

VELSCOPE: A New Outlook Toward Advancing Technology in Early Oral Cancer Detection – A Comprehensive Review

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ABSTRACT

Oral cancer continues to be a significant global health issue, particularly in poorer countries, where people experience high rates of death and serious physical, emotional and social issues due to delayed diagnosis. By far, the most frequent form of oral cancer is oral squamous cell carcinoma (OSCC), which can be caused by several avoidable risk factors, including drinking alcohol, smoking and chewing areca nut. In children, the aetiology of oral mucosal changes is different than that of adults. The best way to improve cancer survival rates and reduce the level of treatment-related morbidity, is to diagnose the condition early. Currently, oral cancer diagnosis is based on conventional oral examination (COE), which limits the ability of the operator to detect subtle or early changes in oral mucosal texture; however, adjunctive diagnostic procedures like tissue autofluorescence devices (such as the VELscope) can provide quick, non-invasive means of enhancing the visualization of abnormal oral mucosa. In this study, in addition to describing standard and other diagnostic methods, the authors will provide a review of the epidemiology and pathophysiology of oral cancer and evaluate the workings of VELscope, including its application, clinical usefulness and limitations. The VELscope presents an improvement in lesion visualization, but does not possess enough accuracy to differentiate among benign, at-risk and malignant lesions. However, coupling the VELscope with AI-based analysis and newer diagnostic technologies may improve accuracy and facilitate early diagnosis, as well as effective monitoring of oral mucosa lesions.

Keywords: VELscope, Oral Neoplasms, Autofluorescence, Early Detection of Cancer, Precancerous Conditions, Artificial Intelligence.

INTRODUCTION

Oral cancer includes malignant tumors of the lips, tongue, buccal mucosa, gingiva, hard palate, and the floor of the mouth. It is estimated that there are 370,000 new cases of oral cancer each year around the world according to GLOBOCAN data.¹ Oral cancer occurs primarily in South Asia, Southeast Asia and large areas of Europe.² Approximately one-third of all cases of oral cancer globally occur in India, primarily due to extensive use of tobacco and areca nut.^{2,3}

Oral squamous cell carcinoma accounts for more than 90% of all oral cancers.⁴ Oral squamous cell carcinomas develop from oral epithelium through cumulative genetic and molecular changes.⁴ Despite advances in surgical techniques, radiotherapy and chemotherapy have marginally improved the survival rate of patients with oral cancers because most patients present with advanced disease.³ When diagnosed at an early stage, patients have a significantly better prognosis, and greater than 80% of patients with early stage oral cancer will survive for five years.⁵

There are very few occurrences of oral malignancies in individuals younger than 20 years of age, accounting for 1% or less of all oral cancers around the world, resulting in approximately 1-2 cases per million in that age group each year.⁶ In this age group, oral squamous cell carcinomas are rare, while there are a high number of other types of cancers affecting the oral cavity including non-epithelial malignancies such as lymphomas, rhabdomyosarcomas and salivary gland tumors. These other malignancies account for approximately 60-70% of all oral malignancies in children and adolescents.

The incidence of premature risk behaviors is becoming a growing concern in India due to the increase in epidemiologically defined risk factors associated with this problem. Nearly 15% of the adolescent population in India may have been exposed to tobacco or areca nut products, therefore putting them at risk for early oral mucosal lesions or potentially malignant oral lesions.⁶ The pediatric dentist has an important role in identifying these conditions early and maintaining long-term surveillance, given that survival rates for pediatric cancers continue to improve. Lesions may not appear at first glance, they may be nonsymptomatic and without any clinical evidence of a lesion. The traditional oral examination continues to be the best screening method, as it is an inexpensive, quick, and straightforward way of identifying lesions in the mouth; however, this form of assessment is subjective in nature and cannot accurately differentiate between inflammatory changes and

precancerous conditions.⁷ The shortcomings associated with conventional oral examinations have driven the development of adjunctive diagnostic tools such as chemiluminescence, toluidine blue staining, narrow-band imaging, and salivary diagnostics, as well as devices that provide fluorescence (such as VELscope).⁸

This device provides better visualization of tissue alterations compared with illumination changes; the VELscope device can provide a real-time noninvasive assessment of oral lesions and is well-suited for children due to the lack of pain associated with the procedure.^{9,10} Despite these advantages, diagnostic accuracy for the VELscope device varies and it should be used as a complementary tool to histopathological evaluation via biopsy.⁷

This review will discuss oral cancer's epidemiology, etiology, and pathogenesis, review the current diagnostic modalities available for practitioners, and discuss VELscope and other adjunctive technologies as they relate to pediatric populations.

EPIDEMIOLOGY OF ORAL CANCER

Worldwide, oral cancer is the 10th most frequent malignancy, with the highest rates found in those countries where there is a high prevalence of tobacco use, alcohol use, and betel quid chewing.^{1,2} Traditionally, more men than women get oral cancer. Recently, however, there has been an increase in the use of tobacco and areca nut products among women and adolescents, which has created a shift in the demographics of patients with oral cancer in certain parts of the world. One of the continuing public health concerns in India is tobacco-related malignancies.³ Cancers of the oral cavity that occur in children make up less than 1% of total oral cancer cases which include rhabdomyosarcoma, lymphoma and tumors of the salivary glands. A major childhood malignancy is leukemia; as such, it is important to know that children with leukemia often have oral manifestations that may include gingival overgrowth, petechiae, ulcerations, and opportunistic infections, among others. Some of these manifestations may be identified prior to the child's systemic diagnosis or may occur later during the child's treatment.

Adolescents are a transitional age group whereby adolescents' behaviors may lead to viral infection (e.g., HPV)², or they may be exposed to other carcinogenic substances (i.e., tobacco smoke from other sources). Exposure to tobacco products at an early age also increases adolescent susceptibility to DNA damage and/or cellular changes in the oral epithelium, which contribute to the development of cancer. Even though, development of oral squamous cell carcinoma (OSCC) is extremely rare among this age group, adolescents who smoke or use any form of tobacco are at an increased risk of developing oral potentially malignant disorders. Early use of tobacco products by adolescents is associated with a 2-4 fold increase in a person's lifetime risk for OSCC; therefore, the behavior of smoking during adolescence is a precursor to the subsequent development of oral cancer following long-term tobacco exposure. These emerging epidemiological trends highlight the importance of comprehensive oral exams and judicious use of adjunctive screening techniques in adolescents.

ETIOLOGY AND RISK FACTORS

Factors that promote oral cancer are many, with the predominant factor being the biological, genetic and chemical interactions between the body and the environmental conditions and factors to which a person is exposed. The principal harmful substance related to oral cancer is tobacco and its chemical compounds which produce DNA damage as well as DNA mutations that are directly related to OSCC. Alcohol acts in a synergistic manner to tobacco by increasing the permeability of the mucosa to allow the carcinogens in tobacco to penetrate into the oral cavity. The use of areca nut and betel quid are also associated with the oral development of submucous fibrosis, and subsequently with the development of malignancies; this is particularly true for the South Asian population. High-risk HPV types, particularly HPV-16 are linked to development of some cancers in the oropharyngeal and oral regions, supporting the concept of viral oncogenesis.^{2,4}

Chronic irritation and inflammation will add to the risk of developing cancer. Examples of this are poor oral hygiene, periodontal infections, sharp teeth, and ill-fitting dental appliances that create chronic trauma to the mucosa, thereby promoting carcinogenesis. Nutritional deficiency (particularly the deficiency of antioxidant vitamins) will impair the mucosal defenses and make a person more susceptible to development of oral cancer. At the molecular level, the accumulation of changes to oncogenes and tumor suppressor genes, and the accumulation of changes to the epigenetic changes, will promote transformation of mucosal cells to malignant neoplasia. In the case of children, the etiologies of the risk factors are different will increase the susceptibility of developing malignancy.

Inherited syndromes that affect DNA repair will also increase the risk of early-onset malignancies, such as Fanconi Anemia and dyskeratosis congenita.¹¹ Immunosuppression (congenital or therapy-associated) will also adversely affect the integrity of epithelial cells.¹² Cancer treatment is a significant contributor to the development of oral pathology in children. Chemotherapy and radiation therapy disrupt the normal turnover of epithelial cells and the function of the salivary glands, thereby causing mucositis, hyposalivation or xerostomia, delay of healing of oral tissues, and developmental abnormalities to teeth, such as enamel hypoplasia and microdontia.¹³ Prolonged hospitalization and limited ability to provide oral self-care can increase the severity of the inflammation in the oral cavity.¹⁴

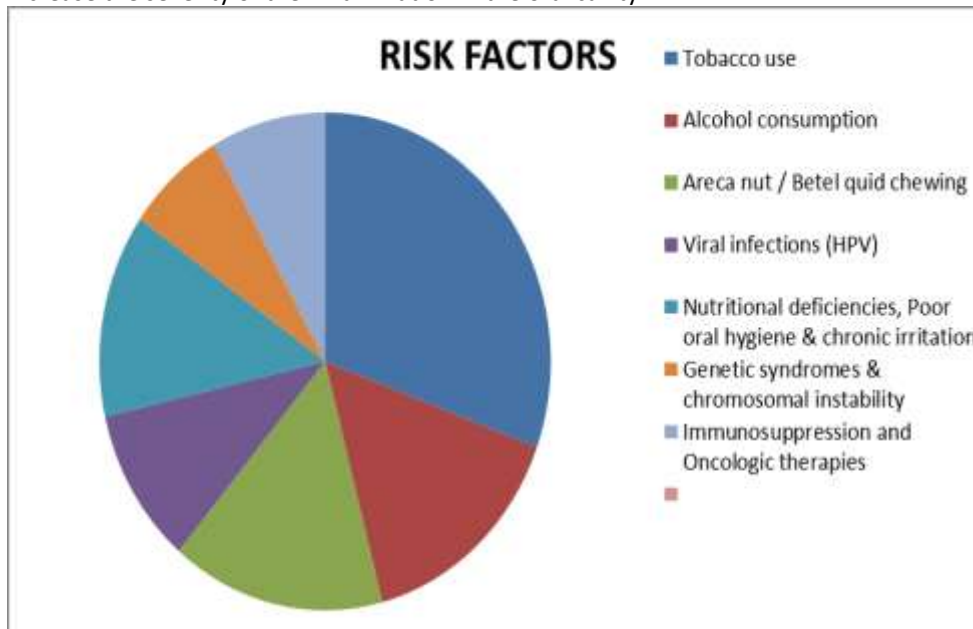


Figure 1: Risk Factors for Oral Squamous Cell Carcinoma²

PATHOGENESIS

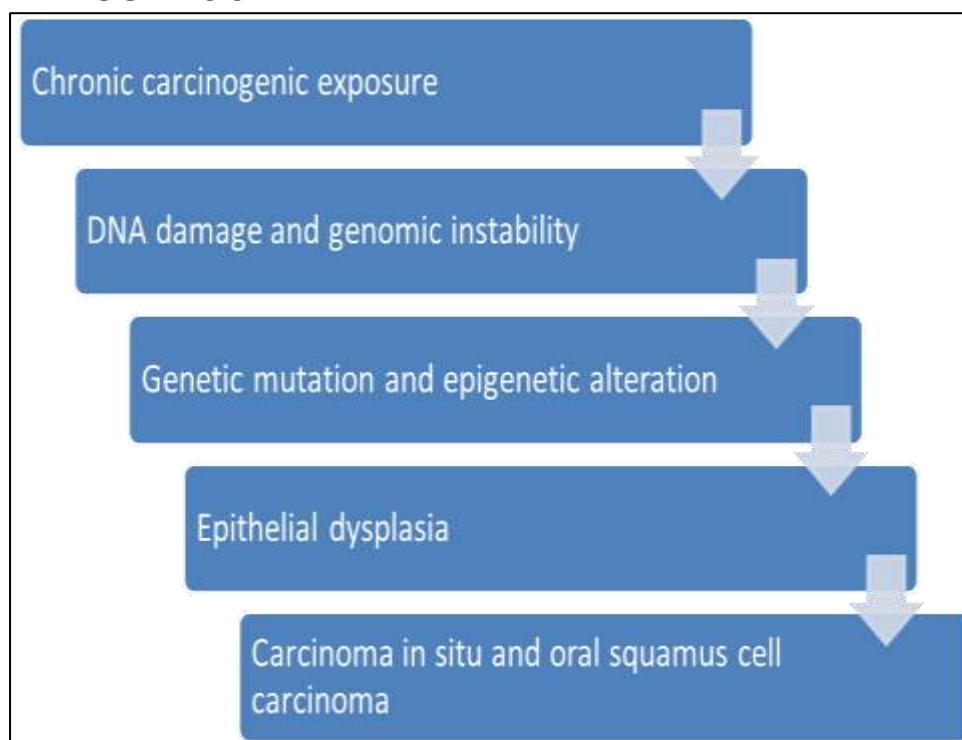


Figure 2: Pathogenesis of OSCC^{5,6,15}

DIAGNOSTIC APPROACHES

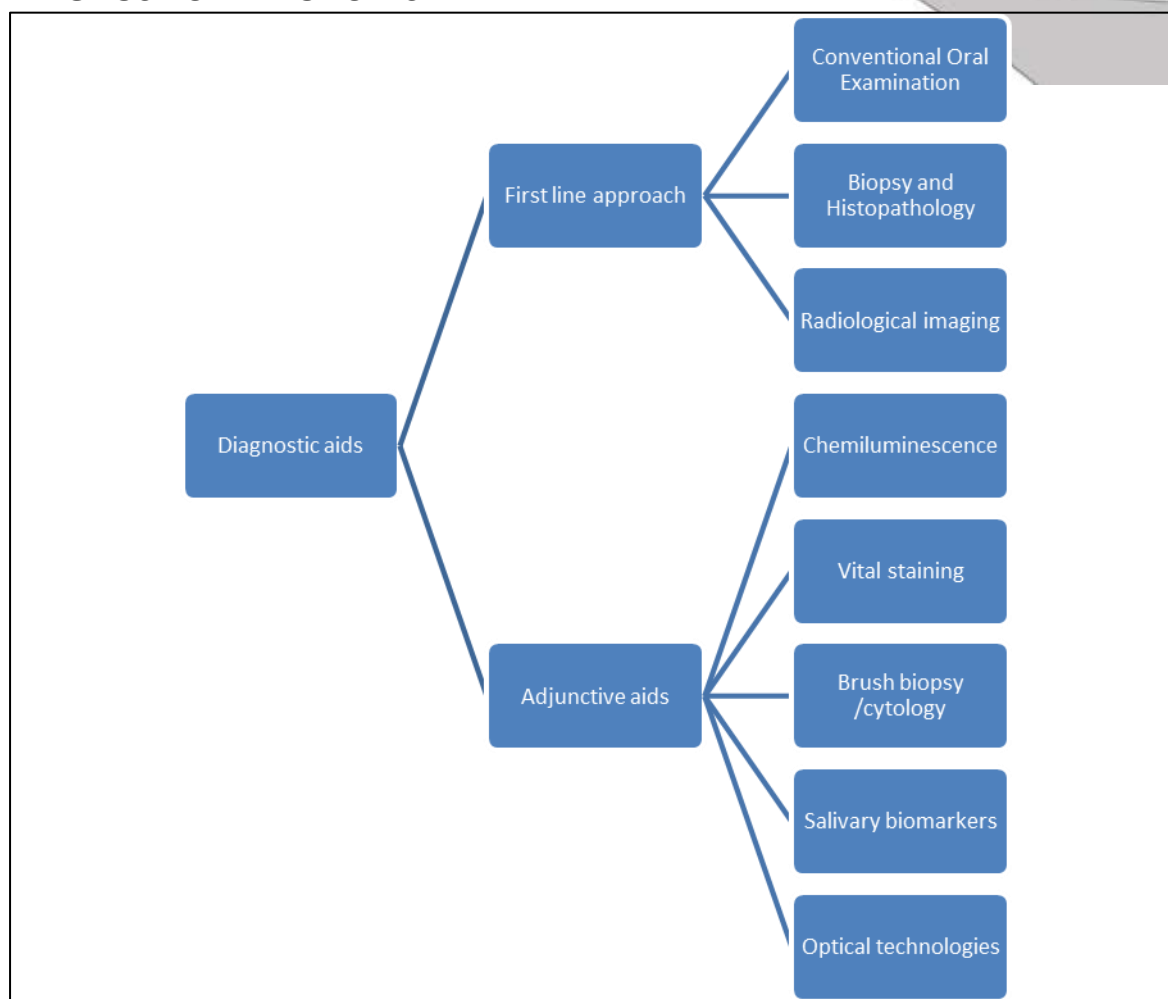


Figure3: Diagnostic approaches for detection of OSCC^{16,17}

VELSCOPE TECHNOLOGY

Overview to VELscope

Early detection is the most important way to improve outcomes for oral cancer patients. To help with this early detection, light-based adjunctive screening devices have been developed to improve the visualization of mucosal abnormalities.^{7, 17} One example of a light-based adjunctive device is the VELscope Vx. The VELscope uses tissue autofluorescence to assist healthcare providers in identifying tissues that may require additional evaluation.^{9,10}

The VELscope has been widely accepted by professionals to directly visualize oral tissues and is routinely used as a chairside adjunctive device in the screening process for oral cancer.⁹ The VELscope emits blue spectrum light, which excites the fluorophores natural to the oral tissues, producing a visual image of the tissues. Under the blue light, clinically healthy mucosa demonstrates a pale green fluorescence allowing for quick inspection of the mucosa for signs of any abnormalities. The assessment process is non-invasive, simple in nature, and typically takes less than 5 minutes to complete, all of which support making it a practical adjunct to any dental visit.^{11,12}

In a pediatric practice, adjusting the VELscope to accommodate children with minimal discomfort is possible through environmental modifications, such as dimming the operatory lights, along with providing age-appropriate explanations of the procedure to relieve anxiety and improve cooperation. Additionally, when performing periodic VELscope assessments on medically compromised children (e.g., on chemotherapy or with immunodeficiency), the assessment will assist with the early identifying mucosal breakdown, thereby decreasing the likelihood of secondary infections and complications.¹⁷



Figure 4: VEL Scope (Vx)

Principles of Autofluorescence Imaging

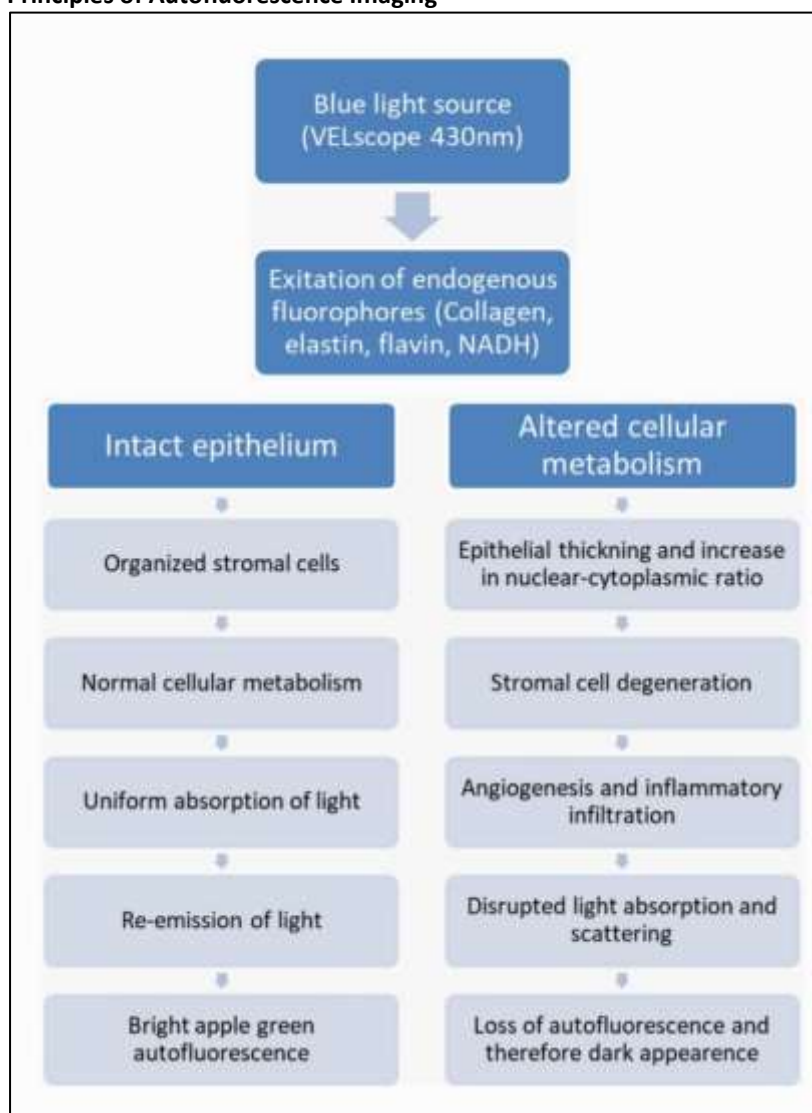


Figure 5: Principles of Autofluorescence Imaging^{9,10}

Clinical Application and Procedure for Using VELscope

A VELscope examination starts with a complete assessment of the oral cavity's soft tissue, visually examining each section to find any visible lesions, asymmetries, or areas of concern.⁷ The operator dims the light to allow the best possible visualization of fluorescence. The operator then performs a systematic examination of the buccal mucosa, labial mucosa, tongue, floor of the mouth and palate under blue light illumination (fluorescent light).⁹ Healthy tissue will fluoresce a uniform green, while tissue with altered metabolic or structural properties will fluoresce less, and therefore appear dark.¹⁸

The results of the examination under autofluorescence are correlated to the results of the examination with white light to determine the clinical significance of the findings under both modalities. The VELscope procedure is painless, requires no medication, and generally lasts two to five minutes.¹⁸ Areas that demonstrate a loss of fluorescence should be interpreted with caution, and when appropriate, further concern should be determined through close follow-up or biopsy for histopathological confirmation.¹⁷



Figure 6: Images of oral cavity and under VELscope

Key Advantages of Using VELscope Vx

One of the greatest strengths of the VELscope is that it allows the clinician to get immediate visual feedback about the fluorescence patterns of the examined tissue during a routine dental visit,¹⁹ eliminating the need for laboratory processing or multiple appointments for results.¹⁸ This immediate assessment is helpful for the timely decision-making of clinicians when they encounter mucosa with subtle changes that are not easily seen by conventional white light methods.

The VELscope procedure is noninvasive, painless, and does not involve the use of any injections, dyes, or manipulation of the tissue. Therefore, the VELscope is accepted by most patients, including children, older people, and people with medical problems.¹⁹ The ease of the VELscope technique supports its use in community dental settings and general dentistry, where complex diagnostic equipment is often not available or practical.

One essential advantage of VELscope's ability to enhance visualization of tissue autofluorescence provides clinicians a means to identify areas where metabolism or the structure of the tissue have been altered even when the alterations cannot be easily detected using conventional fluorescent lighting. Such visualization aids clinicians in defining lesion margins more accurately and in selecting a more representative site for biopsy when it is warranted.²⁰

VELscope's role in the diagnosis of oral cancer has been recognized by many professional organizations, including the FDI World Dental Federation, as a useful adjunct to conventional diagnoses of oral health

through biopsy or histological examination; as such, the recommendations for VELscope emphasize its use only as an adjunct tool rather than as a replacement for biopsy or histological evaluation.¹⁷

Sensitivity and Specificity

Manufacturers of light-based diagnostic systems do not market their devices as good or definitive diagnostic instruments. The reported sensitivity of VELscope has indicated moderate sensitivity for detecting dysplastic and malignant lesions; such results indicate that many premalignant or malignant lesions do not demonstrate sufficient fluorescence loss to result in a positive diagnosis, which can lead to false-negative diagnostic reports.²¹ The limitations of the VELscope's sensitivity can be explained by many biological and technical variables; for instance, early dysplastic lesions may not display significant metabolic disease or loss of normal collagen structure in the surrounding stroma, resulting in minimal fluorescence loss. In addition to the early dysplastic lesions, blue light only penetrates into the uppermost layers of the oral mucosa; consequently, significantly degenerative changes may exist beneath the epithelial surface at the basement membrane, and therefore will not be readily identified as fluorescently altered.²⁰

The sensitivity of the VELscope may also be influenced by the condition of the lesions being screened and by the experience of the clinician. The issue of specificity is a major concern for fluorescence-based screening techniques; the subjective nature of interpreting fluorescence patterns and the success of clinically correlating such patterns require adequate training and experience of the clinician using the device to ensure an accurate diagnosis.¹⁹ There is also potential for obtaining a false positive diagnosis due to fluorescence losses being noted from other causes such as inflammatory lesions, ulcerative lesions due to trauma, infections, and/or lesions secondary to treatment. Ulcerations/inflammatory conditions/infection-related mucosal lesions may reflect fluorescence loss. This can result in falsely-positive findings leading to increased levels of anxiety in patients and the need for additional follow-up appointments and/or biopsies. Consequently, VELscope findings should always be integrated with a comprehensive history, clinical evaluation, and VELscope.¹⁷

Limitations: False-Positive and False-Negative Findings

False positive results occur with non-neoplastic lesions show dark when examined using autofluorescence due to the increase in vascularity and blood content of the lesion, which will attenuate excitation light levels, leading to the reduction of fluorescence emissions. Alternatively, false negative results will occur when dysplastic or malignant lesions have similar fluorescence to adjacent healthy epithelium. In addition, if the pathological change is buried deeper than 2mm from the surface of the epithelium (and therefore outside of the penetrative capability of blue light for excitation), then no identifiable fluorescence loss would be determined. These limitations further cement the need for VELscope to be utilized solely as an adjunctive tool and for all suspected lesions to be followed and/or histologically confirmed regardless of their autofluorescent appearance.

Comparison with Other Emerging Technologies

Numerous advanced imaging techniques are currently being evaluated for the enhancement of early detection of oral cancer. For example, Optical Coherence Tomography (OCT) is capable of obtaining very high resolution cross-sectional images that allow for visualisation of the thickness of the epithelium and the integrity of the basement membrane. Although OCT provides very precise microstructural information, its expense, technical complexity and long duration of procedures limit its ability to be utilized broadly in general dentistry practices, whereas VELscope is much more feasible for rapid screenings in the dental chair.²²

Narrow banded imaging (NBI) provides better visualisation of mucosal vasculature and neovascularisation (both characteristics of malignancy). Evidence exists in the head and neck oncology literature to support that NBI is much more specific than other autofluorescence techniques. However, in routine dental practice, the incorporation of NBI (narrow-band imaging) will be limited by the fact that endoscopy, which is used in an otolaryngology setting and by ENT (ear, nose, and throat) physicians, will be very difficult to integrate into routine dental practice due to the models and equipment that are required in addition to the requirements of using an endoscope to get diagnostic images.²³

In addition, another promising avenue for non-invasive diagnostic tools may be through direct detection of circulating tumor DNA (ctDNA) from bodily fluids such as saliva or molecular biomarkers (molecules produced by cells involved in carcinogenesis or tumor growth). These approaches could ultimately provide greater sensitivity and accuracy compared to optical devices; however, they rely on laboratory infrastructure, standardized testing protocols, and large-scale validation studies to provide conclusive evidence of their efficacy.²⁴

Additionally, artificial intelligence (AI) will play an important role in the enhancement of image-based diagnostic methods by providing an objective interpretation of fluorescence patterns. In contrast to conventional tests, AI-based analysis may provide an alternative way of reducing the subjectivity in assessing fluorescence patterns. Nevertheless, AI tools must be trained using large amounts of data and with sufficient technical resources.²⁵

At this time, VELscope has several demonstrable advantages: simple to use, affordable, portable, and rapid results. While the advent of new technologies may increase diagnostic capabilities in the future, VELscope continues to serve as a practical approach to diagnosis and provides an additional source of clinical assessment that can be applied to a comprehensive diagnostic approach.⁷

Applications in Other Medical Specialties

Although fluoroscopy is often associated with dentistry, various medical specialties have found applications for fluorescence-based technologies. The use of fluorescence-based techniques to detect early cervical epithelial deformities in the field of gynecology,²⁰ bronchoscopy using autofluorescence in the area of pulmonology, to identify premalignant and malignant bronchial lesions, which may not be visualized under traditional white light, have occurred. Optical imaging has been assessed in the breast and prostate to allow for better visualization of abnormal findings in tissue specimens. In ophthalmology, fluorescence imaging has become well-established as a diagnostic tool for the evaluation of retinal disorders and choroidal disorders.²⁰

Future Directions

Future advancements will likely concentrate on putting together auto-fluorescent images with AI and machine learning systems.²⁶ Automation of image analysis may lessen operator bias and provide greater uniformity when detecting subtle changes in mucosa. AI-enhanced evaluation will be advantageous in cases that possess increased inflammation or regenerative alterations where visual examination is difficult.²⁵

There is also potential for multimodal diagnostic platforms that combine autofluorescence with other technologies, such as optical coherence tomography, narrow-band imaging and salivary biomarkers. By using these hybrid techniques, it may be possible to produce a structural, vascular and molecular report concurrently, enhancing diagnostic accuracy while reducing unnecessary biopsy procedures.²⁶

Improved long-term imaging and predictive analytics could also contribute to improved monitoring of OPMDs. Use of serial autofluorescence exam results along with risk stratification models would yield high probabilities for predicting transformation to malignant lesions and directing the development of individualized follow-up schedules.²⁶ VELscope could provide additional assistance in preventive oral health care if it continues to be developed and implemented successfully, maintains affordable costs, and has established simple training protocols for use in clinical or community settings.^{7,9}

CONCLUSION

VELscope is an adjunctive device that assists with the detection and visualization of oral mucosal abnormality during a traditional oral exam. The device is fast, can be used at the chair in a non-invasive manner, and can identify changes to tissue that are otherwise difficult to see, making this device highly valuable for screening and tracking the development or progress of oral premalignant disorders, and for use in primary care and community programmes. VELscope is also applicable in children since patient comfort and the avoidance of invasive procedures is commonly essential.

However, VELscope used in isolation, has a limited ability to discern between benign, non-inflamed, premalignant and malignant lesions. Due to the potential for false-positive findings, false-negative results, and operator-dependent interpretation, it is important to perform clinical correlation with VELscope findings, as well as continue to use biopsy and histopathological examination as the diagnostic gold standard. It is likely that future improvements in oral cancer diagnostics may come from using multiple types of approaches including combining autofluorescence imaging with molecular biomarkers, applying artificial intelligence, and employing advanced optical technologies. Such methods are expected to provide benefits of improved detection at an earlier time, improve risk stratification, decrease additional unnecessary invasive procedures, and ultimately decrease the global burden of oral cancer.

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