and methods

Over a two-year period, a general dentist performed oral cancer

screening examinations on all recall patients age 12 and older. The same patient base was seen by the same practitioner, using one of two protocols for detecting clinically abnormal areas. All examined patients were ambulatory and were American Society of Anesthesiologists (ASA) Class III or less.

Children as young as 12 were included because of recent reports that OSCC occurs in younger populations without risk factors.[7] Other recent reports have associated OSCC with risk factors that include human papilloma virus (HPV) infection, marijuana use, and periodontal disease, in addition to the long-recognized associations with tobacco and alcohol use and genetic predisposition.[8-11] The assumption was made that all adolescent and adult patients are at risk for development of premalignant lesions.

Oral cancer screening examinations were performed during all periodic oral examinations (D0120) and comprehensive oral examinations (D0150 and D0180) for each patient age 12 or older.[12] A documented clinical examination technique with incandescent light illumination, visual inspection, and manual palpation was used to perform a standard oral cancer screening examination.[13]

Standard oral cancer screening examination

From December 1, 2005 to November 30, 2006, 959 patients received a standard oral cancer screening examination using incandescent light illumination. Each examination was conducted as if the patient were a new patient who had not been examined previously by the same practitioner. According to a computerized practice analysis for this 12-month time period, the overall dental practice consisted of 2,133 active patients between the ages of 12 and 99, with a mean age of 55. Of this patient base, 1,006 were male and 1,127 were female.

Standard oral cancer screening examination and direct tissue fluorescence visualization

From December 1, 2006 to November 30, 2007, 905 patients received a standard oral cancer screening examination using incandescent light illumination; in addition, visual screening was performed using a VELscope for direct tissue fluorescence visualization. Each examination was conducted as if the patient were a new patient who had not been examined previously by the same practitioner. However, patients who entered the practice as actual new patients during the second year of the study were excluded from the reported data so that a similar patient population could be compared. According to a computerized practice analysis for this 12-month time period, the overall dental practice consisted of 2,029 active patients between the ages of 12 and 100, with a mean age of 55. Of this patient base, 947 were male and 1,082 were female.

Follow-up

Areas of the oral cavity identified clinically and considered to be abnormal were documented for both groups and the patients were scheduled for a follow-up examination 14 days later, after any suspected etiologic agents were removed. Pathoneumonic normal variations of tissue, such as amalgam tattoos, varices, minor hemangiomas, morsicatio buccarum, and so forth, were not noted because they were considered to be non-pathologic. This protocol was established to minimize false positives produced by inflammation.

Identified lesions that persisted after 14 days were brushed using one of two sample collection methods: the Oral CDx brush test (CDx Laboratories, Inc., Suffern, NY; 877.672.5722) or liquid-based brush cytology (BD SurePath, BD Diagnostics, Burlington, NC; 800.426.2176). Samples collected by Oral CDx were submitted to CDx Laboratories, Inc. for analysis by a cytopathologist. Samples collected for liquid-based brush cytology were placed into SurePath solution and submitted to Tufts Oral Pathology Services in Boston for modified Papanicolaou staining and microscopic examination by an oral pathologist.

Results

Standard oral cancer screening examination

From December 1, 2005 to November 30, 2006, 8 of the 959 patients examined were found to have clinically abnormal areas of the mouth that persisted for 14 days or longer. Brush samples from these patients were collected and examined. Six of the samples had a result of no abnormality, while the other two samples were diagnosed as mild atypia, with further investigation warranted. The two atypical samples were referred for surgical biopsy; histologic diagnoses for both were benign. One case was diagnosed as pigmentation due to exogenous material; the other was reactive hyperkeratosis with normal cellular morphology.

Standard oral cancer screening examination and direct tissue fluorescence visualization

From December 1, 2006 to November 30, 2007, 12 of the 905 patients examined were found to have clinically abnormal areas of the mouth that persisted for

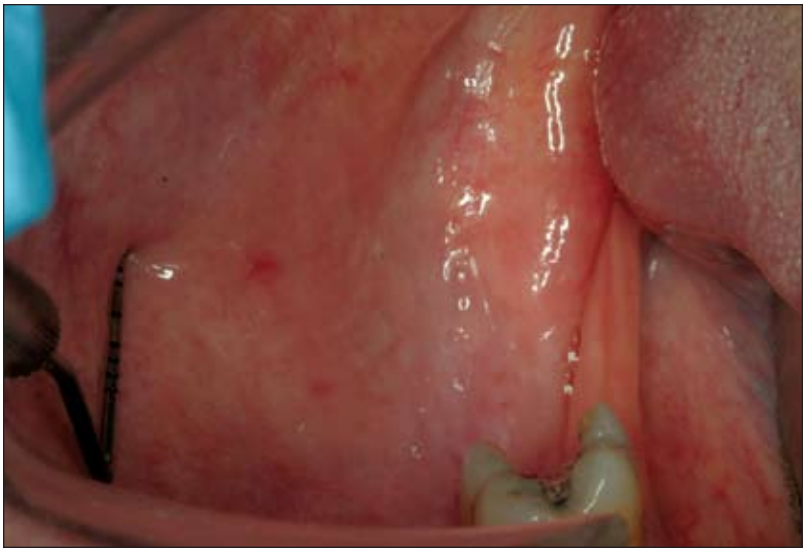

Fig. 1. White light examination reveals an erythematous lesion on the right buccal mucosa, consistent with minor frictional trauma from the fractured mandibular right first molar.

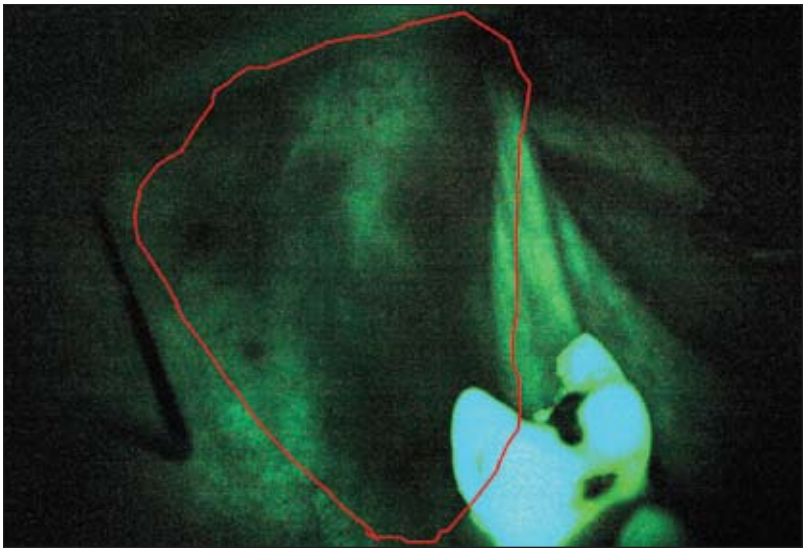

Fig. 2. VELscope examination shows a loss of fluorescence in the outlined retromolar area, which did not blanch with pressure. The histology report of the incisional surgical biopsy diagnosed mild epithelial dysplasia.

14 days or longer (Fig. 1 and 2). Brush samples from these patients were collected and examined. Analysis of the brushed specimens showed abnormal results in all cases; these specimens were referred for surgical biopsy. Two cases were histologically benign; one of these was diagnosed as lichenoid mucositis and the other as a squamous papilloma. The remaining 10 cases were diagnosed as epithelial dysplasia, a potentially premalignant change.

Assuming a constant rate of premalignant and malignant epithelial abnormalities from one year to the next in this stable patient population, the incandescent light examination yielded a 0.83% prevalence of mucosal abnormalities, none of which were premalignant. The incandescent light and direct tissue fluorescence examination yielded a 1.3% prevalence of mucosal abnormalities, 83% of which were potentially premalignant.

Discussion

The standard of practice requires dental practitioners to perform regular clinical screening examinations of the extraoral head and neck and intraoral soft tissues.[13] The screening examination is meant to recognize gross tissue abnormalities and make a clinical provisional diagnosis and a decision on the appropriate management.[14]

Screening for disease entails testing people who apparently are symptom-free from the disease in question, to differentiate between those who probably have the disease and those who probably do not.[3] Usually, screening tools are highly sensitive but are not specific; in addition, they may have high rates of false positive results. A false positive result occurs when the clinical diagnosis of an abnormality is investigated by surgical biopsy but the tissue is histopathologically normal.[3] A screening technique does not provide a diagnosis. A surgical biopsy with microscopic examination by a pathologist remains the standard for diagnosing oral mucosal disease.[14]

The VELscope is a form of direct tissue fluorescence visualization that utilizes the loss of natural fluorescent characteristics of metabolic intermediaries to identify

dysplastic and hypermetabolic activity.[15,16] Inflammation may have a similar appearance to early dysplasia; however, a properly conducted diascopy may be useful for interpreting non-fluorescent findings at the time of the screening examination.[17] Regardless of diascopic results, all irregular findings should be re-evaluated in 14 days and any persistent lesions should be investigated with biopsy, even if they respond to diascopy.

When screening identifies early or occult oral mucosal lesions, general dentists can use minimally invasive epithelial cell collection techniques as case finding and patient education tools. These tests may be used to decide whether a surgical scalpel biopsy is indicated. A recent review by Patton *et al* emphasized that brush cytology is not appropriate for sampling obvious long-standing developmental or submucosal lesions.[18] The review also emphasized that brush cytology is not recommended for assessing clinically suspicious lesions for which the practitioner normally would perform a scalpel or punch biopsy. If clinical judgment indicates that a surgical biopsy is appropriate for an abnormality detected by screening, the biopsy should be performed without a cytology.

Dentists have ethical and legal obligations to be proactive in detecting oral disease.[19] The current standard of care uses direct visualization of the reflected white light from mucosal surfaces to detect gross tissue abnormalities, although reflection alone may fail to identify early epithelial dysplasia. There is a growing realization that some premalignant and early cancerous lesions may not be readily detectable with the naked eye.[20] Additional clinical studies are needed to confirm reported sensitivity, specificity, and positive predictive values of adjunctive screening techniques used to detect oral premalignant and malignant lesions.[3,18,21]

To date, all peer-reviewed VELscope studies have been performed on patients with known oral dysplasia or OSCC confirmed by biopsy.[4,22-24] Routine VELscope use has been challenged by the observation that the current literature pertaining to this particular device does not support all of the principles of evidence-based decision-making.[5] Laronde *et al* emphasized the need to train dentists to use the device.[6]

A recent review of adjunctive techniques for oral cancer examination called for additional study of the VELscope as an adjunct in low-risk populations and for primary care providers.[18] The present study is the first to involve the VELscope as an adjunct for detecting occult abnormal mucosal findings in a low-risk general dental practice. The results of this retrospective, observational pilot study provide data for future studies in a community private practice setting.

Conclusion

In the present study, routine incorporation of the VELscope in the examination protocol for low-risk adolescents and adults in a general dental practice proved useful in identifying occult, potentially premalignant lesions.

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References

1. Oral cancer facts. Available at: http://www.oralcancerfoundation.org/facts/index.htm. Accessed October 2008.
2. Choong N, Vokes E. Expanding role of the medical oncologist in the management of head and neck cancer. CA Cancer J Clin 2008;58(1):32-53.
3. Lingen MW, Kalmar JR, Karrison T, Speight PM. Critical evaluation of diagnostic aids for the detection of oral cancer. Oral Oncol 2008;44 (1): 10-22.
4. Poh CF, Ng SP, Williams PM, Zhang L, Laronde DM, Lane P, Macaulay C, Rosin MP. Direct fluorescence visualization of clinically occult high-risk oral premalignant disease using a simple hand-held device. Head Neck 2007;29(1):71-76.
5. Balevi B. Evidence-based decision making: Should the general dentist adopt the use of the VELscope for routine screening for oral cancer? J Can Dent Assoc 2007;73(7):603-606.
6. Laronde DM, Poh CF, Williams PM, Hislop TG, Zhang L, MacAulay C, Rosin MP. A magic wand for the community dental office? Observations from the British Columbia Oral Cancer Prevention Program. J Can Dent Assoc 2007;73(7): 607-609.
7. Jepsen SA, Closmann JJ. The insidious nature and presentation of oral squamous cell carcinoma in the low-risk population. Gen Dent 2008; 56(1):78-82.
8. Llewellyn CD, Johnson NW, Warnakulasuriya KA. Risk factors for oral cancer in newly diagnosed patients aged 45 years and younger: A case-control study in Southern England. J Oral Pathol Med 2004;33(9):525-532.
9. Syrjanen S. Human papillomaviruses in head and neck carcinomas. N Engl J Med 2007;356 (19):1993-1995.
10. Hashibe M, Morgenstern H, Cui Y, Tashkin DP, Zhang ZF, Cozen W, Mack TM, Greenland S. Marijuana use and the risk of lung and upper aerodigestive tract cancers: Results of a population-based case-control study. Cancer Epidemiol Biomarkers Prev 2006;15(10):1829-1834.
11. Tezal M, Sullivan MA, Reid ME, Marshall JR, Hyland A, Loree T, Lillis C, Hauck L, Wactawski-Wende J, Scannapieco FA. Chronic periodontitis and the risk of tongue cancer. Arch Otolaryngol Head Neck Surg 2007;133(5):450-454.
12. Current dental terminology. Chicago: American Dental Association;2006:3-4.
13. Horowitz AM, Alfano MC. Performing a death-defying act. J Am Dent Assoc 2001;132 Suppl: 5S-6S.
14. Melrose RJ, Handlers JP, Kerpel S, Summerlin DJ, Tomich CJ; American Academy of Oral and Maxillofacial Pathology. The use of biopsy in dental practice. The position of the American Academy of Oral and Maxillofacial Pathology. Gen Dent 2007;55(5):457-461.

15. De Veld DC, Witjes MJ, Sterenborg HJ, Roodenburg JL. The status of *in vivo* autofluorescence spectroscopy and imaging for oral oncology. Oral Oncol 2005;41(2):117-131.
16. Gillenwater A, Jacob R, Richards-Kortum R. Fluorescence spectroscopy: A technique with potential to improve the early detection of aerodigestive tract neoplasia. Head Neck 1998;20(6):556-562.
17. Rudd M, Eversole R, Carpenter W. Diascopy: A clinical technique for the diagnosis of vascular lesions. Gen Dent 2001;49(2):206-209.
18. Patton LL, Epstein JB, Kerr AR. Adjunctive techniques for oral cancer examination and lesion diagnosis: A systematic review of the literature. J Am Dent Assoc 2008;139(7):896-905.
19. Lydiatt DD. Medical malpractice and head and neck cancer. Curr Opin Otolaryngol Head Neck Surg 2004;12(2):71-75.
20. Thomson PJ. Field change and oral cancer: New evidence for widespread carcinogenesis? Int J Oral Maxillofac Surg 2002;31(3):262-266.
21. Lingen MW. Oral cancer screening aids: Where is the science? Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103(2):153-154.
22. Lane PM, Gilhuly T, Whitehead P, Zeng H, Poh CF, Ng S, Williams PM, Zhang L, Rosin MP, MacAulay CE. Simple device for the direct visualization of oral-cavity tissue fluorescence. J Biomed Opt 2006;11(2):024006.
23. Poh CF, Zhang L, Anderson DW, Durham JS, Williams PM, Priddy RW, Berean KW, Ng S, Tseng OL, MacAulay C, Rosin MP. Fluorescence visualization detection of field alterations in tumor margins of oral cancer patients. Clin Cancer Res 2006;12(22):6716-6722.
24. Kois JC, Truelove E. Detecting oral cancer: A new technique and case reports. Dent Today 2006; 25 (10):94-97.